

Introduction of inactivated poliovirus vaccine into oral poliovirus vaccine using countries, WER 11 July 2003: Selected references

Inactivated polio vaccines (IPV)

Plotkin SA, Vidor E. Poliovirus vaccine – inactivated. In: Plotkin SA, Orenstein WA (eds) Vaccines, 4th edition. Philadelphia, PA: Saunders, 2004: 24: 625-649.

Bottiger M. A study of the sero-immunity that has protected the Swedish population against poliomyelitis for 25 years. Scand J Infect Dis. 1987;19(6):595-601.

Although the population was highly susceptible to poliomyelitis on account of its low natural immunity, the general vaccination with inactivated polio vaccine eliminated poliomyelitis in Sweden within 6 years (1957-62). This status remains after 25 years, although challenges from the introduction of virus occur constantly. Over 99% of the population born in the forties and later is estimated to have been vaccinated, as well as at least 90% of those born earlier. The mean antibody levels of vaccinees against polio range from 100 (type 3) and 500 (type 1) up to 800 (type 2). Seronegative persons are seen only in a small percentage. Evaluation of the duration of immunity indicates that, after the post-vaccination fall in titre which occurs within 2-5 years after immunization, the immune levels remain fairly stable or decline very slowly. Sera from 12-year-old Swedish vaccinees neutralized the type 3 Saukett strain used for vaccine production 5 times better than a type 3 strain isolated during the Finnish outbreak 1984.

Robertson SE, Traverso HP, Drucker JA, Rovira EZ, Fabre-Teste B, Sow A, N'Diaye M, Sy MT, Diouf F. Clinical efficacy of a new, enhanced-potency, inactivated poliovirus vaccine. Lancet. 1988 Apr 23;1(8591):897-9.

The 1986-87 outbreak of paralytic poliomyelitis in Senegal, with 676 reported cases, provided an opportunity to evaluate the efficacy of an enhanced-potency inactivated poliovirus vaccine (N-IPV) in the Kolda region, where this vaccine has been used since 1980. 89 cases, confirmed to have poliomyelitis with residual paralysis, were enrolled in a case-control study, up to 5 matched controls being obtained for each case. The clinical efficacy for one dose of N-IPV was 36% (95% confidence interval 0%, 67%) and for two doses was 89% (95% CI 62%, 97%).

Oral poliovaccines (OPV)

Sabin AB. Oral poliovirus vaccine: history of its development and use and current challenge to eliminate poliomyelitis from the world. J Infect Dis. 1985 Mar;151(3):420-36.

Oral poliovirus vaccine (OPV) is like no other live virus vaccine used in humans: vaccine strains multiply extensively in the intestinal tract, are widely disseminated in the family and community, and immunize a large proportion of the unvaccinated population. During the search for optimal strains for vaccine use, motor neurons in the spinal cord of chimpanzees (and by extrapolation those of humans) were found to be much more resistant to polioviruses than those of monkeys; the reverse was true for the alimentary tract. Various biologic properties of polioviruses also varied quantitatively over a wide spectrum and were genetically distinct. The phenomenon of somewhat increased neurovirulence for monkeys, but not for chimpanzees, encountered in excreted virus was extensively studied in families, in children's homes, and finally among hundreds of thousands of susceptible children and adults in areas where only 50% of the susceptible population received OPV; these studies did not reveal evidence of danger. During the past 20 years approximately 5 million cases of paralytic poliomyelitis were probably prevented by OPV in predominantly temperate-climate countries inhabited by approximately 2 billion people. OPV has also been used less extensively and not optimally in many tropical and subtropical countries, where paralytic poliomyelitis is now known to be an important public health problem, with reduction in numbers of cases but not elimination of the disease except in some countries with better health services. Experience in Cuba during the past 21 years, in Brazil during the past 5 years, and in the Dominican Republic during the past 2 years has shown that the strategy of annual short-term vaccination of all children in the most susceptible age groups can rapidly eliminate the disease from tropical and subtropical countries.

Hull HF, Ward NA, Hull BP, Milstien JB, de Quadros C. Paralytic poliomyelitis: seasoned strategies, disappearing disease. Lancet. 1994 May 28;343(8909):1331-7.

With more than 2 years having elapsed since the last case of paralytic poliomyelitis occurred in the Western Hemisphere, significant progress has been made towards the global eradication of wild polioviruses. Poliomyelitis is disappearing from Europe, North Africa, Southern Africa, the Middle East, China, and the Pacific. Reported poliomyelitis cases declined to 15,587 cases in 1992. Current eradication strategies recommended by the World Health Organization include national mass campaigns administering oral poliovaccine to all children under 5 years of age, enhanced surveillance to detect cases of acute flaccid paralysis, creating a network of laboratories for viral diagnosis, and targeted immunisation to areas and populations where poliovirus transmission is likely to persist. The major obstacles to eradication include inadequate political support for eradication and insufficient funding, especially for the purchase of vaccine. With additional support for the international eradication effort, epidemics of poliomyelitis will cease in developing countries, and industrialised countries will be able to save the large sums spent each year on poliovaccine and rehabilitation.

John TJ. Experience with poliovaccines in the control of poliomyelitis in India. Public Health Rev. 1993-94;21(1-2):83-90.

OPV was introduced in the National Immunisation Programme (NIP) in 1979. The reported number of cases of poliomyelitis was about 20,000 in 1979, 38,000 in 1981; it gradually declined to the pre-immunisation level of 20,000 in 1986, but increased to 28,000 in 1987. In 1989, 10 years after NIP, the reported number of cases fell below the pre-immunisation level, and has further declined to 5669 in 1991. The 3-dose OPV coverage during infancy was estimated to be about 80% in 1991. If reporting efficiency is 10%, then about 60,000 cases would have occurred in 1991, for an incidence of disease of about 7/100,000 in the total population of 840 million. Three questions arise: (1) Why did it take over 10 years of NIP to reduce the disease burden? (2) Why is the disease occurring at a high incidence level in spite of 80% immunisation coverage? (3) Will we be able to eliminate poliomyelitis and eradicate polioviruses by the year 2000 by sustaining the high immunisation coverage using 3 doses of OPV? In most countries, the incidence of disease has declined immediately after instituting NIP including OPV. The vaccine efficacy (VE) of 3 doses of OPV in India is 70-93%. Hence the lack of decline of incidence during 10 years of NIP was most probably because sufficient proportions of infants were not being immunised. The incidence remains high because the VE and herd effect of 3 doses of OPV are insufficient. Vaccine failure cases will account for 2-9 cases per 100,000 per year since pre-immunisation incidence was 30 and VE is 70-93%. (ABSTRACT TRUNCATED AT 250 WORDS)

Oostvogel PM, van Wijngaarden JK, van der Avoort HG, Mulders MN, Conyn-van Spaendonck MA, Rumke HC, van Steenis G, van Loon AM. Poliomyelitis outbreak in an unvaccinated community in The Netherlands, 1992-93. Lancet. 1994 Sep 3;344(8923):665-70.

An outbreak of poliomyelitis occurred in the Netherlands between September, 1992, and February, 1993, after 14 years without endemic cases. The outbreak was due to poliovirus type 3 and involved 71 patients, of whom 2 died and 59 had paralysis. The patients were aged between 10 days and 61 years (median 18 years). None of the patients had been vaccinated, and all but 1 belonged to a socially and geographically clustered group of people who refuse vaccination for religious reasons. Control measures were taken within 5 days of notification of the first patient and included a wide offer of vaccination with the trivalent oral poliovirus vaccine to the population at risk. Sequence analysis of the viral genome showed closest similarity (96.7%) with a strain isolated in India in 1992, indicating that the virus probably originates from the Indian subcontinent. The difference, however, is still too large to assume direct import. Extensive outbreak investigation at schools, in the environment, at virus diagnostic laboratories, and in the general population showed no evidence of widespread circulation of the epidemic virus outside the groups at risk and area where these groups live. As in the previous outbreak in 1978, the general population, including the majority of unvaccinated people who live dispersed in the population, seemed to be well-protected against poliomyelitis.

OPV: transmissibility, persistence and neurovirulence

Fine PE, Carneiro IA. Transmissibility and persistence of oral polio vaccine viruses: implications for the global poliomyelitis eradication initiative. Am J Epidemiol. 1999 Nov 15;150(10):1001-21.

The global poliomyelitis eradication initiative has been a tremendous success, with current evidence suggesting that wild poliovirus will cease to circulate anywhere in the world soon after the year 2000. As the goal of wild poliovirus eradication is approached, concern has been raised about the potential for persistent transmission of oral polio vaccine (OPV) viruses, as these viruses are known to revert toward wild-type neurovirulence. This paper has been extracted from a document prepared for the World Health Organization on the implications of OPV transmissibility for the strategy of stopping OPV vaccination after global eradication of wild polioviruses. The authors review the empirical evidence on OPV transmissibility available from household and community transmission studies and from mass-vaccination experiences. They then consider theoretical measures of transmissibility and persistence for wild and OPV viruses (secondary attack rate, basic reproduction number, and critical populations' size), to assess whether transmissibility of OPV viruses is sufficient to allow persistence of these viruses after cessation of vaccination. The findings indicate that OPV viruses could persist under various plausible circumstances, and that this potential should be a major consideration when planning the cessation of OPV vaccination.

PIP: In view of the growing concern over the potential for persistent transmission of oral polio vaccine (OPV) viruses, this paper examines a document on the implications of OPV transmissibility for the strategy of stopping OPV vaccination after global eradication of wild polio viruses. It reviews the empirical evidence on OPV transmissibility gathered from household and community transmission studies and from mass-vaccination experiences. It assesses whether transmissibility of OPV viruses are sufficient to allow persistence of these viruses after cessation of vaccination by considering theoretical measures of transmissibility and persistence for wild and OPV viruses. This review concludes that there is a risk that OPV viruses will persist and that such persistence could occur in a variety of ways. Further research is needed to assess the implications for OPV virus persistence, especially on issues concerning the long-term excretion by immunodeficient individuals; the ability for OPV viruses to spread and persist in communities with low seroprevalence; the risk of reversion to wild-type transmissibility; environmental survival and potential reservoirs of OPV virus; duration of mucosal immunity; and the prevalence of viable poliovirus in stored samples.

Li J, Zhang LB, Yoneyama T, Yoshida H, Shimizu H, Yoshii K, Hara M, Nomura T, Yoshikura H, Miyamura T, Hagiwara A. Genetic basis of the neurovirulence of type 1 polioviruses isolated from vaccine-associated paralytic patients. Arch Virol. 1996;141(6):1047-54.

We examined four type 1 polioviruses isolated from the stools of patients with vaccine-associated paralytic poliomyelitis in China. All of these isolates were shown to be Sabin derived viruses by restriction fragment length polymorphism assay after polymerase chain reaction and by sequencing of the viral genome encoding the viral

coat protein, VP1. However, the same analysis of the 3D coding region suggested that two of the four isolates had the sequence of wild type poliovirus in the tested region. Furthermore there were also point mutations in the 5' non-coding region. One was a single base change from U to C at nucleotide position 525, and the other three were from G to A at position 480. All the four strains were more neurovirulent than Sabin type 1 virus in transgenic mice with human poliovirus receptor gene. The data showed that the nucleotide positions of type 1 poliovirus which were identified to be in favor of the high neurovirulence were indeed changed during natural transmission, and suggested that the point mutation alone or a recombination of the vaccine type with wild type genome results in an acquisition of neurovirulence.

Kew O, Morris-Glasgow V, Landaverde M, Burns C, Shaw J, Garib Z, Andre J, Blackman E, Freeman CJ, Jorba J, Sutter R, Tambini G, Venczel L, Pedreira C, Laender F, Shimizu H, Yoneyama T, Miyamura T, van Der Avoort H, Oberste MS, Kilpatrick D, Cochi S, Pallansch M, de Quadros C. Outbreak of poliomyelitis in Hispaniola associated with circulating type 1 vaccine-derived poliovirus. *Science*. 2002 Apr 12;296(5566):356-9. Epub 2002 Mar 14.

An outbreak of paralytic poliomyelitis occurred in the Dominican Republic (13 confirmed cases) and Haiti (8 confirmed cases, including 2 fatal cases) during 2000-2001. All but one of the patients were either unvaccinated or incompletely vaccinated children, and cases occurred in communities with very low (7 to 40%) rates of coverage with oral poliovirus vaccine (OPV). The outbreak was associated with the circulation of a derivative of the type 1 OPV strain, probably originating from a single OPV dose given in 1998-1999. The vaccine-derived poliovirus associated with the outbreak had biological properties indistinguishable from those of wild poliovirus.

Comparing OPV and IPV

Kok PW, Leeuwenburg J, Tukei P, van Wezel AL, Kapsenberg JG, van Steenis G, Galazka A, Robertson SE, Robinson D. Serological and virological assessment of oral and inactivated poliovirus vaccines in a rural population in Kenya. *Bull World Health Organ*. 1992;70(1):93-103.

A study was carried out in a rural community in Kenya to compare the humoral and intestinal immunity provided by three doses of oral poliovirus vaccine (OPV) and two or three doses of enhanced-potency inactivated poliovirus vaccine (IPV). The immunization series was started at 8-12 weeks of age and the interval between doses was 2 months. In children with low levels of maternal antibodies (i.e., those most at risk), the first dose of either vaccine stimulated antibody response. Children with high levels of maternal antibodies responded to the first dose of OPV, but not to that of IPV. Subsequent doses led to increases in the mean antibody titres with both vaccines. After three doses of OPV, the proportion of children with antibody titres of greater than or equal to 1:8 was 92% for type 1 virus, 98% for type 2, and 90% for type 3.

After two doses of IPV the proportion of children with antibody titres of greater than or equal to 1:8 was 94%, 88%, and 97% for type 1, type 2, and type 3, respectively; after three doses of IPV, 100% of children had antibodies greater than or equal to 1:8 for types 1 and 3, and 98% for type 2. Intestinal immunity was tested with a challenge dose of type 1 OPV, but the dose used was too small to detect a significant difference between the vaccines.

Faden H, Modlin JF, Thoms ML, McBean AM, Ferdon MB, Ogra PL. Comparative evaluation of immunization with live attenuated and enhanced-potency inactivated trivalent poliovirus vaccines in childhood: systemic and local immune responses. J Infect Dis. 1990 Dec;162(6):1291-7.

Serum neutralizing, nasopharyngeal neutralizing, and IgA antibodies were determined in 123 infants immunized with one of four schedules containing live oral vaccine (OPV), inactivated vaccine (IPV), or combinations of the two trivalent poliovirus vaccines: OPV-OPV-OPV, IPV-IPV-IPV, IPV-OPV-OPV, or IPV-IPV-OPV. Nearly 100% of individuals formed serum neutralizing antibodies. The highest geometric mean titer (GMT) of antibody to polioviruses 1, 2, and 3 occurred in groups IPV-IPV-OPV, IPV-OPV-OPV, and IPV-IPV-IPV, respectively. Local neutralizing and IgA antibody responses were detected in 41%-88% and 75%-100%, respectively. Peak GMT of nasopharyngeal antibodies differed minimally between immunization groups. The data suggest that incorporation of at least one dose of IPV at the start of the immunization schedule tends to increase systemic as well as local antibody production.

Faden H, Duffy L, Sun M, Shuff C. Long-term immunity to poliovirus in children immunized with live attenuated and enhanced-potency inactivated trivalent poliovirus vaccines. J Infect Dis. 1993 Aug;168(2):452-4.

Eighty-six children who completed immunization with the two trivalent poliovirus vaccines, live attenuated (OPV) and enhanced potency inactivated (EIPV), in one of four schedules (OPV-OPV-OPV, EIPV-EIPV-EIPV, EIPV-OPV-OPV, and EIPV-EIPV-OPV) at 1 year of age were monitored serologically over the subsequent 4 years and challenged with OPV at 5 years of age. Each of the immunization groups exhibited an initial 10- to 100-fold decline in neutralizing antibody to poliovirus types 1, 2, and 3 during the first 2 years of follow-up; thereafter antibody titers stabilized. The EIPV-EIPV-OPV group maintained the highest antibody levels throughout the observation period, including the response to OPV challenge at 5 years of age. These data suggest that immunization with OPV, EIPV, and combinations of the two vaccines confers long-term immunity. Optimal systemic immunity was associated with two or more doses of EIPV.

Combining OPV and IPV

Combined immunization of infants with oral and inactivated poliovirus vaccines: results of a randomized trial in The Gambia, Oman, and Thailand. WHO Collaborative Study Group on Oral and Inactivated Poliovirus Vaccines. Bull World Health Organ. 1996;74(3):253-68.

[No authors listed]

To assess an immunization schedule combining oral (OPV) and inactivated poliovirus vaccines (IPV), we conducted a clinical trial in the Gambia, Oman, and Thailand. Children were randomized to receive one of the following schedules: OPV at birth, 6, 10, and 14 weeks of age; OPV at birth followed by both OPV and IPV at 6, 10, and 14 weeks of age; or placebo at birth followed by IPV at 6, 10, and 14 weeks of age. A total of 1685 infants were enrolled; 24-week serum specimens were available for 1291 infants (77%). Across the study sites at 24 weeks of age, the proportion of seropositive children in the combined schedule group was 95-99% for type 1, 99-100% for type 2, and 97-100% for type 3. In the Gambia and Oman, the combined schedule performed significantly better than OPV for type 1 (95-97% versus 88-90%) and type 3 (97-99% versus 72-73%). In the Gambia and Oman, seroprevalences in the IPV group were lower for type 1 (significantly lower in the Gambia); significantly lower for type 2; and significantly higher for type 3, compared with the OPV group. In Thailand, the IPV group had significantly lower proportions of children who were seropositive for each of the three types, compared with the OPV group. The responses to OPV in the Gambia, Oman, and Thailand were consistent with previous studies from these countries. IPV given at 6, 10, and 14 weeks of age provided inadequate serological protection against poliovirus, especially type 1. The combined schedule provided the highest levels of serum antibody response, with mucosal immunity equivalent to that produced by OPV alone.

Sutter RW, Suleiman AJ, Malankar P, Al-Khusaiby S, Mehta F, Clements GB, Pallansch MA, Robertson SE. Trial of a supplemental dose of four poliovirus vaccines. N Engl J Med. 2000 Sep 14;343(11):767-73.

BACKGROUND: The immunogenicity of oral poliovirus vaccine (OPV), particularly the type 3 component, is lower in infants in most developing countries than in infants in industrialized countries. We conducted a multicenter trial in Oman to evaluate the response to a supplemental dose of four poliovirus vaccine formulations. **METHODS:** At nine months of age, infants were randomly assigned to receive inactivated-poliovirus vaccine (IPV), administered subcutaneously; trivalent OPV manufactured in the United States or in Europe; or monovalent type 3 OPV. Serum samples were collected at enrollment and 7 and 30 days later. All of the infants had previously received five doses of OPV. **RESULTS:** We enrolled 1025 infants; 785 (76.6 percent) met all the study requirements. At enrollment, 96.8 percent of the infants were seropositive for poliovirus type 1, 98.0 percent for type 2, and 88.0 percent for type 3. At 30 days there were no significant increases in type 3 seroprevalence or in the median antibody titer in the groups of infants who received OPV. Among the recipients of IPV, type 3 seroprevalence increased from 87.8 percent at enrollment to 97.1 percent at 30 days ($P<0.001$), and the median antibody titer increased from 1:228 to 1:1448 or higher ($P<0.001$). The rapid initial increase in the antibody titer suggests a secondary immune response. **CONCLUSIONS:** A supplemental dose of IPV has

excellent immunogenicity and leads to increases in the titer of antibodies against type 3 poliovirus, whereas supplemental doses of the oral vaccines do not have these effects.

Polio eradication policy

Ghendon Y, Robertson SE. Interrupting the transmission of wild polioviruses with vaccines: immunological considerations. Bull World Health Organ. 1994;72(6):973-83.

In 1988 the World Health Assembly set the goal of global poliomyelitis eradication by the year 2000. Substantial progress has been made, and 143 countries reported no poliomyelitis cases associated with the wild virus in 1993. This article reviews the immunological considerations relevant to interrupting the transmission of wild polioviruses with vaccines. Although serum immunity prevents poliomyelitis in the individual, it is local immunity that is important in preventing the transmission of polioviruses in the community. Natural infection and vaccination with oral polioviruses vaccine (OPV) produce local immunity in the intestine and the nasopharynx in about 70-80% of individuals. In contrast, inactivated poliovirus vaccine (IPV) produces local intestinal immunity in only 20-30% of the individuals. With either vaccine, however, a substantial proportion of the immunized population can transmit the wild virus. Moreover, although serum immunity is long-lasting, limited data suggest that local immunity may not be as persistent. To interrupt the transmission of wild polioviruses efforts should be made to achieve and sustain high levels of poliovirus vaccine coverage. Recent outbreaks show that wild poliovirus poses a risk for unimmunized individuals, even when overall coverage levels are high. Delivery of poliovirus vaccine to hard-to-reach populations will be of increasing importance as countries progress toward the final stages of poliomyelitis eradication. The immunization status of persons from poliomyelitis-free countries should be updated prior to travel to poliomyelitis-endemic areas.

Plotkin SA. Developed countries should use inactivated polio vaccine for the prevention of poliomyelitis. Rev Med Virol. 1997 Jul;7(2):75-81.

As the public health situation regarding polio changes, we should not be afraid to change our thinking about vaccination policy. OPV is still the vaccine of choice to eradicate wild poliomyelitis from the developing world. However, in developed countries free of poliomyelitis there is no longer a necessity to tolerate VAPP as the consequence of vaccination. IPV as part of combination vaccines or in mixed schedules with OPV is preferable and is in process of becoming the norm for those countries. Copyright 1997 John Wiley & Sons, Ltd.

Tangermann RH, Hull HF, Jafari H, Nkowane B, Everts H, Aylward RB. Eradication of poliomyelitis in countries affected by conflict. Bull World Health Organ. 2000;78(3):330-8.

The global initiative to eradicate poliomyelitis is focusing on a small number of countries in Africa (Angola, Democratic Republic of the Congo, Liberia, Sierra Leone, Somalia, Sudan) and Asia (Afghanistan, Tajikistan), where progress has been hindered by armed conflict. In these countries the disintegration of health systems and difficulties of access are major obstacles to the immunization and surveillance strategies necessary for polio eradication. In such circumstances, eradication requires special endeavours, such as the negotiation of ceasefires and truces and the winning of increased direct involvement by communities. Transmission of poliovirus was interrupted during conflicts in Cambodia, Colombia, El Salvador, Peru, the Philippines, and Sri Lanka. Efforts to achieve eradication in areas of conflict have led to extra health benefits: equity in access to immunization, brought about because every child has to be reached; the revitalization and strengthening of routine immunization services through additional externally provided resources; and the establishment of disease surveillance systems. The goal of polio eradication by the end of 2000 remains attainable if supplementary immunization and surveillance can be accelerated in countries affected by conflict.

Aylward RB, Hull HF, Cochi SL, Sutter RW, Olive JM, Melgaard B. Disease eradication as a public health strategy: a case study of poliomyelitis eradication. Bull World Health Organ. 2000;78(3):285-97.

Disease eradication as a public health strategy was discussed at international meetings in 1997 and 1998. In this article, the ongoing poliomyelitis eradication initiative is examined using the criteria for evaluating candidate diseases for eradication proposed at these meetings, which covered costs and benefits, biological determinants of eradicability (technical feasibility) and societal and political considerations (operational feasibility). The benefits of poliomyelitis eradication are shown to include a substantial investment in health services delivery, the elimination of a major cause of disability, and far-reaching intangible effects, such as establishment of a "culture of prevention". The costs are found to be financial and finite, despite some disturbances to the delivery of other health services. The "technical" feasibility of poliomyelitis eradication is seen in the absence of a non-human reservoir and the presence of both an effective intervention and delivery strategy (oral poliovirus vaccine and national immunization days) and a sensitive and specific diagnostic tool (viral culture of specimens from acute flaccid paralysis cases). The certification of poliomyelitis eradication in the Americas in 1994 and interruption of endemic transmission in the Western Pacific since March 1997 confirm the operational feasibility of this goal. When the humanitarian, economic and consequent benefits of this initiative are measured against the costs, a strong argument is made for eradication as a valuable disease control strategy.

Sutter RW, Tangermann RH, Aylward RB, Cochi SL. Poliomyelitis eradication: progress, challenges for the end game, and preparation for the post-eradication

era. Infect Dis Clin North Am. 2001 Mar;15(1):41-64.

In 1988, the World Health Assembly resolved to eradicate poliomyelitis globally by the year 2000. Dramatic progress toward this goal has occurred: three of the six WHO regions (Region of the Americas, European Region, and Western Pacific Region) are now polio free; and the number of polio-endemic countries decreased from over 125 in 1988 to 30 in 1999. Intensified efforts currently are underway to reach the target as soon as possible after 2000 in the three remaining polio-endemic WHO regions (African Region, Eastern Mediterranean Region, and South-East Asia Region). Even in polio-endemic regions, many countries are already polio free as the geographic extent of poliovirus shrinks while others, especially those experiencing conflict and war, pose substantial challenges to implementing the proven polio eradication strategies. Increasing attention and research now are devoted to the certification of polio eradication in the polio-free regions (that will include the first phase of implementing the Global Plan of Action for the laboratory containment of wild poliovirus) and formulating a policy for stopping all polio vaccination once eradication, containment, and global certification have been achieved. This report outlines the progress toward polio eradication and highlights some of the remaining issues and challenges that must be addressed before polio becomes a disease that future generations know only by history.

Cochi SL, Sutter RW, Aylward RB. Possible global strategies for stopping polio vaccination and how they could be harmonized. Dev Biol (Basel). 2001;105:153-8; discussion 159.

One of the challenges of the polio eradication initiative over the next few years will be the formulation of an optimal strategy for stopping poliovirus vaccination after global certification of polio eradication has been accomplished. This strategy must maximize the benefits and minimize the risks. A number of strategies are currently under consideration, including: (i) synchronized global discontinuation of use of oral poliovirus vaccine (OPV); (ii) regional or subregional coordinated OPV discontinuation; and (iii) moving from trivalent to bivalent or monovalent OPV. Other options include moving from OPV to global use of IPV for an interim period before cessation of IPV use (to eliminate circulation of vaccine-derived poliovirus, if necessary) or development of new OPV strains that are not transmissible. Each of these strategies is associated with specific advantages (financial benefits for OPV discontinuation) and disadvantages (cost of switch to IPV) and inherent uncertainties (risk of continued poliovirus circulation in certain populations or prolonged virus replication in immunodeficient persons). An ambitious research agenda addresses the remaining questions and issues. Nevertheless, several generalities are already clear. Unprecedented collaboration between countries, regions, and indeed the entire world will be required to implement a global OPV discontinuation strategy. Regulatory approval will be needed for an interim bivalent OPV or for monovalent OPV in many countries. Manufacturers will need sufficient lead time to produce sufficient quantities of IPV. Finally, the financial implications for any of these strategies need to be considered. Whatever strategy is followed it will be necessary to stockpile supplies of a poliovirus-containing vaccine (most probably all three types of monovalent OPV),

and to develop contingency plans to respond should an outbreak of polio occur after stopping vaccination.

Endgame" issues for the global polio eradication initiative. Technical Consultative Group to the World Health Organization on the Global Eradication of Poliomyelitis. Clin Infect Dis. 2002 Jan 1;34(1):72-7. Epub 2001 Nov 19.

The polio eradication initiative, created after the World Health Assembly resolved, in 1988, to eradicate poliomyelitis globally by 2000, has made remarkable progress. From 1988 through 2000, the number of countries where polio was endemic decreased from >125 to 20, and the estimated number of polio cases decreased from 350,000 to <3500, for a percentage decrease of >99%. Wild-type 2 poliovirus has not been detected worldwide since October 1999, despite improving surveillance. The major focus of the eradication effort is to complete the task of stopping wild-type poliovirus transmission. Given the rapid progress made toward this goal, planning for the posteradication era has begun in earnest (1) to minimize the risk of reintroduction of virus into the population from laboratory stocks or long-term carriers, and (2) to prevent vaccine-derived polioviruses from circulating and causing outbreaks. This report summarizes the current thinking about these "endgame" issues, as put forth by the World Health Organization's technical advisory body for the initiative, the Technical Consultative Group on the Global Eradication of Poliomyelitis.

Relevant WHO documents

Vaccines & Biologicals Department. Report of the interim meeting of the Technical Consultative Group (TCG) on the Global Eradication of Poliomyelitis, Geneva, 13-14 Nov 2002. Geneva, World health Organization, 2003 (WHO/V&B/03.04).

The immunological basis for immunization. Module 6: Poliomyelitis. Geneva 1993 (unpublished document WHO/EPI/GEN/93.16: available from Vaccines and Biologicals, World Health Organization, 1211 Geneva 27, Switzerland, and on the internet at www.who.int/vaccines-documents/DocsPDF-ibi-e/mod6_E.PDF).

Transmission of wild poliovirus type 2--apparent global interruption. Wkly Epidemiol Rec. 2001 Mar 30;76(13):95-7.
[No authors listed]

Global eradication of poliomyelitis. Report of the meeting on the scientific basis for stopping polio immunization, Geneva, 23-25 March 1998, WHO/EPI/GEN/98.12

New polio vaccines for the post-eradication era, Geneva, 19-20 January 2000, WHO/V&B/00.20

Polio vaccines for the post-eradication era: regulatory and biosafety issues, Geneva, 20-21 September 2000, WHO/V&B/in press. (NB check most recent version)

Field guide for supplementary immunization activities aimed at achieving polio eradication. 1996 revision. Geneva, 1997 (unpublished document WHO/EPI/GEN/95.1 Rev.1; available from Vaccines and Biologicals, World Health Organization, 1211 Geneva 27, Switzerland, and on the internet at www.who.int/vaccines-documents/DocsWord/word9669.zip).

Report of the first meeting of the Global Commission for the Certification of the Eradication of Poliomyelitis. Geneva: World Health Organization; 1995 (unpublished document WHO/EPI/GEN/95.06).

Disease eradication: friend or foe to the health system? Synthesis report from field studies on the Polio Eradication Initiative in Tanzania, Nepal and the Lao People's Democratic Republic. Sigrun Moegedal and Bo Stenson. WHO/V&B/00.28

World Health Organization. WHO global action plan for laboratory containment of wild poliovirus. Geneva Switzerland: World Health Organization. Available at http://www.who.int/vaccines-polio/all/newa/files/pdf/globalactionplan_2nd.pdf.
NB check most recent version