SL Vaccines And Vaccination Journal

Special Issue Article : "Polio Vaccines"

Review Article

# Polio Vaccines: The Global Effort to Eradicate Polio

**Mulan Zeng and Hua Zhu***

Department of Microbiology, Biochemistry and Molecular Genetics, Rutgers University, USA

**ARTICLE INFO**

Received Date: August 05, 2022
Accepted Date: September 01, 2022
Published Date: September 02, 2022

**KEYWORDS**

Oral polio vaccine
Inactivated polio vaccine
Global polio eradication initiative
WHO



**Citation for this article:** Mulan Zeng and Hua Zhu. Polio Vaccines: The Global Effort to Eradicate Polio. SL Vaccines And Vaccination Journal. 2022; 3(2):124

**Corresponding author:**
Hua Zhu
Department of Microbiology, Biochemistry and Molecular Genetics, Rutgers University – New Jersey Medical School, 225 Warren Street, Newark, NJ 07103, USA, Tel: +973-972-6488,
Email: hua.zhu@rutgers.edu

## ABSTRACT

Poliomyelitis is an infectious disease that may lead to paralysis or even death. In addition to potential damage to the central nervous system, polio symptoms may also resurface in a condition called post-polio syndrome decades after initial infection. The disease is caused by poliovirus, a virus that spreads through the fecal-oral route and has three distinct serotypes (types 1, 2, and 3). Although two of the three wild poliovirus serotypes (types 2 and 3) have already been eradicated and polio cases have decreased significantly since the late 20th century, because of the risks associated with polio and its infectiousness, it is critical that polio disease is completely eradicated globally. Two vaccines are used to accomplish this goal: Jonas Salk's Inactivated Polio Vaccine (IPV) and Albert Sabin's live attenuated Oral Polio Vaccine (OPV). However, due to the mutable nature of OPV, it is possible for additional poliovirus outbreaks to occur, making the disease difficult to fully eliminate. The effort to eradicate polio continues today with the coordination of organizations such as the Global Polio Eradication Initiative (GPEI), the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), and the Bill & Melinda Gates Foundation.

## INTRODUCTION

Poliomyelitis, commonly known as polio, is an acute paralytic diseasecaused by the enterovirus Poliovirus (PV), which belongs to the Picornaviridae family [1]. The poliovirus is a single-stranded RNA virus that has a diameter of 25-30 nm. It has a dense central core with a naked protein capsid, which consists of 60 protomers that are each made of 4 structural proteins, arranged in icosahedral symmetry: VP1, VP2, VP3, and VP4. There are three antigenically distinct poliovirus serotypescalled types 1, 2, and 3 (PV1, PV2, and PV3). Despite the different serotypes having an average nucleotide identity of 70%, there is minimal heterotypic immunity between them, meaning that immunity to one serotype does not equate to immunity to another serotype [2-4].

Polio exclusively affects humans, though experimental infections can be replicated in animals, such as monkeys and transgenic mice [2]. The virus is most often transmitted through the fecal-oral route, though it can also be spread through a common vehicle, such as contaminated water. The disease is usually diagnosed with cultures of the throat and stool, or less commonly, blood levels or cerebrospinal fluid testing [5]. Most polio patients are young children under the age of 5 [6]. Although about 72% of people infected with polio have no visible symptoms, a situation called inapparent infection, others are categorized to either have abortive, nonparalytic, or paralytic polio [4,5]. Abortive polio, in which the poliovirus does not enter the central nervous

system or damage neurons, makes up 80-90% of all polio cases. It is the mildest form of the disease, with symptoms that include fever, decreased appetite, and nausea. Nonparalytic polio is similar to abortive polio, but with additional symptoms such as stiffness along the spine. The rarest form of polio is paralytic polio, which occurs in 1 in 200 cases.Infection can lead to irreversible paralysis, and 5-10% of those paralyzed can die if their breathing muscles also become immobilized. Other symptoms include muscle wasting, loss of reflexes, loose and floppy limbs (flaccid paralysis), orother conditions that affect the brain and spinal cord. After recovering from initial polio illness, patients may be affected by additional symptoms decades later in a condition called noninfectious Post-Polio Syndrome (PPS). Post-polio syndrome develops in about 40% of people who have had polio, in nonparalytic and paralytic polio cases. This is due to the acute central nervous system damage patients can possibly receive with nonparalytic and paralytic polio, despite the milder symptoms of nonparalytic polio. Symptoms of post-polio syndrome include muscle atrophy, fatigue, joint and muscle weakness, and breathing problems [6-8]. Notable people who have had polio include the musician Neil Young, the author of "A Space Odyssey," Arthur C. Clarke, and most significantly, the 32nd President of the United States, Franklin D. Roosevelt, who was also paralyzed from the waist down [9].

However, since an estimated 350,000 cases globally in 1988, the number of wild poliovirus cases has decreased by over 99%, to 33 cases in 2018. This is largely due in part to increased global efforts to eradicate polio, such as the launch of the Global Polio Eradication Initiative (GPEI) in 1988 and the development of the first polio vaccine in 1955. Even so, despite the low number of reported cases globally, this disease is highly infectious and could easily spread again if not completely eradicated [10]. Because polio has no cure, vaccines are critical for prevention; today, the live attenuated Oral Polio Vaccine (OPV) and Inactivated Polio Vaccine (IPV) are used to control the spread of this disease [1].

## HISTORY OF POLIO

The word "poliomyelitis" is derived from the Greek words "polio," which means "gray," and "myelon," which means "marrow" [11]. Polio is estimated to have been around for centuries, including in ancient times, due to its presence in Egyptian hieroglyphs dating back to 1400 B.C. [1]. The disease would often break out in epidemics every few years, often in summer, but it is not clearly mentioned until 1789, when a London pediatrician described it as a paralytic disease in infants [11,12]. The first documented outbreaks occurred in Norway in 1868, and later, the U.S.'s first documented outbreak occurred in 1884. Though previously known as "infantile paralysis" during the 19th century, Austrian physicians Karl Landsteiner and Erwin Popper named the disease "poliovirus" in 1908. They had detected the viral nature of polio by filtering withdrawn spinal cord fluid from a deceased polio patient to trap bacteria, and through intraperitoneal injection of the fluid, Landsteiner and Popper were able to transmit the disease to a Cynocephalus monkey and a rhesus monkey [1,13]. The monkeys developed lesions in the spinal cord, medulla, pons, and brain stem, symptoms that were also exhibited in human cases of poliomyelitis. The rhesus monkey even developed complete flaccid paralysis in both of its legs. Landsteiner and Popper were then able to conclude that polio was caused by an infectious particle—poliovirus. Later, in 1931, different serotypes of poliovirus were identified by Australian researchers Frank Macfarlane Burnet and Jean Macnamara. It had previously been believed that poliovirus had the same antigenic qualities globally; however, the two researchers disproved this assumption through cross-immunity experiments and neutralization tests [12,14]. They infected monkeys, whom had already been previously infected with polio and recovered, with polio from a fatal human case. The monkeys developed paralysis from the new infection, indicating that previous infections, which would supposedly have caused immunity to polio, would not create immunity to a different strain of polio [15]. The three strains of poliovirus were later identified as Brunhilde (PV1), Lansing (PV2), and Leon (PV3) [1]. However, poliomyelitis was unable to be cultivated outside of nervous tissueuntil John Enders, Thomas Weller, and Frederick Robbins successfully multiplied poliovirus in non-nervous cell structures *in vitro*. They tested the multiplication of PV2 in human embryonic cultures, human embryonic intestinal cultures, and nervous tissue, and in 1949, they demonstrated how all three poliovirus strains could be multiplied in large amounts in various tissues, including non-nervous tissues, *in vitro*. This discovery allowed for more efficient methods of studying

poliovirus, in addition to other prominent viruses, since viral research had previously been limited to expensive *in vivo* testing on animals. Enders, Weller, and Robbins were later awarded with the Novel Prize of Physiology and Medicine in 1954 for their work [14,16]. Eventually, in 1953, Jonas Salk announced that he had developed an effective vaccine against polio, the inactivated polio vaccine (IPV), which is the predominantly used polio vaccine in the United States today. In 1961, Albert Sabin introduced the live attenuated vaccine, also known as the Oral Poliovirus Vaccine (OPV) [1,12].

## INACTIVATED POLIO VACCINE (IPV)

The inactivated polio vaccine (IPV) was developed by Jonas Salk in 1953 and contains killed, or inactivated, poliovirus strains of all three serotypes [17]. Salk developed it by choosing to use non-infectious killed viruses to induce immunity, rather than isolate weakened live viruses-the norm in vaccine development at the time [18]. To make the vaccine, he and his team grew samples of types 1, 2, and 3poliovirus in kidney tissue from monkeys and used a 1:250 concentration of formalin to inactivate (kill) the virus without destroying its immunogenicity [19,20]. Salk and his team used the poliovirus strains Mahoney (type 1), MEF-I (type 2), and Saukett (type 3). The vaccine was stored at +2°C to +8°C, protected from light, and it was to be administered as an intramuscular injection in either the upper arm or anterolateral thigh. They finally tested the vaccine in 1954, in a placebo-controlled trial consisting of 1.6 million children in Canada, Finland, and the United States, despite controversies regarding the safety of the vaccine and flaws in the field trial's design [1,3,20]. Salk once said, "I have had dreams and I have had nightmares, but I have conquered my nightmares because of my dreams." In 1955, he finally announced that his vaccine was both safe and efficacious, and it was adopted in the United States. Polio cases in the United States subsequently decreased from 13.9 cases per 100,000 in 1954 to 0.8 cases per 100,000 in 1961 [1,18].

However, Salk's polio vaccine faced challenges. IPV travels through the blood to the brain or the spinal cord, inducing antibodies in the bloodstream rather than the intestines [21]. Because of this, in the late 1950s, there was increasing doubt whether IPV prevented poliovirus infection in the gastrointestinal system [22]. Additionally, the Cutter incident also occurred shortly after the start of mass vaccination with IPV in the United States in 1955. Cutter Laboratories, based in Berkeley, California, had failed to inactivate the poliovirus in the Salk vaccines it manufactured, causing 40,000 cases of polio and killing 10. This was due to possible poliovirus resistance to formaldehyde, which was used to deactivate the virus. Because of this, a second filtration step was added to the production process to remove additional aggregates, and safety tests were improved. The incident lowered trust in IPV, but it also led to increased federal regulation of vaccines [1,23].

By the 1960s, most countries in the world had stopped using IPV, except for Finland, the Netherlands, and Sweden. However, interest in IPV was boosted again in 1978, when researchers at the National Institute for Public Health in the Netherlands created enhanced potency IPV (eIPV). eIPV was made from a new culture technique in which purified virus was grown in large bioreactors, and the enhanced vaccine could also be combined with other vaccines, such as DTP. It also contained more D-antigen units [24]. The original IPV developed by Salk contained 20, 2, and 4 D-antigen units of PV1, PV2, and PV3, while the enhanced potency IPV contained 40, 8, and 32 D antigen units of PV1, PV2, and PV3. Trials show that due to its greater antigen content, after one dose, eIPV demonstrates over 90% seropositivity against all three poliovirus serotypes, and after two doses, it demonstrates 100% seropositivity. In 1987, eIPV was licensed in the United States [1].

## ORAL POLIO VACCINE (OPV)

In 1961, Albert Sabin developed the live attenuated polio vaccine, or the Oral Polio Vaccine (OPV) by growing attenuated (weakened) poliovirus in monkey kidney cells. To develop the vaccine, he experimented with over 9,000 monkeys and 100 chimpanzees to isolate a form of poliovirus that would reproduce in the intestinal tract but not the central nervous system, an experimental feat that would not be possible today. Sabin ended up creating a trivalent OPV (tOPV) vaccine containing the three Sabin poliovirus strains, which were obtained from the virulent wild poliovirus strains [12,21,25]. Sabin's tOPV had equal amounts of the three poliovirus serotypes, with a formula that contained $10^6$, $10^5$, and $10^{5.5}$ TCID50 (50% tissue culture infective dose) of Sabin types 1, 2, and 3. This induces protective antibodies

against all three strains in almost all people, but an improved formula recommended by the Expanded Program on Immunization Global Advisory Group, which had an increased amount of PV3 ($10^{5.8}$), was found to be 2.7 times more likely to cause seroconversion to type 3 [1,26]. OPV is stored at +2°C to +8°C, protected from light, and is administered orally as drops [3].

Polio enters the body through the gastrointestinal system, and because OPV is administered orally, it induces antibodies in the intestines, providing a first line of defense against polio. This gives it an advantage over IPV, which provides a second line of defense by inducing antibodies in the bloodstream, therefore preventing the virus from traveling in the bloodstream to the brain or spinal cord [21]. However, because of this, IPV offers low levels of immunity in the intestines, which allows the virus to still multiply within the intestines and be shed in the feces [17]. This means that with IPV, there is still a risk of the virus spreading to others and therefore does not offer herd protection the way OPV does. Additionally, OPV has lower costs is easier to administrate, since IPV requires trained health workers and sterile injection equipment. OPV can also be offered in different forms other than tOPV, such as monovalent OPV (mOPV), which induces immune responses against either PV1 or PV3 (mOPV1 or mOPV3), or bivalent OPV (bOPV), which targets both PV1 and PV3 and was developed for countries that no longer had cases of PV2. mOPV and bOPV both cause more robust immune responses than tOPV, with bOPV being the most effective of the OPV vaccines [12,27].

However, despite OPV's appeal, it came with more adverse side effects than IPV [3]. Genetic instability in the live attenuated Sabin strains allowed the virus to mutate in certain cases [24]. When administered, the weakened poliovirus usually replicates in the intestines and enters the bloodstream to induce an immune response, but in about 1% of those given OPV per year, the attenuated virus may genetically mutate during the replication process with point mutations at an average frequency of $10^{-4}$, either due to RNA polymerase or through natural recombination, and it can revert to being a neurovirulent virus. The neurovirulent virus is also called a vaccine-derived poliovirus (VDPV) and has a nucleotide divergence from the original Sabin strain of at least 1% in the VP1 sequence. There are three types of VDPV strains known: circulating VDPVs (cVDPs), immunodeficiency-associated VDPVs (iVDPVs), and ambiguous VDPVs (aVDPVs). cVDPV can spread in populations with low population immunity and cause paralysis, iVDPV is found in immunodeficient people exposed to OPV, and aVDPV is identified when the source is not from circulation or immunodeficiency. Additionally, in 1 of 2.4 million recipients, OPV can cause individual cases of paralysis, or Vaccine-Associated Paralytic Poliomyelitis (VAPP) [1,21,28,29]. Mutated neurovirulent VPDV strains in the intestines cause VAPP. There is little evidence to support that VAPP cases are infectious, but VDPVs such as cVDPV can lead to polio outbreaks [30]. As a result, many countries adopted a sequential vaccination schedule involving both IPV and OPV; however, this approach was not shown to eliminate the risk of VAPP [1].

## POLIO ERADICATION TODAY

Despite the risk of contracting VAPP, OPV continued to be used until wild type poliovirus was eradicated in most industrialized nations, making OPV the remaining source of paralytic polio due to VDPV outbreaks and VAPP cases [24]. In 2000, the United States stopped administering OPV due to the risk of VDPVs, and many industrialized nations have done the same, especially after the creation of eIPV [30]. In 2015, type 2 wild poliovirus was officially eradicated, and type 3 wild poliovirus was officially eradicated in 2019 [31]. Because of this, tOPV was withdrawn in April 2016 in favor of bOPV, which contains only PV types 1 and 3 due to the possibility of type 2 Circulating Vaccine-Derived Polioviruses (cVDPV2) strains being created. However, since bOPV does not cause immunity against type 2 poliovirus, there is low immunity to cVDPV2 in many communities [32]. To address this issue, a Novel Oral Polio Vaccine for type 2 poliovirus (nOPV2) is being considered to ensure immunity against cVDPV2. nOPV2 is an improved version of the type 2 monovalent OPV (mOPV2), and clinical trials have shown that it is both effective and less likely to cause VDPV2 [33].

The global effort to eradicate polio has been the largest public health initiative in history. The initiative was established in 1988 by the World Health Assembly, which set the goal of eradicating polio by the year 2000 while strengthening the capacity to control other major childhood diseases. The last

natural polio case in the United States was recorded in 1979, and in 1984, the United Kingdom officially eradicated polio [3,34]. The WHO Region of the Americas was certified polio-free in 1994, the WHO Western Pacific Region in 2000, the WHO European Region in 2002, the WHO Southeast Asia region in 2014, which officially made 80% of the global population live in polio-free regions [10]. In 2020, the WHO African Region was certified polio-free, making 5 of 6 WHO regions free of polio [35]. Today, there are only two polio-endemic countries with wild poliovirus in circulation: Afghanistan and Pakistan [36]. In January 1997, the WHO immunized 127 million Indian children in more than 650,000 villages in a single day [37]. Nonetheless, despite all the milestones achieved in polio eradication effort, there are many barriers to completely eliminating polio globally. Extraordinary progress has been made to achieve polio eradication by 2000, the goal set by the World Health Assembly, but the initiative was later extended to the year 2005. OPV must eventually stop being used due to the risk of VDPVs and VAPP; however, OPV remains the best vaccination option for many less industrialized nations because of its ease of access in mass immunization programs. As a result, VDPV outbreaks may break out in communities with low immunity, leading to more cases of polio. Between January 2018 and June 2019, cVDPV outbreaks of both types 1 and 2 were documented in 25 countries and 4 WHO regions, including in places where wild poliovirus had already been eradicated. Additionally, wild poliovirus may be carried over to polio-free countries and reinvigorate polio infection in those places. In 2011, Xinjiang, China, a province that had previously been polio-free for the past 10 years, suffered from a polio outbreak originating from a wild polio strain from Pakistan. It is also sometimes difficult to deliver vaccines across geographically difficult terrains, receive cooperation from local communities and administrations (a major problem is the politicization of the national polio program in Pakistan), and create a systematic vaccination program. Because of this, multiple programs have been launched, such as the Stop Transmission of Polio (STOP) program in 1988, which strengthens polio surveillance and promotes vaccination campaigns [3,38]. Major modern polio eradication efforts include the Global Polio Eradication Initiative (GPEI), the World Health Organization (WHO), Rotary International, the U.S. Centers for Disease Control and Prevention (CDC), and the United Nations Children's Fund (UNICEF), as well as additional organizations such as the Bill & Melinda Gates Foundation and Gavi, the Vaccine Alliance [10].

## DISCUSSION

Polio, an infectious disease caused by a virus called poliovirus, has been present in humankind for thousands of years, infecting many people, mainly children, over the course of human history. There are three antigenically distinct poliovirus serotypes (PV1, PV2, and PV3) that cause polio, and immunity to one serotype caused by a previous polio infection does not translate to immunity to another serotype. This means that a polio vaccine would have to offer immunity to all three poliovirus serotypes. Jonas Salk accomplished this with the formalin-Inactivated Polio Vaccine (IPV), which inactivated, or killed, the poliovirus and is administered as an injection; later, Albert Sabin would discover the live-attenuated Oral Polio Vaccine (OPV), created with attenuated, or weakened, poliovirus strains and administered orally. For decades, these two polio vaccines have dramatically decreased the number of polio cases around the world, successfully eradicating the disease in most countries. However, due to new poliovirus strains, there have been polio resurgences in multiple countries. These new poliovirus strains are Vaccine-Derived Polioviruses (VDPVs) and are created when weakened poliovirus strains in OPV mutate within the intestines. Polio resurgences caused by VDPVs can reinfect even countries that have stopped indigenous wild poliovirus, including Nigeria, Senegal, Ukraine, China, and various other countries found in the regions of Africa, the Eastern Mediterranean, Europe, and Western Pacific. In response to these resurgences of mutated poliovirus, the Global Polio Eradication Initiative (GPEI) is distributing type 2 monovalent OPV (mOPV2) containing only PV type 2, administering IPV shots for routine immunizations, and advancing a novel oral polio vaccine for type 2 poliovirus (nOPV2), which may be less likely to cause type 2 VDPVs. Currently, to use nOPV2, countries must meet strict WHO Emergency Use Listing Procedure (EUL) requirements, but as data is collected on the safety and efficacy of nOPV2, it will be more accessible [33]. To monitor the spread of poliovirus cases, there has also been an increase in polio surveillance consisting of virologic studies of stool or environment wastewater samples and acute flaccid

paralysis (AFP) surveillance, which detects where polio is circulating. When a case is discovered, such as when a VDPV case was found in Nigeria in 2015, stool samples of contacts and non-contacts were investigated, and a total of 5478 children were vaccinated during the mop-up response, door-to-door vaccinations in areas where the virus may be circulating [39]. Once wild type poliovirus is eradicated, the usage of OPV must cease to eliminate the possibility of VDPVs; however, OPV currently remains as the more accessible polio vaccine.

Additionally, even countries that have fully eradicated polio, such as the United States and Canada, are at risk of importation of polio since wild poliovirus still circulates in two countries today: Afghanistan and Pakistan. A number of difficulties are associated with the circulation of polio in these countries, including poor management and health communication strategies, financial deficits, ineffective immunization campaigns, and active conflict. Pakistan's Expanded Program on Immunizations (EPI) involves 10,000 vaccinators across 6000 fixed centers; however, it is difficult to carry out vaccination campaigns and Supplementary Immunization Activities (SIAs) due to the geography, which includes the complicated terrain of the Himalayan Mountains and Balochistan. There is also distrust in the vaccine in many areas, due to cultural issues and conflict. Negative propaganda against the polio vaccine has caused many areas to believe that polio vaccination programs are an effort to sterilize Muslim children [40]. The situation in Pakistan is similar to that of Afghanistan's, where in 2018, more than 840,000 children missed vaccination opportunities in inaccessible regions. The COVID-19 pandemic has also hindered vaccination programs in Afghanistan and Pakistan: travel bans disrupted supply chains, and nationwide programs were suspended [41].

The World Health Organization (WHO) estimates that if the continued transmission of wild polio in Afghanistan and Pakistan is not stopped, there could be as many as 200,000 new cases every year within 10 years [10]. Currently, strategies such as contact-tracing, intensive surveillance, mop-up campaigns, and SIAs are in place to control the spread of polio; although control of polio can be sustained, it is difficult to fully eradicate polio as the GPEI plans to. To eradicate polio, wild poliovirus must first be eradicated, OPV must be phased out of use to eliminate VDPVs, and safe containment measures must be implemented at facilities to minimize the risk of reintroducing the virus [42]. The Global Polio Eradication Initiative (GPEI) has also recently established a new eradication strategy, the 2022-2026 Strategy, which hopes to boost polio eradication efforts again after the various challenges caused by COVID-19 [43]. To overcome setbacks regarding vaccine access in areas in Pakistan and Afghanistan, the number of fixed vaccine centers must be increased, and existing health workers and even military personnel can be trained to administer vaccines [40]. With the increasing efforts of local health authorities in Afghanistan and Pakistan, financial support from organizations such as the GPEI and WHO, and cooperation from individual countries, it may be possible to globally eradicate polio soon.

## REFERENCES


1. Baicus A. (2012). History of polio vaccination. World J Virol. 1: 108 -114.
2. Troy SB, Maldonado YA. (2012). 235 - Polioviruses. In Long SS, (editors), Principles and Practice of Pediatric Infectious Diseases (4th edn ). 1168-1172.e1. Elsevier.
3. Mehndiratta MM, Mehndiratta P. Pande R. (2014). Poliomyelitis: historical facts. Epidemiology and current challenges in eradication. Neurohospitalist. 4: 223-229.
4. Centers for Disease Control and Prevention (2019). Polio: For Healthcare Providers. Centers for Disease Control and Prevention.
5. University of Rochester Medical Center, Polio (Poliomyelitis), L.R.W.M.R. Barry Zingman MD, Raymond Turley Jr PA-C, Editor., University of Rochester Medical Center.
6. Mayo Clinic Staff. (2020). Polio. Mayo Clinic.
7. Bruno RL. (2000). Paralytic vs "Nonparalytic" Polio: Distinction Without a Difference? American Journal of Physical Medicine & Rehabilitation. 79: 4-12.
8. Cleveland Clinic. Polio. Cleveland Clinic.
9. Disabled World. (2017). Famous People Who Had and Have Polio. Disabled World.
10. World Health Organization. (2019). Poliomyelitis. World Health Organization.
11. History of Vaccines. History of Polio (Poliomyelitis). History of Vaccines.
12. (2020). Britannica Polio in Britannica. Britannica The Editors of Encyclopaedia.
13. Toole L. (2013). The History of Polio. The Borgen Project.

14. Eggers HJ. (1999). Milestones in early poliomyelitis research (1840 to 1949). Journal of virology. 73: 4533-4535.
15. History of Vaccines. More Than One Type of Polio Proposed. History of Vaccines.
16. Chastel C. (2009). [Sixty years ago, cell cultures finally permitted the poliomyelitis virus to multiply easily] Hist Sci Med. 43: 345-354.
17. Global Polio Eradication Initiative. IPV. Global Polio Eradication Initiative.
18. Tan SY, Ponstein N. (2019). Jonas Salk (1914-1995): A vaccine against polio. Singapore medical journal. 60: 9-10.
19. Shampo MA, Kyle RA. (1998). Jonas E. Salk—Discoverer of a Vaccine Against Poliomyelitis. Mayo Clinic Proceedings, 73: 1176.
20. Juskewitch JE, CJ Tapia CJ, Windebank AJ. (2010). Lessons from the Salk Polio Vaccine: Methods for and Risks of Rapid Translation. Clinical and Translational Science. 3: 182-185.
21. Children's Hospital of Philadelphia. A Look at Each Vaccine: Polio Vaccine. Children's Hospital of Philadelphia.
22. Sutter RW. (2018). Unraveling the Mucosal Immunity of Inactivated Poliovirus Vaccine. The Journal of Infectious Diseases. 217: 344-346.
23. Fitzpatrick M. (2006). The Cutter Incident: How America's First Polio Vaccine Led to a Growing Vaccine Crisis. Journal of the Royal Society of Medicine. 99: 156.
24. Chumakov K, Ehrenfeld E. (2008). New generation of inactivated poliovirus vaccines for universal immunization after eradication of poliomyelitis. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 47: 1587-1592.
25. Polio vaccine developed.
26. Patriarca PA, Laender F, Palmeira G, Oliveira MJ, Lima Filho J. et al. (1988). Randomised trial of alternative formulations of oral poliovaccine in Brazil. Lancet. 1: 429-433.
27. Jehan F, Nisar MI, Lassi ZS, Omer SB, Zaidi A. (2013). Oral polio vaccine plus inactivated polio vaccine versus oral polio vaccine alone for reducing polio in children under two years of age. The Cochrane Database of Systematic Reviews. CD010857.
28. Global Polio Eradication Initiative. Vaccine-derived Polioviruses: Managing the risks. Global Polio Eradication Initiative.
29. Wringe A, Fine PEM, Sutter RW, Kew OM. (2008). Estimating the extent of vaccine-derived poliovirus infection. PloS one. 3: e3433.
30. Centers for Disease Control and Prevention. Vaccine-derived Poliovirus. Centers for Disease Control and Prevention.
31. Global Polio Eradication Initiative. History of Polio. Global Polio Eradication Initiative.
32. Global Polio Eradication Initiative. OPV. Global Polio Eradication Initiative.
33. Global Polio Eradication Initiative. nOPV. Global Polio Eradication Initiative.
34. Centers for Disease Control and Prevention. Polio Elimination in the United States. Centers for Disease Control and Prevention.
35. (2020). World Health Organization, Global polio eradication initiative applauds WHO African region for wild polio-free certification. 2020. World Health Organization.
36. Centers for Disease Control and Prevention. Our Progress Against Polio. Centers for Disease Control and Prevention.
37. History of Vaccines. Massive Vaccination Efforts in India. History of Vaccines.
38. Alonge O. (2020). What can over 30 years of efforts to eradicate polio teach us about global health? BMC Public Health. 20: 1177.
39. Fatiregun A, Famiyesin E, Bawa S, Ogunbodede N. (2020). Field investigation and response to a vaccine-derivedpoliovirus pre-tOPV switch in Southwest Nigeria, October 2015. The Pan African medical journal. 37: 6.
40. Hussain SF, Boyle P, Patel P, Sullivan R. (2016). Eradicating polio in Pakistan: an analysis of the challenges and solutions to this security and health issue. Globalization and Health. 12: 63.
41. Ahmadi A, Essar MY, Lin X, Adebisi YA, Lucero-Prisno DE. (2020). Polio in Afghanistan: The Current Situation amid COVID-19. Am J Trop Med Hyg. 103: 1367-1369.
42. Zambon M., Martin J. (2018). Polio eradication: next steps and future challenges. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin, 23: 1800625.
43. (2021). World Health Organization, Countries reaffirm commitment to ending polio at launch of new eradication strategy. World Health Organization.