

Polio: Virus and Vaccine - Historical Perspective

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The world has fewer crippled people in the early 21st century than it did in the early 20th, due to the remarkable effort that went into the conquest of poliomyelitis.

Polio has been depicted in a picture etched into an Egyptian stele and described in the writings of Hippocrates and Galen. The Scottish author Sir Walter Scott suffered its ravages. Later it was called infantile Paralysis, somewhat misleadingly, for children rather than infants were most susceptible. The current name comes from two Greek words *polios* ("grey") and *myelos* ("marrow"), referring to the grey matter of the spinal cord which is inflamed by the disease, hence the suffix *itis*. Poliomyelitis was always in the news in the 20th century, and journalists shortened the name to "Polio" to fit their headlines.

Although polio was an ancient disease, for most of its history it was not feared. It did not cause epidemics nor erupt into sweeping pandemics the way of smallpox, syphilis, influenza, and the plague. But from the mid 1800s, polio outbreaks popped up regularly in Western Europe and North America. Soon the great polio epidemics began. This virus was suddenly attacking people in a way it had never done before.

We associate infectious diseases like cholera and typhoid with poor sanitation and hygiene. With polio, it was contrary. In the bad old days of poor hygiene, babies were exposed to poliovirus early, while still protected with antibodies they had acquired from their mothers. Later (if they survived the other diseases associated with poor hygiene), these children developed their own antibodies to poliovirus. The net effect was that in communities with poor hygiene, most had already possessed immunity to polio. As sanitary conditions improved, such immunity was lost. A disease that festered as an endemic for centuries turned epidemic.

Poliomyelitis

Polio is an intestinal infection spread from person to person from contact with faecal material through unwashed hands, contaminated water and food, and shared objects. Poliovirus enters the body through the mouth, travels down the gut and is excreted through the stools. It multiplies in lymph tissues in the intestines (Peyer's Patches) and usually causes no symptoms or may cause a mild illness with fever, headache, nausea, and neck stiffness. In most people, lifelong immunity is acquired.

In about 1% of infected people, the virus sneaks into the bloodstream and invades the nervous system, destroying the motor neurons (the nerve cells that make the muscles contract) resulting in paralysis, most often in the lower limbs. The extent and severity of the paralysis depends on how much the body is able to fight back. And if the virus attacks the brain stem ('the bulb of the brain'), the resultant 'bulbar polio' paralyzes the respiratory muscles and, in effect, slowly asphyxiates the person to death.

Victim

Polio might still be with us in a big way had Franklin Delano Roosevelt not succumbed to poliovirus in the summer of 1921. The news shocked America. If an athletic upper class gentleman with a singular pedigree could succumb to polio at age 39 (no infant, this), then no one in America was safe. Roosevelt was determined not to let his malady cut short his political career. He ran successfully for Governor of New York in 1928 and for the presidency four years later. He struck a gentleman's agreement with the press that continued through his presidential years. The press would not write about his affliction or film him looking helpless and vulnerable. If an errant journalist, photographed Roosevelt being lifted out of his chair, the Secret Service stepped in and confiscated the film.

The strategy worked. Most Americans had little idea of the extent of Roosevelt's handicap, and re-elected him thrice. Roosevelt, the longest serving president of the United States, led his country out of the Great Depression and shepherded it through World War II, while totally and absolutely paralysed below the waist. In 1938, Roosevelt started an organisation called the National Foundation for Infantile Paralysis to discover the cure for polio and provide the best treatment for polio-stricken

Americans. Money was scarce. The Foundation came up with a campaign called March of Dimes, calling on every American to contribute a dime to the President to fight polio.

On the first day of the campaign, 30,000 letters were delivered; on the second, 50,000. Thousands of dollars arrived through banknotes and cheques as well.

In 1926, bacteriologist Paul de Kruif published *Microbe Hunters*, a dossier of 12 stories starting with Leeuwenhoek squinting down a lens at 'animalcules,' and ending with Ehrlich's work on salvarsan, the 'magic bullet.' in between, other pioneers like Pasteur, Koch, Spallanzani, Ross, and Metchnikoff commanded the stage. *Microbe Hunters* inspired hundreds to pursue careers in medicine and science, including two boys. The older boy was Albert Sabin, the younger one, Jonas Salk.

Salk and Sabin

Salk and Sabin had different approaches to their common quarry, poliovirus. Bacteria could be defeated by antibiotics, but not viruses. The solution was a vaccine that would make the immune system spew out antibodies against poliovirus before it invaded, so that any such invasion would be stymied before it took root. However, Salk favoured a killed vaccine where the virus was dead, but still had intact its structure that could trigger an immune response by way of antibody production. Sabin favoured a vaccine where the virus was alive but attenuated, that is, weakened to the point where it was incapable of causing disease but would provoke an immune response. The general medical opinion of the day sided with Sabin, as it was believed that a live vaccine generated a more robust immune response than a killed vaccine did.

What was poliovirus like? There were three serotypes. Type i was the most common, responsible for most epidemics that resulted in paralyzed limbs. Type ii was milder, likely to cause damage only if the infected patient was already weakened from other causes. Type iii was the least common but the most lethal, the one that went for the medulla oblongata and caused bulbar polio, paralyzing the respiratory muscles, leading to an invisible garrotting and death. This placed the patient into an iron lung, a tank-like contraption into which the body was inserted up to the neck, the fluctuating pressure within the tank making the chest expand and contract. An effective vaccine would have to combat all three.

The National Foundation had raked in millions of dollars each year from the public through the March of Dimes campaigns. While the Foundation helped polio patients across America, paying for treatment whether the patient was indigent or not, the public expected a cure. The Foundation prodded the scientists whose research it was funding, including Salk and Sabin, implicitly turning it into a case of who would get there first.

A killed vaccine was easy to prepare. Salk killed poliovirus with formalin. Attenuating the virus was akin to capturing a herd of kangaroos whose members were leaping in different directions. The virus had to be passed in rapid succession through a series of animals or animal tissue, during which some viruses became weak. These had to be identified, isolated, and then grown in sufficient quantities for vaccine production. As Sabin plodded on, Salk announced in 1953 that his vaccine was ready.

The Salk Vaccine

The following year, the Salk vaccine was tested in a stupendous clinical trial. The trial engaged some 20,000 doctors, 40,000 nurses and 1000 health care workers, and enrolled 1.3 million children, about 423,000 received the vaccine, 201,000 the placebo control, and in addition there were several hundreds of thousands who did not receive anything but were followed up and observed as controls. Almost 95 percent of those injected got the stipulated three shots of either vaccine or placebo. Most of the trial sites were schools.

The results were announced on 12 April 1955, the 10th anniversary of Roosevelt's death. The vaccine was safe, and 60-70 percent effective against Type i and over 90 percent effective against Type ii and iii. Salk became an American icon, lionized by the public, gracing the cover of TIME magazine, and the recipient of numerous awards.

Once the government approved the Salk vaccine, thousands of children were inoculated. Then disaster uncoiled. Several children developed polio after receiving the vaccine. At first, people were not alarmed; the child could well have contracted the disease before the vaccination. But there were too many cases for comfort. The U.S. Surgeon-General halted polio vaccinations. Salk was devastated.

While he was willing to concede that the vaccine that carried his name might not protect against polio a hundred percent, it certainly wouldn't, couldn't, *cause* polio.

Then it was discovered that every vaccine lot that led to polio came from one manufacturer: Cutter. As a result of dubious quality control, some lots had live viruses besides the killed ones. Once the problem was identified and fixed, normalcy returned. So did Salk's reputation when it was clear he wasn't person-ally at fault. But it took much longer to restore public confidence.

Sabin Vaccine

in 1959, Sabin found few takers when he announced his vaccine was now ready. America had no stomach for another massive clinical trial, especially for a dis-ease for which they now had a protective vaccine. Sabin did something unexpected: he boarded a plane to Moscow to a warm welcome from the Soviets. Amid the searing heat of the Cold War, Albert Sabin conducted his clinical trial on enemy soil.

Concerned that the trial results would be dis-missed as Soviet propaganda, Sabin requested the World Health Organisation to validate his results. The U.S. still wanted Sabin to run another clinical trial, however small, on its territory, which he did in 1960.

Sabin's vaccine was approved. it was easier to manufacture, transport and administer, and children were happy to lick down a blob of syrup. The virus in the vaccine followed the path that occurred in nature: entering through the mouth, multiplying in the gut, and evoking immunity with IgA antibodies, which stopped wild (naturally occurring) poliovirus from invading in contrast to Salk's vaccine, which mainly evoked IgG antibodies that did not stop the wild virus from infecting a person and replicating in the gut; they only stopped it from invading the nervous system.

By 1963, the Sabin vaccine had supplanted the Salk vaccine in America and was soon in use in most countries. Jonas Salk was the hero but Albert Sabin was the victor.

Bacteria grow in broth or agar in Petri dishes and test tubes. A virus only multiplies within another living host, so cultivating it in the lab involves artificially maintaining the host tissue, a process called tissue culture. Early erroneous research concluded that poliovirus only multiplied in neurological tissue, which was hard to maintain as tissue culture. This set back polio research by years, until John Enders and his team demonstrated that poliovirus grew in non-neurological tissue as well. But for this discovery, nobody could have worked on a vaccine. Enders and his team won the Nobel Prize in 1954; as far as the Nobel Committee was concerned, the semi-nal work in polio research had been recognized.

There is much still unknown. Why did the virus strike mostly during summer? Was it because it needed a co-factor, maybe an allergen like pollen or rag-weed, in order to infect people? Why were children more susceptible than adults, and boys infected much more than girls? We might never know the exact answers. Polio has been almost eradicated from the globe. The consensus is that time and money are better spent researching other pressing issues.

Poliomyelitis Today

Polio remains endemic in three nations: Pakistan, Afghanistan, and Nigeria. Then, there are the impor-tation countries, where migrants or visitors with polio can cause outbreaks. These countries extend from West Africa eastward to the Horn of Africa. (Link: <http://www.polioeradication.org/infectedcountries.aspx>) To underline the difficulty of extinguishing polio for all time, three countries that were declared polio-free saw fresh outbreaks of wild polio this year (figures as of September 3, 2013): Somalia (160 cases), Kenya (13) and Ethiopia (1). Poliovirus has also been detected this year in sewage samples in israel, prompting a massive re-vaccination of israeli chil-dren.

One of the heartening polio success stories is india. in 2009, india reported 741 new polio cases, more than any country in the world. Since January 2011, there have been no new cases caused by wild (occurring in nature) poliovirus. it is a much lauded public-health achievement (Link: <http://world.time.com/2013/01/13/how-india-fought-polio-and-won/>) but a few months without new cases has to pass before WHO declares india polio-free. However, there may be vast numbers of vaccine-induced polio cases in india, masked by other clinical terms (Link: <http://www.thehindu.com/opinion/lead/polio-free-does-not-mean-paralysis-free/article4266043.ece>).

The Sabin vaccine was an attenuated vaccine. Very occasionally, a virus could back-mutate to virulence and produce polio. The benefits of the vaccine over-whelmingly outweighed this slight risk. However, the last naturally occurring polio case in the U.S. was in 1979. All the few subsequent cases

were due to the live vaccine. And sometimes the disease didn't occur in the vaccinated child, but in another member of the household to whom the child had passed on the virus. People with compromised immunity - such as those on chemotherapy, immunosuppressive drugs, or infected with the Human immune-deficiency Virus -were especially vulnerable. The Centers for Disease Control and Prevention strongly recommended that the Sabin vaccine be phased out and the Salk vaccine reintroduced. By January 1, 2000, the transition was complete. Salk was back.

Other industrialized countries have followed the American example. The Sabin vaccine continues to be in use in the rest of the world, though, as countries become polio-free, they too will have switch to the Salk vaccine to avoid vaccine-induced polio and become truly polio-free.

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