The Unsung Heroes Who Ended a Deadly Plague

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How a team of fearless American women overcame medical skepticism to stop whooping cough, a vicious infectious disease, and save countless lives



This seven-foot statue of Pearl Kendrick, center, and Grace Eldering, left, was unveiled in Grand Rapids in 2019. Lab assistant Loney Clinton stands to the right with a microscope.

Lisa Spindler By <u>Richard Conniff</u>

Photographs by Lisa Spindler

In late November of 1932, the weather cold and windy, two women set out at the end of their normal workday into the streets of Grand Rapids, Michigan. The Great Depression was entering its fourth year. Banks across the country had shut down. The city's dominant

furniture industry had collapsed. Pearl Kendrick and Grace Eldering, both bacteriologists for a state laboratory, were working on their own time to visit sick children and determine if they were infected with a potentially deadly disease. Many of the families were living in "pitiful" conditions, the scientists later recalled. "We listened to sad stories told by desperate fathers who could find no work. We collected specimens by the light of kerosene lamps, from whooping, vomiting, strangling children. We saw what the disease could do."

Pertussis, otherwise known as whooping cough, means little to most parents in the developed world today. But it was once among the great terrors of family life.

Diagnosing pertussis is difficult on the basis of symptoms alone. It can seem like nothing at first: a runny nose and a mild cough. A parent watching a baby in her crib might notice a pause in her breathing but relax when the steady rise and fall of the chest resumes. A doctor can miss it, too: Just a cold, nothing to worry about. One to two weeks in, though, the coughing can begin to come in violent spasms, too fast to allow for breathing, until the sharp, strangled bark breaks through of the child desperately gasping to get air down her throat. That whooping sound makes the diagnosis unmistakable.

"It's awful, it's awful. You wonder how they can survive the crisis," says Camille Locht, a researcher at the Pasteur Institute in Lille, France. "They're suffocating. They're choking. They become completely blue. They cannot overcome the cough, and you have the impression that the child is dying in your hands." It could go on like that for up to three months. To this day, there is little any doctor can do once that whooping stage sets in.





Left, Pearl Kendrick at work in the 1940s, photographed for a Grand Rapids news story. "This is what I'd like to be doing all the time," she told a reporter. Center and right, a culture and an artist's rendering of *Bordetella pertussis*, the pathogen that causes whooping cough. The bacteria spread through airborne droplets and colonize cells in the lungs. They have only one known host species: humans. Grand Rapids History Center, Grand Rapids Public Library; Dr. Camille Locht Institut de Lille; Sarah Bailey Cutchin / CDC

Until the mid-20th century, there was also nothing anyone could do to prevent the disease. It was so contagious that one child with pertussis was likely to infect half his classmates and all of his siblings at home. Pertussis killed up to 7,500 Americans a year in the early 1930s, most of them infants and young children. Survivors sometimes suffered permanent physical and cognitive damage.

All of that changed because of Kendrick and Eldering. They'd been hired to do routine daily testing of medical and environmental samples. But research on whooping cough became their obsession. They worked late into the night, with almost no funding at first, in what one reporter described as a "dumpy broken-down stucco" building. They benefited from the work of their own hand-picked research team, which was remarkably diverse for that era. They also enlisted the trust and enthusiasm of the public. The city government and private donors stepped forward to cover the cost of their first clinical trial. Doctors, nurses and ordinary city residents rallied to help. Mothers volunteered not just their time but also their children as experimental subjects.

Medical men with better credentials were deeply skeptical. But where other researchers had failed repeatedly over the previous 30 years, Kendrick, Eldering, and their team succeeded in developing the first safe and effective whooping cough vaccine. Through their innovations, childhood deaths from whooping cough plummeted in the United States and then the world.

Pearl Kendrick, born in 1890, grew up in upstate New York, where her father was a Methodist preacher. She went on to earn her degree in science from Syracuse University and then spent the summer of 1917 studying bacteriology at Columbia. But while educational opportunities for women had been expanding for decades, job opportunities had not followed. The conventional attitude, as one medical educator put it in 1922, was that "education enhances womanly charm, attractiveness and fitness for domestic happiness." For a time, Kendrick became a schoolteacher and principal in upstate New York, the expected career path for an educated woman then, preferably leading to marriage.

Public health was one of the few scientific areas that had begun to seek out educated women. The lifesaving success of infectious disease control in World War I had opened minds to the possibilities for improving public health at home. Much of the new work fell to state departments of health, and their laboratories needed staff to bring new diagnostic tests, vaccines and other tools of disease control into routine use. Men with public health training tended to seek the prestige and higher pay of jobs at universities or research institutions. State laboratories offered lower wages, less status and mostly repetitious tasks. Women with science degrees seemed ideal for that rote work.

Kendrick found employment at a lab run by the New York State Department of Health. Then, in 1920, C.C. Young, Michigan's enterprising director of state laboratories, offered her a job, promising to "make it interesting" and "with every chance for advancement." He was true to his word. When the Michigan State Department of Health opened a laboratory in Grand Rapids in 1926, Kendrick became its first director. In 1932, on leave from her job, Kendrick completed her doctorate in science from Johns Hopkins School of Hygiene and Public Health. She came back to Grand Rapids with the goal of studying a single disease: pertussis. That year, the city was suffering a major outbreak. When Kendrick wrote to Young for permission to work with local pediatricians on vaccine research, he replied, "Go ahead and do all you can with pertussis if it amuses you."

The lab where Kendrick and Eldering began their work was housed in the administration building of an old sanitarium, above. A 1926 article announced the building's new purpose, though the reporter got Kendrick's name wrong. Grand Rapids History Center, Grand Rapids Public Library; MLive Media Group / The Grand Rapids Press

Grace Eldering, born in 1900, had gone to college at the University of Montana, and then worked as a schoolteacher in Hysham, the ranching and farming community where she grew up. As with Kendrick, teaching didn't hold her interest. Starting in 1928, she became a volunteer and then a paid employee at the Michigan state laboratory in Lansing, later transferring to Grand Rapids to work on pertussis. There, she and Kendrick began their lifelong partnership.

In the beginning, their main goal was to diagnose the disease faster and more accurately so contagious patients could be isolated as early as possible, and return to school or work as soon as the contagious stage ended. Their weapon of choice was the cough plate, basically a



BRANCH STATE LABORATORY OPENS AT CITY HOSPITAL

A laboratory for diagnosis of contagious diseases is open for physiolans at the city hospital on Fullerav., N. E. The inboratory is a branch of the state department of health and is in charge of Miss Pearl Kendall. Dr. R. M. Olin, state health commissioner, is sending to Grand Rapids physiclans announcements of the laboratory opening.

petri dish with the culture medium painted on the bottom. The two women, along with

doctors, nurses and others on their team, would hold the open dish a few inches away while a patient coughed onto it. The dish, covered with a lid, then went back to the laboratory and into an incubator, to grow the bacteria into colonies suitable for analysis.

On November 28, 1932, the laboratory confirmed its first *Bordetella pertussis* specimens. The pathogen had first been identified in Belgium a quarter century earlier, but no one on the staff had ever seen it. They had to compare the specimens on their cough plate against published accounts. Kendrick and Eldering reported that the colonies appeared "smooth, raised, glistening, pearly, and almost transparent," encircled by a pale halo where the bacteria had eaten into the blood in the surrounding culture medium.



Grace Eldering traced her interest in pertussis to her battle with the illness at age 5. Decades later, she still remembered the terrifying coughing fits. Grand Rapids History Center, Grand Rapids Public Library

They soon expanded their study into an ambitious citywide cough plate service for monitoring and controlling the whooping cough outbreak. Instead of using human blood as a culture medium, the way other scientists had done for much smaller studies, they turned to sheep blood, because it was less expensive and more readily available in the volumes they needed. (Having grown up on a ranch, Eldering knew about sheep.) It was one of many such improvements by their laboratory that allowed them to vastly expand the city's testing program.

And then, in January 1933, just seven weeks after their first glimpse of the pathogen, Kendrick and Eldering produced their first experimental pertussis vaccine.

Coming up with a vaccine for any disease was still a rudimentary, cooking-without-recipes enterprise. Researchers had to experiment with different methods of killing or weakening the pathogen, to make it safe enough to inject into human patients, but still strong enough to elicit lasting immune resistance to the disease. In 1931, the American Medical Association declined to endorse any of the pertussis vaccines then available, concluding that they had "absolutely no influence" on prevention and were "useless" as remedies after onset of the illness.

Kendrick and Eldering's vaccine consisted of whole-cell *Bordetella* bacteria killed with a common antiseptic, purified, sterilized and suspended in a saline solution. Others who had developed vaccines before them often neglected to provide critical information on preparation, dosage and other considerations, with the result that one batch could vary wildly from the next. Kendrick and Eldering took a far more systematic approach at every step, from the initial collection of bacteria through testing whether their vaccine actually protected children. They learned as they went—for instance, that bacteria collected at a certain stage were more likely to elicit a strong immune response—and they tested various iterations of the vaccine for safety by injecting them into experimental animals, and themselves.

The two researchers had no prior experience with clinical trials, which were practically a new science then. But testing whether their vaccine could safely and effectively protect children would require a large-scale, controlled field study—comparing a group of vaccinated test subjects against a similar, but untreated, control group. Designing the trial would have to be part of what Kendrick called "our midnight work," after business hours.

"I never thought there was anything I couldn't do," Kendrick later told a reporter. She was describing a time in college when she'd had to organize meal service for 75 fellow students during a two-week Christmas break. Her point was that she was single-minded about every task she took on. That determination showed up even in her driving: Eldering's niece Shirley Redland, reached in Montana, where she still lives on the family ranch, recalled that Kendrick had a "heavy foot, and people better get out of her way."

In their dealings with the public, though, neither Kendrick nor Eldering came across as bold or commanding. Instead, they were both unfailingly polite, gracious and a little formal. For women experienced in the gender politics of their era, modesty may have seemed obligatory. In college, Kendrick recalled, she'd gotten male science faculty to give her the instruction she needed by acting "as humble as I could be." Once she started working in labs, she said, keeping her head down and focusing on the work at hand "kept me from worrying if I was getting as much as my friend John, say, who was working beside me—though I knew very well I wasn't."

That peculiar mix of self-confidence and humility helped them win local support as they launched their clinical trial. Grand Rapids was also willing. It had a proud reputation then as a leader in putting medical advances to work saving lives.

In the first round of the field study, 1,592 children took part, 712 of them as vaccine recipients and 880 as untreated controls. After each vaccination clinic, the two women waited in dread for a call about a bad reaction, beyond the usual mild fever. "I felt scared to death most of the time," Kendrick later admitted. "You just didn't sleep very well those nights." But that urgent call never arrived. Instead, the data came in: The untreated group had 63 cases of whooping cough, 53 of them serious. The vaccinated group had only four cases, all of them mild.



Kendrick, far right, watches a colleague inoculate a child against pertussis in 1942. Government officials had begun distributing her team's vaccine in 1940, drastically reducing deaths. Grand Rapids History Center, Grand Rapids Public Library

At first, the medical establishment didn't believe the results. A respected epidemiologist— James Doull of Case Western Reserve University School of Medicine in Cleveland—had carried out a similar study around the same time, using a different vaccine, and shown no real benefit from vaccination. When public health leaders asked the renowned Johns Hopkins epidemiologist Wade Hampton Frost to review the results of both studies and make a recommendation, Frost seemed reluctant to undertake a trip to Michigan. "I very strongly suspect that Miss Kendrick's field studies are not set up in such a way as to give a really good control," he wrote. Getting it right was hard even for specialists in clinical testing, and "the odds are strongly against Miss Kendrick's experiment being sound."

Frost ended up visiting Grand Rapids after all. There, he soon came to appreciate Kendrick and Eldering's commitment to careful science. He recommended improvements in the design of their clinical trial, and the two women and their team went back to work. Their new study would require a larger staff and more frequent visits to follow patients over a period of years. This time they enlisted the help of first lady Eleanor Roosevelt, who visited the laboratory on a busy 1936 tour of Grand Rapids. She was one of the few outsiders, Kendrick later recalled, who seemed to understand what she and Eldering were doing. Funding for additional staff soon followed from the federal Works Progress Administration. The new study attracted 4,212 test subjects, and the vaccinated group again experienced whooping cough at a dramatically lower rate than their unvaccinated counterparts. The same protective effect showed up in an independent clinical trial of the vaccine in New York State.



A kit from the late 1940s contained an early version of the DTP vaccine, along with a brochure touting the advantages of giving the inoculations using fewer shots. Rachel Anderson / NMAH

In 1944, the <u>American Medical Association</u> added Kendrick and Eldering's vaccine to its list of recommended immunizations. As a result, incidence of pertussis in the United States fell by more than half just in that decade. Deaths dropped from 7,518 in 1934—the peak year for pertussis cases—to just ten a year by the early 1970s. Throughout that period, Kendrick traveled to other countries, from Mexico to Russia, to help introduce the vaccine there, with similar success in saving children's lives.

Margaret Pittman, shown here working with meningitis germs, spent years helping Kendrick and Eldering improve the safety and effectiveness of the whole-cell pertussis inoculation. NIH / Smithsonian Institution Archives



To minimize the "pincushion effect" of giving so many different shots in the early years of a child's life, Kendrick and Eldering had by then already begun to work on a combined diphtheria, tetanus and pertussis vaccine, a forerunner of the vaccine that now routinely protects 85 percent of the world's children. To standardize the vaccine everywhere, Kendrick, Eldering and Margaret Pittman, at the <u>National Institutes of Health</u>, also developed what has become the required method for testing the effectiveness of every batch of whole-cell pertussis vaccine worldwide. In place of the hodgepodge cooking-without-recipes past, these women made whooping cough prevention standardized, reliable, reproducible—in a word, scientific.

"What did Kendrick and Eldering really do?" asks Michael Decker, a pertussis specialist at Vanderbilt University Medical Center. "They persevered in their belief that a successful vaccine could be made. They figured out how to make it. They engineered a clinical trial using novel techniques to prove their point. And in the face of intense criticism from people of high standing, they showed that their results were correct. They basically laid the pathway for modern pertussis vaccination."

It may seem surprising that such monumental achievements did not make Kendrick and Eldering famous. Both women held doctorates from Johns Hopkins (Eldering earned hers in 1942), and over the years, they co-authored dozens of papers together. But they were intensely private and never meant the work to be about them. "All these medical breakthroughs are a result of the work of many persons," Eldering told a reporter who wondered in 1985 why their vaccine hadn't become known as the Kendrick-Eldering vaccine, on the model, for instance, of the Salk vaccine for polio. "We disapproved of that notion," Eldering said, "because there were just too many people involved and we didn't want the sole credit. You'd have to put a whole string of names on the vaccine." In the 1970s, when the feminist movement was shining a light on women's overlooked contributions, an invitation arrived for Kendrick and Eldering to appear on NBC's "Today" show. They politely declined.



Carolyn Shapiro-Shapin says Kendrick and Eldering "believed in the development of their people," giving their staff members ample opportunity to learn and shine. Lisa Spindler

The contributions of Kendrick and Eldering might have been forgotten if it hadn't been for Carolyn Shapiro-Shapin, a history professor at Grand Valley State University just outside Grand Rapids. In the 1990s, she heard local women talking about Kendrick and Eldering's lab and dug into their story, ultimately publishing articles in academic journals.

One of the retired lab technicians Shapiro-Shapin interviewed was Loney Clinton Gordon, an African American woman who had a bachelor's degree in home economics and chemistry but had been unable to get work as a dietitian in Grand Rapids. Prospective employers had praised her credentials but explained that they didn't think chefs would take orders from a black woman. A friend mentioned her plight to Kendrick, who offered her a job at the lab. Her assignment, Gordon told Shapiro-Shapin, was to help find a suitable strain of *Bordetella* for the vaccine. One pertussis strain could be up to 10,000 times more virulent than another, and finding the right strain was crucial to improving the vaccine. "Every day I worked so hard," she said. "Millions of plates. It's a wonder I still have eyes."

Loney Clinton Gordon (shown in 1951) started her science career at Kendrick's lab. She continued working in microbiology and public health until 1978, traveling the world and training hospital staff to identify pathogens. Grand Rapids History Center, Grand Rapids Public Library



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One morning, she went into work thinking, "This has to be the day." She started sorting through the plates—and suddenly, she found it. "My God, it was so big and so clear," she later recalled, describing the halo where the bacteria had eaten into the blood in the surrounding culture medium. "It just talked to me: 'Here I am.'" She brought that plate to the attention of Kendrick and Eldering, who put it through "all of these processes, repeated and repeated and repeated—and, bingo, there it was," Gordon said. No other record of Gordon's contribution exists. But like the others who remembered working at the lab, Gordon mainly expressed gratitude at having been part of the work of saving lives.

Neither Kendrick nor Eldering ever married. For decades, they lived together in a comfortable four-bedroom house in an old apple orchard, on a hilltop overlooking the city. They shared the same leisure activities: reading, gardening and birdwatching. They owned pets and often traveled together. Redland spent time with her aunt and Kendrick at the cabin they owned on Lake Michigan; once, she says, they hosted her there for a month in an effort to discourage her from getting married at the age of 19. (It didn't work.) The two women took care of each other. After Eldering lost a finger while attempting to repair an air conditioner at work, it was Kendrick who trimmed her gloves, stitching that finger down. "They had a wonderful life together," Redland told me. "I don't think there was ever a harsh word."

Were Kendrick and Eldering more than colleagues and devoted friends? It was common for single working women to live together then as they eked out meager salaries. At one point in her research, Shapiro-Shapin was interviewing a chemist named Lucile Portwood, who had worked in the laboratory in the 1940s. She asked about the relationship and Portwood, who was then in her 80s and hard of hearing, yelled into Shapiro-Shapin's recorder: "I'm a lesbian and I would've known if those gals were up to something." In any case, their private lives were nobody's business but their own.

There is another reason history has largely ignored two such important medical pioneers. It has to do with the paradoxical nature of prevention: When a vaccine or some other health care measure prevents a disease, it leads people to forget the disease that it prevents. The vaccine itself can then become a target, because real or imagined adverse effects now suddenly seem worse than the disease.

That happened to Kendrick and Eldering's pertussis vaccine. It caused fever and injection site reactions and in rare cases temporary neurological problems, according to Decker, the Vanderbilt pertussis specialist. Anti-vaccine activists accused it of more serious adverse effects, though a scientific review debunked most of those accusations. The vaccine was steadily improved over time, but even in Kendrick and Eldering's day, getting it was dramatically safer than risking the disease. Yet public confidence was shaken.

In 1997, a stripped-down acellular vaccine—with just a few of the original 3,000 or so antigens—replaced the whole-cell vaccine in the United States and some other developed nations. The acellular vaccine has, however, lately turned out to provide strong protection for only a few years. Together with increasing vaccine resistance, that short-lived protection has contributed to a pertussis resurgence in the United States. Undervaccination in poor and middle-income countries has also allowed the disease to persist there, killing an estimated 160,700 people each year, most of them children. The death toll is likely to get worse: In 2020, an estimated 23 million children missed out on their pertussis vaccinations, largely due to disruptions caused by the Covid-19 pandemic.



A 12-year-old receives a Tdap booster. The Tdap, approved in 2005, added an acellular pertussis component to a booster shot for tetanus and diphtheria. John Ewing / Portland Press Herald via Getty Images

An answer to these problems may soon be available. Locht, the Pasteur Institute researcher, has developed a new whole-cell vaccine and may begin a Phase 3 trial as early as this year. He is a devoted admirer of Kendrick and Eldering. But his vaccine will be different from theirs—made with live bacteria that are genetically altered to be harmless, and not injected in the arm, but sprayed into the nose. In addition to being easier to administer and avoiding needle

fear, the vaccine will not require refrigeration, all of which are advantages in remote or impoverished areas. If all goes well, Locht's vaccine could be available in as little as three years.

Meanwhile, state laboratories like the one where Kendrick and Eldering carried out their midnight work are now struggling. It's another paradoxical result of vaccine successes: Because medical advances have largely eliminated so many infectious diseases that were once routine, from smallpox to polio, governments have felt comfortable cutting public health budgets and laying off staff. Emergency funding helped to address the 2009 H1N1 and 2015-16 Zika epidemics. But then the scary headlines went away, and so did the funding. When Covid-19 hit, the staff needed to introduce safety measures, process tests quickly, or administer vaccines that didn't exist. "We continue to go from crisis to crisis, instead of appreciating that this is a service that's needed all the time," says Frances Pouch Downes, Michigan's former state public health laboratory director. "Would we do that with a fire department?"

The rise of vaccine skepticism in America also means older diseases have rebounded. Reported cases of pertussis in the U.S. have more than doubled already in this century, from 7,867 in 2000 to 18,617—and seven deaths—in 2019. That's still well below the 215,343 cases that struck Americans in 1932, the year Kendrick and Eldering began their research. But it's a powerful argument for the kind of community-based public health work, built on trust between parents and local officials, that Kendrick and Eldering helped to pioneer.

After Kendrick's death in 1980, one of her colleagues, Richard Remington, estimated the number of lives saved by the pertussis vaccine in the hundreds of thousands in the U.S. alone. By now, it is probably in the tens of millions worldwide. "Who are the men and women living today who would be dead from whooping cough had it not been for Pearl Kendrick's vaccine?" Remington wrote in the newsletter of the University of Michigan's School of Public Health. "Name one. You can't do it and neither can I....The accomplishments of disease prevention are statistical and epidemiological. Where's the news value, the human interest in that?"

News value, of course, had little meaning for Kendrick and Eldering. They wanted only to save children's lives. Having achieved that, they were content to be forgotten. But we should remember.

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