Pearl Luella Kendrick (1890–1980) [1]


Pearl Luella Kendrick researched prevention for pertussis, commonly known as whooping cough, in Grand Rapids, Michigan, during the mid-1900s. Pertussis is a respiratory disease that mainly affects infants and young children. During the 1920s, pertussis was responsible for more deaths in children in the United States than any other disease. In the 1930s, Kendrick created one of the first pertussis vaccines that underwent large-scale clinical trials. Toward the end of her career, Kendrick helped developed combination vaccines for other common childhood diseases at the time, including diphtheria, tetanus, pertussis, and poliomyelitis. She also studied immune responses in infants whose mothers had pertussis antibodies that transferred to them during pregnancy [6]. Kendrick helped lower the incidence and death rate of pertussis and other common childhood diseases in the US through the creation of vaccines.

Kendrick was born 24 August 1890 in Wheaton, Illinois, to Ella and Milton Kendrick. Her father was a Free Methodist preacher in New York. At the age of three, Kendrick survived a pertussis infection. Kendrick attended high school in Sherburne, New York, and graduated in 1908. She attended Greenville College in Greenville, Illinois, for one year in 1910. Later that year, Kendrick transferred to Syracuse University in Syracuse, New York, where she majored in zoology and minored in philosophy. She received her Bachelor of Science degree in 1914. After graduation, Kendrick taught science at the Saint Johnsville Public Schools in St. Johnsville, New York, for five years. During the summer of 1917, she continued her education by studying bacteriology at Columbia University [7] in New York City, New York, under Hans Zinsser, who was a scientist who specialized in bacteriology and immunology.

From 1919 to 1920, Kendrick worked as a research assistant for the New York State Department of Health. In 1920, Cy Young, who was the director of the Bureau of Laboratories for the Michigan Department of Health, invited Kendrick to relocate to the Lansing, Michigan, branch to research syphilis, which is a sexually transmitted bacterial infection. In 1926, Kendrick was promoted to Associate Director of Laboratories and Chief of the Western Michigan Branch Laboratory at the Grand Rapids, Michigan, branch. During the summers of 1928 and 1931, she continued her research while also studying serology and pathology, which are the studies of the immune system’s response to infections, at the University of Michigan [8]. Kendrick then took a leave of absence from the Grand Rapids laboratory to attend Johns Hopkins University [9] in Baltimore, Maryland, where she received her Doctor of Science degree in bacteriology in 1932.

Kendrick returned to the Grand Rapids laboratory in 1932. While there, she recruited Grace Eldering, a bacteriologist from the Lansing branch who had also contracted pertussis as a child, to work with her on researching the disease that affected them as children. In 1906, Jules Bordet and Octave Gengou, researchers who studied bacteria and the immune system in France, identified Bordetella pertussis [10] as the bacteria that causes pertussis, which manifests as a severe cough with a whooping sound. In the 1920s, more than 6,000 children in the US died from pertussis each year. In 1925, Thorvald Madsen, a physician in Denmark, developed a pertussis vaccine. However, it was ineffective at preventing pertussis and even resulted in the death of two children in the study.

Kendrick and Eldering began working on a pertussis vaccine in 1932, when a particular strain, or subtype, of Bordetella pertussis appeared in Grand Rapids and began infecting the children in the city. The researchers worked on a vaccine that would undergo standardized trials to ensure efficacy. They partnered with the local community for resources and funding support. Local physicians provided Bordetella pertussis samples on cough plates, which are plates containing a jelly media that patients coughed on to collect bacteria. Kendrick and Eldering also collected samples by personally knocking on the doors of those infected with pertussis.

Kendrick had difficulties culturing the pertussis bacteria since the existing standard growth medium, called the Bordet-Gengou medium, did not fit the ideal conditions for Bordetella pertussis to grow. Bacteria cultures must grow in large quantities to create a vaccine, which often entailed inactivating, or killing, the bacteria prior to injection. Therefore, Kendrick devised a modified version of the medium that incorporated sheep’s blood, allowing for rapid growth of Bordetella pertussis. Although Kendrick developed the new medium for pertussis vaccine research, it also helped doctors and researchers in other ways. The increased rate of bacterial growth in those cough plates led to a more efficient tool for pertussis diagnosis, which local physicians began to implement in their clinics. Furthermore, the rapid-growth plates allowed Kendrick to determine the appropriate quarantine timeframes for children with pertussis.

Kendrick published her cough plate findings in 1934 in "Cough Plate Examinations for B. Pertussis" in the American Journal of Public Health and the Nation’s Health, stating that there was enough active Bordetella pertussis in a child's cough to infect others within the first three weeks of infection. However, Kendrick reported that after four to five weeks, a child with pertussis was not likely to infect others. The Grand Rapids Health Department incorporated Kendrick’s quarantine length recommendations into the Grand Rapids Communicable Disease Regulations later that year.
Kendrick and Eldering began conducting large-scale studies of the pertussis vaccine in 1934. They inactivated the live pertussis bacteria cells so that the cells could no longer cause infection by using thimerosal, which is an agent that kills bacteria and prevents contamination. To ensure that the vaccine was safer than previously developed vaccines, Kendrick performed multiple sterility tests and even injected it into her own arm to account for potential adverse side effects. She then performed several field trials for the pertussis vaccine, which entailed studies on people in a community environment, rather than admitting them to an institution for testing. During that time, most scientists did not conduct field trials due to lack of established standards with human participants. Previous field tests primarily used orphans or people in institutions as test subjects, rather than people from the general public. Kendrick instead used volunteer outreach to bring in a more representative cohort from the community at-large. Kendrick used pre-school aged children and nursing records to document how the vaccine worked in different demographics. From 1934 to 1935, Kendrick conducted a field trial with 1,592 children, vaccinating approximately half of them. She summarized the results in her 1936 paper, "Progress Report on Pertussis Immunization," in the American Journal of Public Health and the Nation's Health. Of the 712 vaccinated children in the field trial, only four developed pertussis, which presented as mild cases. In addition to the eighty-nine percent efficacy rate of the vaccine, Kendrick’s studies established field trials as a standard method of conducting immunization and public health experiments.

Like many others in the 1930s, Kendrick had limited research funding during the economic downturn from the Great Depression. In 1936, First Lady Eleanor Roosevelt traveled around the US to learn about projects sponsored by the Works Progress Administration, or WPA, which was an employment program implemented during the Great Depression. Kendrick’s pertussis study was a WPA-funded project, and so Roosevelt visited the Grand Rapids laboratory to learn more about Kendrick’s work in 1936. At a time where federal funding for research was not common, Congress accused many research groups of boondoggling, which meant that they were wasting money on unnecessary projects. Upon recognizing that Kendrick’s project was not boondoggling, Roosevelt helped obtain additional funding from the WPA, which, according to Kendrick, was critical to supporting the laboratory financially. Kendrick published the results of her field trial on the pertussis vaccine later that year.

Following the publication of Kendrick’s 1936 paper on the field trial results, some scientists raised concerns over the validity of the study. James Doull, an epidemiologist from Cleveland, Ohio, published opposing results in 1936, claiming that his pertussis vaccine conferred no protection to children. Due to the appearance of two contrasting studies around the same time, other scientists questioned the validity of Kendrick’s vaccine and whether she had designed the experiment properly. However, the results of subsequent administration of Kendrick’s vaccine effectively addressed Doull’s and other scientists’ concerns.

In 1938, the Michigan Department of Health began distributing Kendrick’s pertussis vaccine throughout the state. Then, in 1940, the US federal government distributed the vaccine across the country. From 1934 to 1948, the pertussis incidence decreased from 209 cases per 100,000 residents to fifty-one cases per 100,000 residents. Approximately a decade later, in 1960, the incidence was less than ten cases per 100,000 residents. Furthermore, the vaccine lowered the death rate from 5.9 per 100,000 residents to less than one per 100,000 by 1960. In 1943, the American Academy of Pediatrics approved Kendrick’s vaccine for routine use in the US, with the American Medical Association doing the same in 1944.

In 1942, Kendrick began experimenting with combination vaccines to protect individuals against multiple diseases in one injection. Combination vaccines require mixing multiple disease-specific antigens, which are foreign proteins from the bacteria that cause a particular disease. Other researchers used that technique before Kendrick. For example, the Army Medical School in the US combined several strains of typhoid fever, which is a bacterial infection that causes severe fever in patients, to develop the triple typhoid vaccine in 1917. Kendrick first worked to develop a vaccine that protected against both pertussis and diphtheria, which was another common childhood disease at the time that affected the mucous membranes of the respiratory tract.

In Kendrick’s 1942 paper, "Use of Alum-Treated Pertussis Vaccine, and of Alum-Precipitated Combined Pertussis Vaccine and Diphtheria Toxoid, for Active Immunization" in the American Journal of Public Health and the Nation's Health she reported the results of a field trial she conducted after combining pertussis and diphtheria toxins into a single vaccine. In the field trial, Kendrick divided 2,194 children into three groups: no vaccine, standard single vaccine, and combined vaccine. She found that the incidence of diphtheria or pertussis infection per 100 person-years was 10.9 cases in the no vaccine group, 1.6 cases in the standard single vaccine group, and 0.7 cases in the combined vaccine group, indicating that the combination vaccine was effective. Person-years is a time measurement that summates the total number of years all participants spend in a study.

In 1936, Kendrick left the Michigan Department of Health in 1951 and started teaching at the University of Michigan in Ann Arbor, Michigan. She lectured for the Department of Epidemiology in the School of Public Health while continuing her research on pertussis until her retirement in 1960. She also researched other common childhood diseases such as tetanus and poliomyelitis. Tetanus is a disease that causes muscles in the neck and jaw to lock, while poliomyelitis affects the nervous system and can lead to paralysis.

In 1960, Kendrick published her study on the combination vaccine for diphtheria, tetanus, pertussis, and poliomyelitis, or DPT-polio, and the effect of maternal immunization on the neonate after birth. She noted that thirty of the forty-eight neonates in the study had high levels of maternal antibodies immediately after delivery for at least one strain of virus, meaning that they were more protected against disease. During pregnancy, maternal antibodies produced from prior vaccination or infection can transfer to the fetus via the placenta. After birth, the maternal antibodies protect the infant for several months. That phenomenon is an example of passive immunity, which is where people receive immunity through another person’s antibodies.
Instead of their own. However, previous studies from David Talmage, an immunologist who studied antibodies in the US showed that individuals who had passive immunity to a disease did not develop a robust immune response to later vaccination. Kendrick reported similar results where infants with maternal antibodies after birth had lower antibody levels after vaccination compared to infants without maternal antibodies. Therefore, in her 1960 paper, Kendrick proposed delaying the vaccination of infants until maternal antibodies are gone.

Despite retiring from the University of Michigan in 1960, Kendrick remained involved in the scientific community. In 1962, she participated in the US-Union of Soviet Socialist Republics exchange program where she visited Soviet Union laboratories on behalf of the Immunology Delegation. During that time, Kendrick also consulted for the World Health Organization, or WHO, on immunization programs in regions such as Mexico, Eastern Europe, and Central and South America. She retired from the WHO in 1965. Throughout her career, Kendrick was active in multiple professional organizations such as the American Public Health Association and the American Board of Bacteriologists. She also served as President of the Michigan Branch of the American Society for Microbiology. In 1983, Kendrick was inducted in the Historical Honors Division of the Michigan Women’s Hall of Fame.

Kendrick’s DPT vaccine later became a prototype for the DTaP vaccine commonly administered to children in the US as of 2022. Despite both targeting diphtheria, pertussis, and tetanus, the two vaccines differ on the cellular level. Kendrick’s DPT vaccine utilized whole-cell pertussis bacteria, which means that whole pertussis bacterial cells were inactivated and then placed in the vaccine mixture. However, the whole-cell vaccine caused adverse side effects such as fever, redness, swelling, and seizures. The DTaP vaccine, which Yuji Sato and Hiroko Sato developed in Japan in 1974, uses acellular pertussis, or components from the pertussis bacteria, instead of the whole cell. The acellular component of DTaP decreased the likelihood of having an adverse reaction to the vaccine. By the 1990s, the DTaP vaccine became regularly distributed in the US. The US Centers for Disease Control and Prevention recommends a five-dose schedule of DTaP vaccination between the ages of two months and six years.

Kendrick and her colleagues published over sixty articles on their studies of pertussis and vaccination. Her 1960 findings on how having maternal antibodies may repress later vaccination responses have been supported in later studies. In the Netherlands in 2019, a trial showed that infants born to people immunized during pregnancy had higher levels of antibodies to pertussis, but having maternal antibodies interfered with primary and booster vaccinations. They still had an antibody response to the vaccination, but at a lower level compared to infants without maternal antibodies. In addition, Kendrick’s research with combination vaccines for diphtheria, pertussis, and tetanus led to the development of the DTaP vaccine currently administered in the US. In 2019, more than eighty percent of children in the US had been vaccinated for the diphtheria, tetanus, and pertussis combination vaccine. Kendrick’s development and field testing of the pertussis vaccine helped alleviate the pertussis crisis at the time and served as a prototype for vaccines administered today.

Kendrick died at age ninety on 8 October 1980 in Grand Rapids, Michigan.

Sources

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