Polio and Eli Lilly and Company

While polio has a history that some say dates back to ancient times, it was not until 1789 that British physician Michael Underwood provided the first clinical description of the disease.[1] The first outbreaks of polio in the United States were in 1894, with a major epidemic occurring in the summer of 1916 when thousands of children in New York, New Jersey, Pennsylvania, and Connecticut experienced unusual and frightening symptoms.[2] First, they came down with an apparent cold accompanied by a headache and chills. Soon, without warning, they might wake up partially paralyzed. Some victims even became unable to swallow or breathe due to paralyzed muscles. By mid-August that year, 9,000 children had exhibited these symptoms.[3]

No one knew what the disease was or how it was contracted, but they did know that children were disproportionately affected, which led to increased fear and panic. Autopsies revealed an inflammation of the anterior spinal cord. Thus the disease got its name – poliomyelitis.[4] Various measures were taken to try to control the disease and to stop its spread. According to one source, New York City scrubbed the streets with four million gallons of water a day and killed 72,000 stray cats in an effort to destroy polio germs.[5] In her book *Patenting the Sun: Polio and the Salk Vaccine*, Jane S. Smith noted:

> Nonresident bathing was banned at the Hudson Park Beach. Sunday schools were closed, and children under sixteen were forbidden to attend the local vaudeville theatres. Travelers were stopped at the city limits and issued transit passes good for one-half hour. Ferry service from the Bronx was suspended, and meetings were held almost daily for doctors to inform parents how best to care for their children. Sutton Manor, an exclusive residential enclave with a private marina off the main harbor, declared itself in voluntary isolation from the rest of the city. The local board of health printed quarantine signs in English, Italian, and Yiddish.[6]

As the public searched for explanations, it looked to the poor and new immigrants, suspecting these groups of being carriers of the disease.[7] However, it was the middle class, and not the poor, who were the most affected.[8] Indeed, it seemed to be a paradox of the disease that it struck in areas where there was relatively good hygiene. This paradox is explained by the Chemical Heritage Foundation. When infants are exposed to polio in the first months of their life, as they commonly were in times when the importance of hygiene was not well understood, they are protected by their

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[1] National Museum of American History, "Whatever Happened to Polio?" Time line, http://americanhistory.si.edu/polio/timeline/index.htm (accessed March 28,, 2012).
[2] Harry M. Marks, "The 1954 Salk Poliomyelitis Vaccine Field Trial," Institute of the History of Medicine, Johns Hopkins University, Baltimore, MD: 2008, p. 3.
[3] Lauren Pomerantz, "To Catch a Killer: The Search for the Vaccine to Prevent Poliomyelitis," p.1 http://www.teachspace.org/personal/research/poliostory/index.html.
[4] Ibid., p. 1.
[5] Ibid., p. 1.
[6] Jane S. Smith, *Patenting the Sun: Polio and the Salk Vaccine,* New York, NY: William Morrow and Company, 1990, p. 32 as quoted in Pomerantz, "To Catch a Killer," 1.
[7] Pomerantz, "To Catch a Killer," 1.
[8] Marks, p. 3.

mother's antibodies (still present in their bodies). "However, as hygienic conditions improved and fewer newborns were exposed to the virus (which is present in human sewage), paralytic poliomyelitis began to appear in older children and adults who did not have an infant's benefit of immunity," the foundation noted.[9] In addition, during the 1916 epidemic, rural children fell ill and died in greater numbers than did children in urban environments.[10]

Then, almost as suddenly as it had come, the disease disappeared. However, it did not stay away. Polio outbreaks came to be commonly associated with the spring and summer months from the 1930s through the mid-1950s, and every time "polio season," which generally lasted from mid-June to mid-October, returned, so did the fear and panic associated with the dreaded disease. Polio remained a relatively rare disease, and most cases of polio were mild, with the patient fully recovering.[11] However, the fact that polio victimized mainly children and sometimes left them crippled, contributed to the hysteria. A 1954 publication noted that children from the ages of five to nine were most susceptible to polio during the postwar epidemic years. A study conducted between July 20 and December 31, 1952, showed that 54 percent of those affected by polio were under the age of ten.[12]

In 1938 a new organization was formed to fight against polio. Established by President Franklin D. Roosevelt, who himself had been paralyzed by polio, the National Foundation for Infantile Paralysis was charged with raising money to aid polio victims and to fund research aimed at finding a cure for polio. Roosevelt appointed his friend and New York City law partner Basil O'Connor to head the NFIP. O'Connor immediately made combating polio his personal passion and mission.

O'Connor built the organization from the ground up, establishing a large network of local chapters (3,100 chapters by 1950) that were almost entirely staffed by volunteers.[13] These local chapters responded to the needs of polio victims in their communities, working with local hospitals, treatments centers, and patients' families to provide equipment and funding for patient care. On the national level, the NFIP outlined and executed a "scientific plan of attack against polio," working with scientists who studied the polio virus and searched for a vaccine or cure.[14] The NFIP established scientific committees that funded research on the polio virus and partnered with the U.S. armed forces to study the way polio affected troops. Until the NFIP provided the funding and

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[9] Chemical Heritage Foundation, "Jonas Salk and Albert Bruce Sabin," http://www.chemheritage.org/discover/online-resources/chemistry-in-history/themes/pharmaceuticals/preventing-and-treating-infectious-diseases/salk-and-sabin.aspx (accessed February 20, 2012) p. 1.

[10] Pomerantz, "To Catch a Killer," 1.

[11] According to the "History of Vaccines" Web site, in approximately 98 percent of cases, polio is a mild illness with no symptoms or viral-like symptoms. Fewer than 1 to 2 percent of people who get polio become paralyzed. In paralytic polio, the polio virus enters the bloodstream and from there attacks the central nervous system. In severe cases, a patient's throat and chest may become paralyzed. http://www.historyofvaccines.org/content/timelines/polio (accessed February 20, 2012).

[12] Robert Coughlan, *The Coming Victory Over Polio* (New York: Simon and Schuster, 1954,) 48-49.

[13] March of Dimes, "A History of the March of Dimes," http://www.marchofdimes.com/history_indepth.html (accessed February 20, 2012,) 1.

[14] National Foundation for Infantile Paralysis, "A Statement Prepared by the National Foundation for Infantile Paralysis for The House Committee on Interstate and Foreign Commerce, Charles A. Wolverton, Chairman, October 12, 1953," (Hereafter cited as NFIP Statement).

spurred a systematic research program, "scientific knowledge of the disease was sparse, uncoordinated, and in many important phases, contradictory."[15]

During the height of the epidemic years, it became clear that people perceived the chief threat of polio to be paralysis and not death. In a 1953 statement to the House Committee on Interstate and Foreign Commerce, the NFIP noted, "Since [polio] strikes chiefly at youngsters - small children and teenagers - a large number of its victims must be cared for many years and many carry a burdensome handicap throughout their lives."[16] Arresting images of children in leg braces and wheelchairs were used extensively and effectively in fund-raising materials by the NFIP, which noted not only a severe emotional and physical toll on paralyzed children and their families, but also a high economic cost associated with the long-term care of these patients. According to the foundation, "There is no way of estimating manpower loss accurately in terms of interruption of schooling or denial of playtime for children. The high incidence among women of 20 and over strikes into the group of young mothers, whose loss to their families is incalculable. Permanent crippling of the boys and girls under 20 means perhaps 50 years of economic handicap. Recovery periods after a poliomyelitis attack often stretch for months, and some patients cannot be restored to earning power for years, if at all."[17]

For the NFIP itself, since the organization continued to pay for patient care for years to come, long-term treatment for paralysis could be extremely expensive. For example, in 1953 the NFIP was still paying for care of some of the victims of the 1916 epidemic. In 1953 the average cost of treatment per patient was $629, of which the NFIP contributed $550. This did not include the cost of equipment provided to the patients (such as an iron lung, rocking bed, portable chest respirator, hot-pack machine, wheelchair, or leg braces).[18]

Polio outbreaks were particularly severe in the 1940s and 1950s, but despite years of research, scientists had few answers as to what caused the disease and how it spread. One important milestone in scientific research related to polio occurred in 1949. In that year John F. Enders, MD, a virologist at Harvard University and the Boston Children's Medical Center, and his partner, Thomas Weller, developed a method of culturing tissue that "allowed for large-scale production of poliovirus in non-nervous tissue."[19] This meant that the virus that would be necessary to produce a polio vaccine no longer had to be obtained from the infected brains or spinal cords of monkeys or other animals. It could be cultured in non nervous tissue in a test tube. This was important because of the dangers involved in injecting nervous tissue from one species into another.[20] This discovery did not eliminate animal testing or the use of animals in poliovirus and vaccine research, however.

Between 1948 and 1951 another major scientific breakthrough came with the typing of the poliovirus. The NFIP had awarded $1.37 million in grants to scientists at the University of Southern

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[15] Ibid., 6.
[16] NFIP Statement, 1.
[17] Ibid, 2-3.
[18] Ibid., 2-3.
[19] Marks, "1954 Salk Poliomyelitis Vaccine Field Trial,"4.
[20] NFIP Statement, 7.

California, Utah, Kansas, and Pittsburgh, and had asked them to work together to determine how many viruses caused polio. These scientists studied hundreds of polio virus specimens obtained from patients worldwide. By 1951 they had determined that there were three major types of polio virus: the Brunhilde type, the Lansing type, and the Leon type. A vaccine would have to be effective against all three of these viruses in order to conquer polio.[21]

In addition, as scientists continued their work with the financial support of the NFIP, they discovered that the poliovirus did not go directly from the intestinal tract to the brain or spinal cord, but that it entered the bloodstream for a brief period of time. This meant that a vaccine could be injected intravenously and be successful.

These discoveries opened the door for the work of scientists Jonas Salk and Albert Sabin, who focused on developing a safe and viable polio vaccine. Earlier attempts at creating a vaccine had not gone well. In 1934 and 1935, researchers Maruice Brodie (New York) and John Kolmer (Philadelphia) each developed a vaccine. Brodie's vaccine was a killed virus vaccine and Kolmer's used "attenuated," or weakened, live polio virus. The tests of Kolmer's vaccine ended in disaster when it was suspected to have caused ten cases of paralysis and five deaths among the 10,000 children vaccinated. Reports of anaphylactic reactions to Brodie's vaccine shut down further trials.[22]

However, by the early 1950s, armed with the techniques pioneered by scientists such as Enders and Weller and the typing of the poliovirus, several scientists were once again experimenting with developing a polio vaccine.[23] By this point, Salk was thinking about how he might produce a polio vaccine using killed virus, as he had previously done with an influenza vaccine (developed in 1943).[24] Building on the work of Enders and Weller (who developed a method for growing polio virus in non nervous tissue cultures), Salk developed methods for growing large amounts of the three types of poliovirus in cultures of monkey kidney cells. He then killed the virus with formaldehyde. He found that when he injected this killed virus vaccine into monkeys it appeared to provide some protection against paralytic poliomyelitis.[25] He began testing the vaccine in humans in 1952, using small populations, including 98 children at the D. T. Watson Home for Crippled Children, 63 students at the Polk State School, and ultimately several thousand children in Allegheny County.[26]

Around the same time that Salk began working on his killed-virus vaccine, Sabin began work on an attenuated live-virus vaccine. Sabin found three mutant strains of the polio virus that appeared to stimulate antibody production and developed an oral vaccine from them. He first administered his vaccine on himself, his family, research associates, and prisoners in the Chillicothe Penitentiary.[27]

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[21] Ibid., 8.
[22] Marks, "1954 Salk Poliomyelitis Vaccine Field Trial," 3.
[23] Ibid., 4.
[24] Chemical Heritage Foundation, "Jonas Salk and Albert Bruce Sabin," http://www.chemheritage.org/discover/online-resources/chemistry-in-history/themes/pharmaceuticals/preventing-and-treating-infectious-diseases/salk-and-sabin.aspx, 2 (accessed February 20, 2012).
[25] "Jonas Salk and Albert Bruce Sabin," 2.
[26] Marks, "1954 Salk Poliomyelitis Vaccine Field Trial," 5-6.
[27] "Jonas Salk and Albert Bruce Sabin," 3.

However, it was Salk, not Sabin, that gained support for a large-scale field trial in the United States because he simply beat Sabin to the punch. A vaccine would normally be tested first in a handful of children and then progress to tests of several hundred, all "while collecting detailed data about antibody responses to the vaccine."[28] O'Connor knew that this would take a very long time, and in an attempt to speed up the process he convened a committee of national authorities on public health in May 1953 to advise the NFIP on a field trial of the Salk vaccine.

The committee struggled to come up with a design for the field trials and to start them before polio season hit in 1954. They finally agreed on a compromise plan – the trial would be a double-blind trial with randomized controls. However, in some areas the control group would receive a saline shot, while in others they would receive the influenza vaccine. The trial group would receive the polio vaccine. In eleven states, first, second, and third graders were randomized by blocks of ten within each classroom, with some children receiving the vaccine and others receiving placebo shots. In thirty-three states the second graders received the vaccine, while first and third graders received placebo shots (serving as the control group). All children participating would need to provide blood samples for testing the effectiveness of the vaccine, and all would be termed "polio pioneers."[29]

The NFIP contracted with five pharmaceutical companies to produce vaccine for the trials: Eli Lilly and Company, Indianapolis; Parke, Davis and Company, Detroit; Cutter Laboratories, Berkeley; Wyeth Laboratories, Philadelphia; and Pitman-Moore Company, Indianapolis. The NFIP also contracted with Connaught Laboratories in Toronto to produce poliovirus that was then shipped to Lilly and Parke, Davis for use in vaccine production. Cutter Laboratories, Wyeth Laboratories, and Pitman-Moore Laboratories had an integrated production process in which they produced both the poliovirus and the vaccine.[30] According to Eugene N. Beesley, president of Lilly in 1955, "When it appeared to be feasible to manufacture a vaccine for immunization against poliomyelitis, we again considered it a privilege to take part in its development."[31] By the 1950s the Lilly research team consisted of more than 900 employees working in the areas of research, development, and control. "The company, cheered on by an enthusiastic Eli and J. K. Lilly, grandsons of the company's founder, was ready to take the risks involved in early polio vaccine work. These included the need to invest in research and production technologies, equipment, and brainpower before the vaccine received approval for public use. Had the trials not succeeded, Eli Lilly and Company would have been left with a stockpile of unusable vaccine," according to an Indiana Historical Society exhibition on Lilly and the polio vaccine.[32]

However, the trials were successful. By the end of June 1954, 626,779 children around the country had received the full series of three vaccine shots. Compiling the data took several months, but on April 12, 1955, Thomas Francis Jr., a professor of epidemiology at the University of Michigan and

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[28] Ibid., p. 6.
[29] Marks, "1954 Salk Poliomyelitis Vaccine Field Trials," 8 - 11, 13.
[30] Coughlan, *The Coming Victory Over Polio*, 58 - 59.
[31] Eugene N. Beesely, "Welcome to Eli Lilly and Company" (speech delivered to visiting congressmen February 24, 1956), 3.
[32] Eloise Batic, *You Are There 1955: Ending Polio* exhibit text (2012), 8.

Salk's mentor who had been chosen to run the field trials, announced at a press conference in Ann Arbor, Michigan, that the results of the trials seemed quite favorable. Though the vaccine did not provide complete protection against paralytic poliomyelitis, "For the handful of cases (85) where virus was recovered," the Michigan University Poliomyelitis Evaluation Center reported that, "it appeared that the vaccine's effectiveness against the commonest poliovirus strain (Type I) was 68% as compared to 100% against Type II and 92% against Type III. For reasons never fully explained, polio rates among six year olds enrolled in the study did not show the protective effects seen in seven, eight and nine year olds."[33] News reporters heard only good news and ran with the headline "Triumph Over Polio." That evening a group of virologists met and sent a recommendation to the U.S. Surgeon General that the vaccine should be licensed. It is the quickest federal approval on record. On April 13, 1955, manufacturers began delivering the vaccine.[34]

Production of the vaccine was temporarily suspended when the Public Health Service received word of eleven cases of polio in children who had been vaccinated with the Cutter Laboratories' vaccine. U.S. Surgeon General Dr. Leonard A. Scheele, immediately banned Cutter from continuing vaccine production. The public panicked. Could it be that a vaccine they were told would protect their children instead would paralyze them or worse, kill them? Although it appeared that the problem was limited to vaccine produced by Cutter, Scheele decided to "play it safe" by ordering a complete halt to the immunization program.[35] For the next several weeks, PHS officials visited vaccine plants. Ultimately, a new series of safety protocols was put into place and manufacture and distribution of the vaccine resumed by the end of May 1955. It was determined that the affected Cutter vaccine had traces of live virus in it. In all, at least 200 cases of polio were traced to the defective Cutter vaccine.[36]

When vaccination of children resumed, the effect was nearly immediate. "An average of 35,000 polio cases per year were reported in the 1940s and 1950s, but by 1957 the number of reported cases had dropped to 2,500. By 1965, just ten years after the vaccine became available, only sixty-one cases were reported in the United States," according to the IHS exhibit text.[37] American children could once again look forward to summer – to hours splashing in public pools, friends made at summer camps, and to being free from the fear of polio.

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[33] Michigan University. Poliomyelitis Evaluation Center (1955), An evaluation mof the 1954 poliomyelitis vaccine trials; summary report. Ann Arbor: n.p. , pp. 17-18 as quoted in Marks, Harry M. "The 1954 Salk Poliomyelitis Vaccine Field Trial." Institute of the History of Medicine, Johns Hopkins University. Baltimore: 2008, p. 20.
[34] Marks, p. 21.
[35] Harper's Magazine. "'Who is responsible, and why, for the chaotic confusion over the polio inoculations?' A noted medical journalist disentangles the essential facts." August, 1955. Pp, 2
[36] Marks, "1954 Salk Poliomyelitis Vaccine Field Trials," 22.
[37] Batic, *You Are* There, 9.