**Polio vaccines: WHO position paper, January 2014**

References with abstracts cited in the position paper

*Polio Eradication and Endgame Strategic Plan 2013–2018*


Since 1974, greater than 100 different surveys have been carried out throughout the developing world to estimate the prevalence of lameness due to poliomyelitis. Reported prevalence rates have ranged from less than 1 to a high of 25 per 1,000 children surveyed and have prompted many countries to undertake polio vaccination programs. A review of surveys conducted to date reveals considerable variation in both the choice and use of survey methods and in the assumptions made in the analysis and interpretation of findings. More precise and comparable data about the risk of poliomyelitis could be obtained in future surveys by incorporating a standard case definition, by using house-to-house case-finding methods in representative community-based samples, by analyzing and presenting rates in more clearly defined ways, and by selecting stable populations for study.

Inactivated and trivalent oral poliovirus vaccines contain either formalin-inactivated or live, attenuated poliovirus, respectively, of the three serotypes. Interference among the three attenuated poliovirus serotypes was minimized with a "balanced-formulation" vaccine, and serologic responses after IPV were optimized by adjusting the antigenic content of each inactivated poliovirus serotype. Seroconversion is dependent on both the relative content as well as the absolute quantity of virus in the vaccine. The "gold standard" method to assess humoral antibody responses following vaccination is the neutralization assay. Any detectable titer of neutralizing antibody against poliovirus is considered protective against clinical paralytic diseases. Recently, standard procedures were adopted for conducting neutralization assays. Efforts are being undertaken now to develop a combined diphtheria and tetanus toxoids and pertussis vaccine and IPV vaccine in the United States using a dual-chambered syringe that mixes the content of both vaccines at the time of injection; this approach is necessary to overcome the potential detrimental effect of thimerosal on IPV (the preservative in DTP). Other vaccines that combine DTP and/or Haemophilus influenzae type b and/or hepatitis B with IPV appear feasible but require further investigation. New combination vaccines should induce similar or superior levels of neutralizing antibody in serum for individual protection against paralytic disease and mucosal immunity that effectively decreases viral replication in the intestine and pharynx for population protection against transmission of poliovirus.

The full data concerning the history of attenuated poliovirus strains developed by one of us (Sabin, 1965) for vaccine production do not appear in a single journal. Over the past few years we have had frequent requests for the details such as isolation and attenuation and accordingly we felt that bringing the data together in the report below would be both helpful and informative to those involved in the production and control of poliovirus vaccine (oral) prepared from these strains.


An epidemiologic classification of paralytic poliomyelitis cases (ECPPC) has been in use in the United States since 1976. In 1985, this classification system was reviewed because of recent changes in the epidemiology of paralytic poliomyelitis and improved laboratory capability to definitively characterize poliovirus strains. An alternative classification system was devised, the epidemiologic and laboratory classification of paralytic polio cases (ELCPPC), that incorporated virus isolation and strain characterization with epidemiologic information. Reported paralytic poliomyelitis cases for 1980-86 were classified by both the ECPPC and the ELCPPC classification systems. The new ELCPPC system classified 91 per cent of the reported cases as vaccine-associated, while the ECPPC system classified only 71 per cent of the reported cases as vaccine-associated. The proposed classification system provides more specific and useful information particularly concerning vaccine-associated paralytic poliomyelitis.

Poliomyelitis caused by wild poliovirus has been virtually nonexistent in the United States since 1980, and vaccine-associated paralytic poliomyelitis (VAPP) has emerged as the predominant form of the disease. We reviewed national surveillance data on poliomyelitis for 1960-1989 to assess the changing risks of wild-virus, vaccine-associated, and imported paralytic disease; we also sought to characterize the epidemiology of poliomyelitis for the period 1980-1989. The risk of VAPP has remained exceedingly low but stable since the mid-1960s, with approximately 1 case occurring per 2.5 million doses of oral poliovirus vaccine (OPV) distributed during 1980-1989. Since 1980 no indigenous cases of wild-virus disease, 80 cases of VAPP, and five cases of imported disease have been reported in the United States. Three distinct groups are at risk of vaccine-associated disease: recipients of OPV (usually infants receiving their first dose), persons in contact with OPV recipients (mostly unvaccinated or inadequately vaccinated adults), and immunologically abnormal individuals. Overall, 93% of cases in OPV recipients and 76% of vaccine-associated cases have been related to administration of the first or second dose of OPV. Our findings suggest that adoption of a sequential vaccination schedule (inactivated poliovirus vaccine followed by OPV) would be effective in decreasing the risk of VAPP while retaining the proven public health benefits of OPV.

OBJECTIVE: Vaccine-associated paralytic poliomyelitis (VAPP) is a rare but serious consequence of the administration of oral polio vaccine (OPV). Intensified OPV administration has reduced wild poliovirus transmission in India but VAPP is becoming a matter of concern.

METHODS: We analysed acute flaccid paralysis (AFP) surveillance data in order to estimate the VAPP risk in this country. VAPP was defined as occurring in AFP cases with onset of paralysis in 1999, residual weakness 60 days after onset, and isolation of vaccine-related poliovirus. Recipient VAPP cases were a subset with onset of paralysis between 4 and 40 days after receipt of OPV.

FINDINGS: A total of 181 AFP cases met the case definition. The following estimates of VAPP risk were made: overall risk, 1 case per 4.1 to 4.6 million OPV doses administered; recipient risk, 1 case per 12.2 million; first-dose recipient risk, 1 case per 2.8 million; and subsequent-dose recipient risk, 1 case per 13.9 million.

CONCLUSION: On the basis of data from a highly sensitive surveillance system the estimated VAPP risk in India is evidently lower than that in other countries, notwithstanding the administration of multiple OPV doses to children in mass immunization campaigns.


Live Sabin poliomyelitis vaccine has been given in Hungary since December 1959. Generally, monovalent vaccines--administered in the sequence type 1, 3, and 2--have been used in annually repeated nationwide campaigns. Each type was administered within a week all over the country, with an interval of five to eight weeks between administrations. In the initial campaigns, children younger than 14 years of age were vaccinated. Since 1962, children between two and 38 months of age have been vaccinated annually. As a result of the vaccination program, the mean annual incidence of poliomyelitis declined to 0.03 per 100,000 population between 1961 and 1982 from a level of 12 per 100,000 observed over the previous five years. Epidemiologic and virologic evidence indicated that 47 (82%) of 57 cases registered since 1961 were vaccine-associated. Circumstances connected with the special vaccination practice in Hungary gave an opportunity to estimate the risk of vaccine-associated poliomyelitis. For recipients receiving the vaccine for the first time, the estimated risks for each type of vaccine were type 1, 0.99; type 2, 0.65; and type 3, 8.91 per million and for susceptible contacts, type 1, 0; type 2, 3.62; and type 3, 4.97 per million. The author's opinion is that these rates of risk are acceptable in view of the benefits provided by the live vaccine, especially under circumstances when importation of wild polioviruses that circulate widely in extended regions of the world may commonly occur.


Between June and October 2005, 45 laboratory-confirmed type 1 vaccine-derived poliovirus (VDPV) cases were identified on Madura Island in Indonesia. Genetic sequencing data on VDPV isolates were
consistent with replication and circulation for up to approximately 2 years. Concurrent circulation with type 1 wild poliovirus (WPV) enabled comparisons of VDPV and WPV cases and found that clinical and epidemiological features of both were similar. Attack rates for VDPV were as high as those for WPV. Of 41 VDPV case patients with known vaccination status, 25 (61%) had received zero oral polio vaccine (OPV) doses. Low population immunity due to low routine OPV coverage in rural areas and the absence of WPV circulation for more than a decade were major predisposing factors for the emergence of VDPV. Suboptimal surveillance and a limited initial immunization response may have contributed to widespread circulation. Sensitive surveillance and prompt high-quality immunization responses are recommended to prevent the spread of VDPVs.


BACKGROUND: The largest recorded outbreak of a circulating vaccine-derived poliovirus (cVDPV), detected in Nigeria, provides a unique opportunity to analyze the pathogenicity of the virus, the clinical severity of the disease, and the effectiveness of control measures for cVDPVs as compared with wild-type poliovirus (WPV).

METHODS: We identified cases of acute flaccid paralysis associated with fecal excretion of type 2 cVDPV, type 1 WPV, or type 3 WPV reported in Nigeria through routine surveillance from January 1, 2005, through June 30, 2009. The clinical characteristics of these cases, the clinical attack rates for each virus, and the effectiveness of oral polio vaccines in preventing paralysis from each virus were compared.

RESULTS: No significant differences were found in the clinical severity of paralysis among the 278 cases of type 2 cVDPV, the 2323 cases of type 1 WPV, and the 1059 cases of type 3 WPV. The estimated average annual clinical attack rates of type 1 WPV, type 2 cVDPV, and type 3 WPV per 100,000 susceptible children under 5 years of age were 6.8 (95% confidence interval [CI], 5.9 to 7.7), 2.7 (95% CI, 1.9 to 3.6), and 4.0 (95% CI, 3.4 to 4.7), respectively. The estimated effectiveness of trivalent oral polio vaccine against paralysis from type 2 cVDPV was 38% (95% CI, 15 to 54%) per dose, which was substantially higher than that against paralysis from type 1 WPV (13%; 95% CI, 8 to 18%), or type 3 WPV (20%; 95% CI, 12 to 26%). The more frequent use of serotype 1 and serotype 3 monovalent oral polio vaccines has resulted in improvements in vaccine-induced population immunity against these serotypes and in declines in immunity to type 2 cVDPV.

CONCLUSIONS: The attack rate and severity of disease associated with the recent cVDPV identified in Nigeria are similar to those associated with WPV. International planning for the management of the risk of WPV, both before and after eradication, must include scenarios in which equally virulent and pathogenic cVDPVs could emerge.

Centers for Disease Control and Prevention, Update on vaccine-derived polioviruses. MMWR. 2006;55:1093-1097. (no abstract available)


The live, attenuated oral poliovirus vaccine (OPV) provides a powerful tool for controlling and stopping the transmission of wild polioviruses (WPVs), although the risks of vaccine-associated paralytic polio (VAPP) and circulating vaccine-derived poliovirus (cVDPV) outbreaks exist as long as OPV remains in use. Understanding the dynamics of cVDPV emergence and outbreaks as a function of population immunity and other risk factors may help to improve risk management and the development of strategies to respond to possible outbreaks. We performed a comprehensive review of the literature related to the process of OPV evolution and information available from actual experiences with cVDPV outbreaks. Only a relatively small fraction of poliovirus infections cause symptoms, which makes direct observation of the trajectory of OPV evolution within a population
impractical and leads to significant uncertainty. Despite a large global surveillance system, the existing genetic sequence data largely provide information about transmitted virulent polioviruses that caused acute flaccid paralysis, and essentially no data track the changes that occur in OPV sequences as the viruses transmit largely asymptomatically through real populations with suboptimal immunity. We updated estimates of cVDPV risks based on actual experiences and identified the many limitations in the existing data on poliovirus transmission and immunity and OPV virus evolution that complicate modeling. Modelers should explore the space of potential model formulations and inputs consistent with the available evidence and future studies should seek to improve our understanding of the OPV virus evolution process to provide better information for policymakers working to manage cVDPV risks.

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.

From 1988 to 1993, 30 cases of poliomyelitis associated with poliovirus type 2 were found in seven governorates of Egypt. Because many of the cases were geographically and temporally clustered and because the case isolates differed antigenically from the vaccine strain, it was initially assumed that the cases signaled the continued circulation of wild type 2 poliovirus. However, comparison of sequences encoding the major capsid protein, VP1 (903 nucleotides), revealed that the isolates were related (93 to 97% nucleotide sequence identity) to the Sabin type 2 oral poliovirus vaccine (OPV) strain and unrelated (<82% nucleotide sequence identity) to the wild type 2 polioviruses previously indigenous to Egypt (last known isolate: 1979) or to any contemporary wild type 2 polioviruses found elsewhere. The rate and pattern of VP1 divergence among the circulating vaccine-derived poliovirus (cVDPV) isolates suggested that all lineages were derived from a single OPV infection that occurred around 1983 and that progeny from the initiating infection circulated for approximately a decade within Egypt along several independent chains of transmission. Complete genomic sequences of an early (1988) and a late (1993) cVDPV isolate revealed that their 5’ untranslated region (5’ UTR) and noncapsid- 3’ UTR sequences were derived from other species C enteroviruses. Circulation of type 2 cVDPVs occurred at a time of low OPV coverage in the affected communities and ceased when OPV coverage rates increased. The potential for cVDPVs to circulate in populations with low immunity to poliovirus has important implications for current and future strategies to eradicate polio worldwide.

BACKGROUND: Oral poliovirus vaccine (OPV) has not been used in the United States since 2000. Type 1 vaccine-derived poliovirus (VDPV) was identified in September 2005, from an unvaccinated Amish infant hospitalized in Minnesota with severe combined immunodeficiency. An investigation was conducted to determine the source of the virus and its means of transmission.
METHODS: The infant was tested serially for poliovirus excretion. Investigations were conducted to detect poliovirus infections or paralytic poliomyelitis in Amish communities in Minnesota,
neighboring states, and Ontario, Canada. Genomic sequences of poliovirus isolates were determined for phylogenetic analysis.

RESULTS: No source for the VDPV could be identified. In the index community, 8 (35%) of 23 children tested, including the infant, had evidence of type 1 poliovirus or VDPV infection. Phylogenetic analysis suggested that the VDPV circulated in the community for approximately 2 months before the infant’s infection was detected and that the initiating OPV dose had been given before her birth. No paralytic disease was found in the community, and no poliovirus infections were found in other Amish communities investigated.

CONCLUSIONS: This is the first demonstrated transmission of VDPV in an undervaccinated community in a developed country. Continued vigilance is needed in all countries to identify poliovirus infections in communities at high risk of poliovirus transmission.


Inactivated poliovirus vaccine (IPV) may be used in mass vaccination campaigns during the final stages of polio eradication. It is also likely to be adopted by many countries following the coordinated global cessation of vaccination with oral poliovirus vaccine (OPV) after eradication. The success of IPV in the control of poliomyelitis outbreaks will depend on the degree of nasopharyngeal and intestinal mucosal immunity induced against poliovirus infection. We performed a systematic review of studies published through May 2011 that recorded the prevalence of poliovirus shedding in stool samples or nasopharyngeal secretions collected 5-30 days after a "challenge" dose of OPV. Studies were combined in a meta-analysis of the odds of shedding among children vaccinated according to IPV, OPV, and combination schedules. We identified 31 studies of shedding in stool and four in nasopharyngeal samples that met the inclusion criteria. Individuals vaccinated with OPV were protected against infection and shedding of poliovirus in stool samples collected after challenge compared with unvaccinated individuals (summary odds ratio [OR] for shedding 0.13 [95% confidence interval [CI] 0.08-0.24]). In contrast, IPV provided no protection against shedding compared with unvaccinated individuals (summary OR 0.81 [95% CI 0.59-1.11]) or when given in addition to OPV, compared with individuals given OPV alone (summary OR 1.14 [95% CI 0.82-1.58]). There were insufficient studies of nasopharyngeal shedding to draw a conclusion. IPV does not induce sufficient intestinal mucosal immunity to reduce the prevalence of fecal poliovirus shedding after challenge, although there was some evidence that it can reduce the quantity of virus shed. The impact of IPV on poliovirus transmission in countries where fecal-oral spread is common is unknown but is likely to be limited compared with OPV.


BACKGROUND: Advantages to combining childhood vaccines include reducing the number of visits, injections and patient discomfort, increasing compliance and optimising prevention. The World Health Organization (WHO) recommends that routine infant immunisation programmes include a vaccination against Haemophilus influenzae (H. influenzae) type B (HIB) in the combined diphtheria-tetanus-pertussis (DTP)-hepatitis B virus (HBV) vaccination. The effectiveness and safety of the
combined vaccine should be carefully and systematically assessed to ensure its acceptability by the community.

OBJECTIVES: To compare the effectiveness of combined DTP-HBV-HIB vaccines versus combined DTP-HBV and separate HIB vaccinations.

SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2011, Issue 4), which contains the Cochrane Acute Respiratory Infections Group’s Specialised Register, MEDLINE (January 1966 to week 1, November 2011), EMBASE (January 1990 to November 2011) and www.clinicaltrials.gov (up to April 2011).

SELECTION CRITERIA: Randomised controlled trials (RCTs) or quasi-RCTs comparing vaccination with any combined DTP-HBV-HIB vaccine, with or without three types of inactivated poliovirus (IPV) or concomitant oral polio vaccine (OPV) in any dose, preparation or time schedule, compared with separate vaccines or placebo, administered to infants up to two years old.

DATA COLLECTION AND ANALYSIS: Two review authors independently inspected references identified by the searches and evaluated them against the inclusion criteria, extracted data and assessed the methodological quality of included trials.

MAIN RESULTS: Data for the primary outcome (prevention of disease) were lacking. We performed a meta-analysis to pool the results of 20 studies with 5874 participants in an immunogenicity analysis and 5232 participants in the reactogenicity analysis. There were no data on clinical outcomes for the primary outcome (prevention of disease) and all studies used immunogenicity and reactogenicity (adverse events). The number of vaccine doses differed significantly between the studies. Heterogeneous interventions, study location, healthcare environment and combining research across disparate geographical locations, may have lead to bias. The risk of bias was unclear across most of the included studies. Comparisons found little heterogeneity. In two immunological responses the combined vaccine achieved lower responses than the separate vaccines for HIB and tetanus. No significant differences in immunogenicity were found for pertussis, diphtheria, polio and hepatitis B. Serious adverse events were comparable with mainly hospitalisation and acute bronchiolitis cases. Minor adverse events such as pain and redness were more common in children given the combined vaccine. Overall, the direction shown by the results is in favour of the DTPw (diptheria-tetanus-whole cell pertussis)-HBV-HIB vaccine rather than the DTPa (diptheria-tetanus-acellular pertussis)-HBV-HIB vaccine when compared to the separate vaccines (size of effect: risk ratio (RR) 1.43; 95% confidence interval (CI) 0.98 to 2.10, for 5269 participants).

AUTHORS’ CONCLUSIONS: We could not conclude that the immune responses elicited by the combined vaccine were different from or equivalent to the separate vaccines. There was significantly less immunological response for HIB and tetanus and more local reactions in the combined injections. However, these differences rely mostly on one study each. Studies did not use an intention-to-treat (ITT) analysis and we were uncertain about the risk of bias in many of the studies. These results are therefore inconclusive. Studies addressing clinical end points whenever possible, using correct methodology and a large enough sample size should be conducted.


In a randomized, controlled trial carried out from November 1980 to July 1983 involving 1,114 infants in Baltimore City and in Baltimore and Prince George’s counties, Maryland, the serologic response to three doses of two enhanced-potency inactivated polio vaccines was compared with the response to three doses of oral polio vaccine. The mean ages at vaccination were 2.2, 4.7, and 19.9 months, respectively, for the three doses. Seroconversion after the first dose varied from 35% to 84%, and it was higher after oral polio vaccine than after either of the enhanced-potency inactivated polio vaccines for polioviruses types 2 and 3.

Approximately two and one-half and 16 months after the second dose, almost all inactivated polio vaccine recipients had antibodies against all three virus types (98-100%). Fewer oral
polio vaccine recipients had detectable antibodies to type 1 (89-92%) and to type 3 (96%). After three doses of vaccine, all children had antibodies against types 2 and 3. Approximately 1% of the inactivated polio vaccine recipients and 3% of the oral polio vaccine recipients lacked antibody to type 1. One or two doses of oral polio vaccine stimulated higher reciprocal geometric mean antibody titers against type 2 poliovirus than did the inactivated polio vaccine. For the other two types, the results were mixed. The third dose of inactivated polio vaccine produced significant increases in the reciprocal geometric mean titers against each of the three poliovirus types and resulted in significantly higher reciprocal geometric mean titers after three doses of vaccine for recipients of inactivated polio vaccine than for recipients of oral polio vaccine.

Kim–Farley RJ et al Outbreak of paralytic poliomyelitis, Taiwan. Lancet. 1984;2:1322–1324. Taiwan had been free of major poliomyelitis outbreaks since 1975, but from May 29 to Oct 26, 1982, 1031 cases of type 1 paralytic poliomyelitis were reported to the Taiwan health authorities. Before the outbreak approximately 80% of infants had received at least 2 doses of trivalent oral poliovaccine (OPV) by their first birthday. Of the 86% of poliomyelitis patients whose vaccination status was known 65% had not had poliovaccine, 19% had received one dose, 8% had received two doses, and 8% had received three or more doses. Vaccine efficacy was calculated to be 82% after one dose, 96% after two doses, and 98% after three or more doses. Failure to vaccinate rather than vaccine failure was the most important risk factor in this outbreak. A child who had not had any vaccine was 80 times more likely to become a case than one who had received three or more doses of poliovaccine, independent of sanitation facilities at home. A child was 5 times more likely to become a case if he received water from non-municipal rather than municipal sources. Furthermore, for children who received municipal water, the risk was doubled if the family shared a toilet with at least one other family. This outbreak shows that major epidemics can occur in areas that have high overall community vaccination levels. Identification and vaccination of subpopulations with low coverage is essential for the control of poliomyelitis.

Sutter RW et al. Outbreak of paralytic poliomyelitis in Oman: evidence for widespread transmission among fully vaccinated children. Lancet. 1991;338:715–720. From January, 1988, to March, 1989, a widespread outbreak (118 cases) of poliomyelitis type 1 occurred in Oman. Incidence of paralytic disease was highest in children younger than 2 years (87/100,000) despite an immunisation programme that recently had raised coverage with 3 doses of oral poliovirus vaccine (OPV) among 12-month-old children from 67% to 87%. We did a case-control study (70 case-patients, 692 age-matched controls) to estimate the clinical efficacy of OPV, assessed the immunogenicity of OPV and extent of poliovirus spread by serology, retrospectively evaluated the cold chain and vaccine potency, and sought the origin of the outbreak strain by genomic sequencing. 3 doses of OPV reduced the risk of paralysis by 91%; vaccine failures could not be explained by failures in the cold chain nor on suboptimum vaccine potency. Cases and controls had virtually identical type 1 neutralising antibody profiles, suggesting that poliovirus type 1 circulation was widespread. Genomic sequencing indicated that the outbreak strain had been recently imported from South Asia and was distinguishable from isolates indigenous to the Middle East. Accumulation of enough children to sustain the outbreak seems to have been due to previous success of the
immunisation programme in reducing spread of endemic strains, suboptimum efficacy of OPV, and delay in completing the primary immunisation series until 7 months of age. Additionally, the estimated attack rate of infection among children aged 9-23 months exceeded 25% in some regions, suggesting that a substantial proportion of fully vaccinated children had been involved in the chain of transmission.


Although rates of seroconversion following administration of trivalent oral poliovirus vaccine (TOPV) approach 100% in industrialized countries, only 73% (range, 36%-99%) and 70% (range, 40%-99%) of children in developing countries have detectable antibody to poliovirus types 1 and 3, respectively, after three doses. While factors accounting for these differences have not been fully elucidated, available data suggest that type 2 vaccine virus and enteric pathogens often interfere with responses to types 1 and 3 vaccine viruses but that this interference may be overcome by modifying the absolute and relative dosage of the three Sabin types. Increasing the interval between doses beyond 30 days may also be important, in view of the prolonged excretion of vaccine virus and the potential for interference with responses to subsequent doses. Although advances in molecular biology may ultimately lead to the development of more-immunogenic vaccine candidates, approaches such as increasing the number of doses of TOPV, mass vaccination campaigns, and combined use of oral and inactivated vaccines should also be considered.


BACKGROUND: The continued presence of polio in northern India poses challenges to the interruption of wild poliovirus transmission and the management of poliovirus risks in the post-eradication era. We aimed to assess the current immunity profile after routine doses of trivalent oral poliovirus vaccine (OPV) and numerous supplemental doses of type-1 monovalent OPV (mOPV1), and compared the effect of five vaccine formulations and dosages on residual immunity gaps.

METHODS: We did a community-based, randomised controlled trial of healthy infants aged 6-9 months at ten sites in Moradabad, India. Serum neutralising antibody was measured before infants were randomly assigned to a study group and given standard-potency or higher-potency mOPV1, intradermal fractional-dose inactivated poliovirus vaccine (IPV, GlaxoSmithKline), or intramuscular full-dose IPV from two different manufacturers (GlaxoSmithKline or Panacea). Follow-up sera were taken at days 7 and 28. Our primary endpoint was an increase of more than four times in antibody titres. We did analyses by per-protocol in children with a blood sample available before, and 28 days after, receiving study vaccine (or who completed study procedures). This trial is registered with Current Controlled Trials, number ISRCTN90744784.

FINDINGS: Of 1002 children enrolled, 869 (87%) completed study procedures (ie, blood sample available at day 0 and day 28). At baseline, 862 (99%), 625 (72%), and 418 (48%) had detectable antibodies to poliovirus types 1, 2, and 3, respectively. In children who were type-1 seronegative, an increase of more than four times in antibody titre was detected 28 days after they were given standard-potency mOPV1 (5/13 [38%]), higher-potency mOPV1 (6/21 [29%]), intradermal IPV (9/16 [56%]), GlaxoSmithKline intramuscular IPV (19/22 [86%]), and Panacea intramuscular IPV (11/13 [85%]). In those who were type-2 seronegative, 42 (100%) of 42 seroconverted after
GlaxoSmithKline intramuscular IPV, and 24 (59%) of 41 after intradermal IPV (p<0.0001). 87 (90%) of 97 infants who were type-3 seronegative seroconverted after intramuscular IPV, and 21 (36%) of 49 after intradermal IPV (p<0.0001).

INTERPRETATION: Supplemental mOPV1 resulted in almost total seroprevalence against poliovirus type 1, which is consistent with recent absence of poliomyelitis cases; whereas seroprevalence against types 2 and 3 was expected for routine vaccination histories. The immunogenicity of IPV produced in India (Panacea) was similar to that of an internationally manufactured IPV (GSK). Intradermal IPV was less immunogenic.


BACKGROUND: A high-potency monovalent oral type 1 poliovirus vaccine (mOPV1) was developed in 2005 to tackle persistent poliovirus transmission in the last remaining infected countries. Our aim was to assess the efficacy of this vaccine in India.

METHODS: We estimated the efficacy of mOPV1 used in supplementary immunisation activities from 2076 matched case-control pairs of confirmed cases of poliomyelitis caused by type 1 wild poliovirus and cases of non-polio acute flaccid paralysis in India. The effect of the introduction of mOPV1 on population immunity was calculated on the basis of estimates of vaccination coverage from data for non-polio acute flaccid paralysis.

FINDINGS: In areas of persistent poliovirus transmission in Uttar Pradesh, the protective efficacy of mOPV1 was estimated to be 30% (95% CI 19-41) per dose against type 1 paralytic disease, compared with 11% (7-14) for the trivalent oral vaccine. 76-82% of children aged 0-23 months were estimated to be protected by vaccination against type 1 poliovirus at the end of 2006, compared with 59% at the end of 2004, before the introduction of mOPV1.

INTERPRETATION: Under conditions where the efficacy of live-attenuated oral poliovirus vaccines is compromised by a high prevalence of diarrhoea and other infections, a dose of high-potency mOPV1 is almost three times more effective against type 1 poliomyelitis disease than is trivalent vaccine. Achieving high coverage with this new vaccine in areas of persistent poliovirus transmission should substantially improve the probability of rapidly eliminating transmission of the disease.


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 adequate 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.


BACKGROUND: Poliovirus types 1 and 3 co-circulate in poliomyelitis-endemic countries. We aimed to assess the immunogenicity of a novel bivalent types 1 and 3 oral poliovirus vaccine (bOPV).

METHODS: We did a randomised, double-blind, controlled trial to assess the superiority of monovalent type 2 OPV (mOPV2), mOPV3, or bOPV over trivalent OPV (tOPV), and the non-inferiority of bivalent vaccine compared with mOPV1 and mOPV3. The study was done at three centres in India between Aug 6, 2008, and Dec 26, 2008. Random allocation was done by permuted blocks of ten. The primary outcome was seroconversion after one monovalent or bivalent vaccine dose compared with a dose of trivalent vaccine at birth. The secondary endpoints were seroconversion after two vaccine doses compared with after two trivalent vaccine doses and cumulative two-dose seroconversion. Parents or guardians and study investigators were masked to treatment allocation. Because of multiple comparisons, we defined p≤0.01 as statistically significant. This trial is registered with Current Controlled Trials, ISRCTN 64725429.

RESULTS: 900 newborn babies were randomly assigned to one of five vaccine groups (about 180 patients per group); of these 70 (8%) discontinued, leaving 830 (92%) for analysis. After the first dose, seroconversion to poliovirus type 1 was 20% for both mOPV1 (33 of 168) and bOPV (32 of 159) compared with 15% for tOPV (25 of 168; p>0.01), to poliovirus type 2 was 21% (35 of 170) for mOPV2 compared with 25% (42 of 168) for tOPV (p=0.01), and to poliovirus type 3 was 12% (20 of 165) for mOPV3 and 7% (11 of 159) for bOPV compared with 4% (7 of 168) for tOPV (mOPV3 vs tOPV p=0.01; bOPV vs tOPV; p>0.01). Cumulative two-dose seroconversion to poliovirus type 1 was 90% (151 of 168) for mOPV1 and 86% (136 of 159) for bOPV compared with 63% (106 of 168) for tOPV (p<0.0001), to poliovirus type 2 was 90% (153 of 170) for mOPV2 compared with 91% (153 of 168) for tOPV (p>0.01), and to poliovirus type 3 was 84% (138 of 165) for mOPV3 and 74% (117 of 159) for bOPV compared with 52% (87 of 168) for tOPV (p<0.0001). The vaccines were well tolerated. 19 serious adverse events occurred, including one death; however, these events were not attributed to the trial interventions.

INTERPRETATION: The findings show the superiority of bOPV compared with tOPV, and the non-inferiority of bOPV compared with mOPV1 and mOPV3.


Interrupting the transmission of wild polioviruses in developing countries remains the most difficult step towards global eradication of poliomyelitis. The global strategy ought to be to achieve this using either or both vaccines, without waiting for socio-economic development to result in a reduced power of wild virus transmission. In developed countries with low transmission potential, the protective efficacy and the herd effect of either OPV or IPVAPV-E
are sufficient to eradicate wild viruses. Developing countries are not uniform in their poliovirus epidemiology: broadly they can be divided into those in which protective efficacy of OPV is high but herd effect is poor and others in which both are poor. Large countries such as India may have regions representing both epidemiological patterns. The same strategy applies everywhere, but the tactical use of the vaccines should be intelligently designed in order to achieve eradication in all areas with differing epidemiological patterns in the shortest possible time. Where the epidemiology is varied, the tactic of immunisation should also be modified to meet this challenge. Exaggerated claims of the properties of either vaccine have not only led to controversies but also to inadequate immunisation schedules and have resulted in delays in the design and application of appropriate immunisation tactics in many developing countries. Consequently hundreds of thousands of children in developing countries have suffered from paralytic poliomyelitis which could have been prevented if scientists and policymakers had been more objective and dispassionate.


Administration of supplementary dose of oral polio vaccine (OPV) during neonatal period is recommended by WHO in countries like India, where host response to the regular to the regular three-dose schedule is not satisfactory and poliomyelitis continues to be a problem. The efficacy of this dose +3, and +5 doses of OPV in terms of seropositivity, seroconversion, systemic, and mucosal antibody responses were measured in 51 infants in a follow-up study from birth to 30 weeks. Administration of the additional dose in the newborn period significantly improved seropositivity and seroconversion rates compared to the conventional 3 or 5 dose schedules. Systemic antibody titres improved with each dose of the vaccine and 40-60 per cent of infants had > 1:128 titres to the three types of polioviruses that could prevent re-infection of the gut and 50 per cent of them had mucosal antibodies as evidenced by specific IgA in nasopharyngeal secretions. Therefore, administration of OPV in the neonatal period should be made compulsory in countries where poliomyelitis still continues to be a problem.


BACKGROUND: Oral poliovirus vaccine (OPV) remains the vaccine-of-choice for routine immunization and supplemental immunization activities (SIAs) to eradicate poliomyelitis globally. Recent data from India suggested lower than expected immunogenicity of an OPV birth dose, prompting a review of the immunogenicity of OPV or inactivated poliovirus vaccine (IPV) when administered at birth.

METHODS: We evaluated the seroconversion and reported adverse events among infants given a single birth dose (given ≤7 days of life) of OPV or IPV through a systematic review of published articles and conference abstracts from 1959 to 2011 in any language found on PubMed, Google Scholar, or reference lists of selected articles.

RESULTS: 25 articles from 13 countries published between 1959 and 2011 documented seroconversion rates in newborns following an OPV dose given within the first seven days of life. There were 10 studies that measured seroconversion rates between 4 and 8 weeks of a single birth dose of TOPV, using an umbilical cord blood draw at the time of birth to establish baseline antibody levels. The percentage of newborns who seroconverted at 8 weeks range from 6-42% for poliovirus
type 1, 2-63% for type 2, and 1-35% for type 3. For mOPV type 1, seroconversion ranged from 10 to 76%; mOPV type 3, the range was 12-58%; and for the one study reporting bOPV, it was 20% for type 1 and 7% for type 3. There were four studies of IPV in newborns with a seroconversion rate of 8-100% for serotype 1, 15-100% for serotype 2, and 15-94% for serotype 3, measured at 4-6 weeks of life. No serious adverse events related to newborn OPV or IPV dosing were reported, including no cases of acute flaccid paralysis.

CONCLUSIONS: There is great variability of the immunogenicity of a birth dose of OPV for reasons largely unknown. Our review confirms the utility of a birth dose of OPV, particularly in countries where early induction of polio immunity is imperative. IPV has higher seroconversion rates in newborns and may be a superior choice in countries which can afford IPV, but there have been few studies of an IPV dose for newborns.


OBJECTIVE--Due to recent resurgences of measles, mumps, and rubella among young US adults, we sought to generate antibody prevalence data for national and military immunization policy evaluations. DESIGN--We used a questionnaire and serological survey of Army recruits to assess antibody status to measles, mumps, rubella, and varicella by enzyme-linked immunosorbent assay and to poliovirus types 1, 2, and 3 by microneutralization assay. SETTING--Basic training reception centers at Fort Benning, Ga., and Fort Jackson, SC. PATIENTS--The study included 1547 US Army recruits who were inducted during September and October 1989. OUTCOME MEASURES--Seronegativity by various demographic factors. RESULTS--Seronegativity rates, directly adjusted to the 15- to 24-yearold US population in 1980, were 20.7% for measles, 15.6% for mumps, 17.5% for rubella, and 6.9% for varicella. For measles, mumps, and rubella, susceptibility was less in females, blacks, and college-educated recruits, and varicella susceptibility was greater in females and blacks. Recruitment who were born after 1969 lacked measles, mumps, and rubella antibodies more often than older recruits. The adjusted seronegativity rates for poliovirus types 1, 2, and 3 were 2.3%, 0.6%, and 14.6%, respectively; trends by age, sex, and race-ethnicity were generally unremarkable. CONCLUSIONS--Among young adult Americans, susceptibility to measles, mumps, and rubella is unevenly distributed and may be substantial. Our findings support national objectives to further improve immunization coverage in school-age and adult populations and provide further impetus for legislation requiring college entrannts to present evidence of having received at least two doses of measles vaccine, with one on or after entry into elementary school.


The persistence of neutralizing antibody (NA) against three types of poliovirus acquired after two doses of trivalent live attenuated poliovirus vaccine (LPV) has been followed up for ten years in individual vaccinees. Sixty-seven children were bled once a year over a five year period following the primary vaccination. More than 80% of them retained NA against all three types of poliovirus. Thirty-two individuals whose NA titres were 1:16 or over for types 1 and 2 and 1:4 or over for type 3 at the fifth year were further followed up for a further five years and it was shown that during this period some of them had a naturally-acquired antibody
rise, mostly against type 3 virus. At the sixth to eighth year after the primary vaccination, one further dose of the trivalent vaccine was administered to the children whose NA titres were down to 1:8 or less and the effect of booster vaccination on NA was followed. Other subjects were revaccinated with LPV and their fecal excretion of the vaccine virus was investigated. The results showed that a decrease in serum antibody level could be a good indicator of the local resistance of the alimentary tract and that reinfection could occur if serum NA had decreased to 1:8 or less, which allowed a virus excretion in the stools.


In recent years, two live oral rotavirus vaccines have been successfully tested in developing and industrialized countries, and both vaccines are now recommended by the World Health Organization for all children worldwide. Both immunogenicity and efficacy of these rotavirus vaccines has been lower in developing compared to industrialized settings. We reviewed the data on the effect of trivalent OPV on the immunogenicity and efficacy of two rotavirus vaccines currently recommended by the WHO. While rotavirus vaccines have not affected immune responses to OPV, in general, the immune responses (i.e., antibody levels) to rotavirus vaccination were lower when rotavirus vaccines were co-administered with OPV. Limited data suggests that the interference is greater after the first dose of OPV, presumably because the first dose is associated with greatest intestinal replication of vaccine polio virus strains, and this interference is largely overcome with subsequent rotavirus vaccine doses. Despite the lower immunogenicity, one large efficacy study in middle income Latin American countries showed no decrease in protective efficacy of rotavirus vaccine in infants receiving concurrent OPV. While these data are encouraging and support simultaneous administration of rotavirus vaccines and OPV, additional evidence should be gathered as rotavirus vaccines are used more widely in developing country settings, where OPV is routinely used, rather than inactivated polio vaccine.

We determined the complete genomic sequences of nine type 1 immunodeficient vaccine-derived poliovirus (iVDPV) isolates obtained over a 337-day period from a poliomyelitis patient from Taiwan with common variable immunodeficiency. The iVDPV isolates differed from the Sabin type 1 oral poliovirus vaccine (OPV) strain at 1.84% to 3.15% of total open reading frame positions and had diverged into at least five distinct lineages. Phylogenetic analysis suggested that the chronic infection was initiated by the fifth and last OPV dose, given 567 days before onset of paralysis, and that divergence of major lineages began very early in the chronic infection. Key determinants of attenuation in Sabin 1 had reverted in the iVDPV isolates, and representative isolates of each lineage showed increased neurovirulence for PVR-Tg21 transgenic mice. None of the isolates had retained the temperature-sensitive phenotype of Sabin 1. All isolates were antigenic variants of Sabin 1, having multiple amino acid substitutions within or near neutralizing antigenic sites 1, 2, and 3a.
Antigenic divergence of the iVDPV variants from Sabin 1 followed two major independent evolutionary pathways. The emergence of distinct coreplicating lineages suggests that iVDPVs can replicate for many months at separate sites in the gastrointestinal tract. Some isolates had mosaic genome structures indicative of recombination across and within lineages. iVDPV excretion apparently ceased after 30 to 35 months of chronic infection. The appearance of a chronic VDPV excretor in a tropical, developing country has important implications for the strategy to stop OPV immunization after eradication of wild polioviruses.

CDC. Update on Vaccine-Derived Polioviruses — Worldwide, April 2011–June 2012. MMWR. 2012; 61(37);741-746. (no abstract available)


After the global eradication of wild polioviruses, the risk of paralytic poliomyelitis from polioviruses will still exist and require active management. Possible reintroductions of poliovirus that can spread rapidly in unprotected populations present challenges to policymakers. For example, at least one outbreak will likely occur due to circulation of a neurovirlent vaccine-derived poliovirus after discontinuation of oral poliovirus vaccine and also could possibly result from the escape of poliovirus from a laboratory or vaccine production facility or from an intentional act. In addition, continued vaccination with oral poliovirus vaccines would result in the continued occurrence of vaccine-associated paralytic poliomyelitis. The likelihood and impacts of reintroductions in the form of poliomyelitis outbreaks depend on the policy decisions and on the size and characteristics of the vulnerable population, which change over time. A plan for managing these risks must begin with an attempt to characterize and quantify them as a function of time. This article attempts to comprehensively characterize the risks, synthesize the existing data available for modeling them, and present quantitative risk estimates that can provide a starting point for informing policy decisions.


BACKGROUND: As polio eradication nears, the development of immunization policies for an era without the disease has become increasingly important. Outbreaks due to circulating vaccine-derived poliovirus (VDPV) and rare cases of immunodeficient persons with prolonged VDPV shedding lend to the growing consensus that oral poliovirus vaccine (OPV) use should be discontinued as soon after polio eradication as possible. The present study was conducted to assess whether persons infected with human immunodeficiency virus (HIV) experience prolonged VDPV shedding and serve as a source of reintroduction of virus into the population.

METHODS: Adults infected with HIV had specimens tested (1) 8 months after a mass OPV campaign, to determine whether poliovirus related to OPV administered during the campaign was present (i.e., prolonged excretion), and (2) starting 7 weeks after a subsequent campaign, to determine whether poliovirus could be detected after the height of OPV exposure.

RESULTS: A total of 419 participants were enrolled—315 during the 8-12 months after an OPV campaign held in 2001 and 104 during the 7-13 weeks after a 2002 campaign. No poliovirus was isolated from any participants.
CONCLUSIONS: It appears unlikely that adults infected with HIV experience prolonged vaccine virus shedding, and, therefore, they probably represent a minimal risk of reintroducing vaccine virus into the population after poliovirus has been eradicated.


OBJECTIVE: To determine whether the presence of HIV infection and the associated immuno-depression increases the risk of paralytic poliomyelitis in children under the age of 15 years in Kinshasa, Zaire, an area endemic for both infections. METHODS: To ascertain cases of paralytic poliomyelitis, biweekly visits were made from October 1988 thru September 1989 to a network of 27 clinical sites, including the principal pediatric and rehabilitation services in Kinshasa. To identify risk factors associated with possible concurrent HIV and paralytic polio infection, a case-control study was performed. Cases of paralytic polio were children under the age of 15 years with acute onset of asymmetric flaccid paralysis, without sensory changes, and which persisted for at least 60 days if the child survived, and with no other apparent cause. Controls were age (+/- 4 months) and neighborhood-matched children. HIV infection was determined by ELISA and immunoblot. For logistic reasons, the case-control study was limited to a systematic one-third sample of cases.

RESULTS: A total of 131 cases of paralytic poliomyelitis were identified. Two 2(4.5%) of 44 case children and 4(9.5%) of 42 case mothers were HIV(+). Case-control groups have thus far been constituted for 35 cases. The odds ratio comparing the HIV infection rate in case children with that in control children was not significantly different from 1.0 (p greater than 0.05). The same was true for case and control mothers.

CONCLUSION: In our Kinshasa study population, paralytic poliomyelitis was not associated with a statistically significantly increased risk of HIV infection. These data provide support for continued use of live oral polio vaccine in immunization programs in HIV-endemic areas of Africa.


Industrial-scale inactivated polio vaccine (IPV) production dates back to the 1960s when at the Rijks Instituut voor de Volksgezondheid (RIV) in Bilthoven a process was developed based on micro-carrier technology and primary monkey kidney cells. This technology was freely shared with several pharmaceutical companies and institutes worldwide. In this contribution, the history of one of the first cell-culture based large-scale biological production processes is summarized. Also, recent developments and the anticipated upcoming shift from regular IPV to Sabin-IPV are presented. Responding to a call by the World Health Organization (WHO) for new polio vaccines, the development of Sabin-IPV was continued, after demonstrating proof of principle in the 1990s, at the Netherlands Vaccine Institute (NVI). Development of Sabin-IPV plays an important role in the WHO polio eradication strategy as biocontainment will be critical in the post-OPV cessation period. The use of attenuated Sabin strains instead of wild-type Salk polio strains will provide additional safety during vaccine production. Initially, the Sabin-IPV production process will be based on the scale-down model of the current, and well-established, Salk-IPV process. In parallel to clinical trial material
production, process development, optimization and formulation research is being carried out to further optimize the process and reduce cost per dose. Also, results will be shown from large-scale (to prepare for future technology transfer) generation of Master- and Working virus seedlots, and clinical trial material (for phase I studies) production. Finally, the planned technology transfer to vaccine manufacturers in low and middle-income countries is discussed.


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.


BACKGROUND: After poliomyelitis has been eradicated, access to live polioviruses will be highly restricted and the use of oral poliovirus vaccine (OPV) will probably be discontinued. Countries using OPV must decide whether to switch to inactivated poliovirus vaccine (IPV) or stop polio vaccination. Because data on the immunogenicity of IPV in tropical developing countries are limited, we conducted a randomized, controlled trial of IPV in Cuba.

METHODS: The study population consisted of healthy infants born in Havana. A total of 166 infants were randomly assigned to two groups. Group A received a combination of the diphtheria-pertussis-tetanus (DPT) vaccine, the Haemophilus influenzae type b (Hib) vaccine, and IPV (DPT-Hib-IPV) at 6, 10, and 14 weeks of age. Group B, the control group, received a combination of the DPT vaccine and the Hib vaccine at 6, 10, and 14 weeks of age. Another group (group C, 100 infants), which did not undergo randomization at the same time as groups A and B, received the DPT-Hib-IPV combination at 8 and 16 weeks of age. Serum
satisfactory. There were no seroconversions in group B. The seroconversion rates in group C were 90%, 89%, and 90% for poliovirus types 1, 2, and 3, respectively. For groups A, B, and C, the virus isolation rates after challenge with OPV were 94%, 91%, and 97%, respectively, and the mean log10 viral titers of any serotype were 3.46, 3.89, and 3.37, respectively. There was one major adverse event, an episode of hypotonia. CONCLUSIONS: Vaccination with two or three doses of IPV resulted in a rate of seroconversion of at least 90%, except for seroconversion against type 2. The viral titer of OPV shed in the stool after OPV challenge was reduced in both groups receiving IPV.


BACKGROUND: The World Health Organization (WHO) recommends the discontinuation of oral poliovirus vaccine after eradication of wild poliovirus. Studies assessing inactivated poliovirus vaccine (IPV) immunogenicity in tropical countries, using the WHO Expanded Programme on Immunization (EPI) schedule, have been limited. METHODS: We conducted a randomized clinical trial in Ponce, Puerto Rico. Infants were assigned to 1 of 2 study arms: those in the EPI arm received IPV at 6, 10, and 14 weeks of age, and those in the US arm received IPV at 2, 4, and 6 months of age. Neutralizing antibody titers against poliovirus types 1, 2, and 3 were tested on serum specimens obtained before administration of the first dose of IPV and 28-45 days after administration of the last dose of IPV. RESULTS: Seroconversion rates for the EPI (n=225) and US (n=230) arms, respectively, were 85.8% and 99.6% for poliovirus type 1 (P<.001), 86.2% and 100% for poliovirus type 2 (P<.001), and 96.9% and 99.1% for poliovirus type 3 (P=.08). Seroconversion rates were lower among infants in the EPI arm who had high maternal antibody levels for all 3 poliovirus types (P<.001). CONCLUSIONS: The EPI schedule resulted in lower seroconversion rates for poliovirus types 1 and 2. These results are relevant for tropical countries planning to use IPV in a posteradication environment.


**Anis E. Insidious reintroduction of wild poliovirus into Israel, 2013. Euro Surv. 2013;Sep 19;18(38).**

Israel was certified as polio-free country in June 2002, along with the rest of the World Health Organization European Region. Some 11 years later, wild-type polio virus (WPV₁) was isolated initially from routine sewage samples collected between 7 and 13 April 2013 in two cities in the Southern district. WPV₁-specific analysis of samples indicated WPV₁ introduction into that area in
early February 2013. National supplementary immunisation with oral polio vaccine has been ongoing since August 2013.


BACKGROUND: To reduce the costs of maintaining a poliovirus immunization base in low-income areas, we assessed the extent of priming immune responses after the administration of inactivated poliovirus vaccine (IPV).

METHODS: We compared the immunogenicity and reactogenicity of a fractional dose of IPV (one fifth of a full dose) administered intradermally with a full dose administered intramuscularly in Cuban infants at the ages of 4 and 8 months. Blood was collected from infants at the ages of 4 months, 8 months, 8 months 7 days, and 8 months 30 days to assess single-dose seroconversion, single-dose priming of immune responses, and two-dose seroconversion. Specimens were tested with a neutralization assay.

RESULTS: A total of 320 infants underwent randomization, and 310 infants (96.9%) fulfilled the study requirements. In the group receiving the first fractional dose of IPV, seroconversion to poliovirus types 1, 2, and 3 occurred in 16.6%, 47.1%, and 14.7% of participants, respectively, as compared with 46.6%, 62.8%, and 32.0% in the group receiving the first full dose of IPV (P<0.008 for all comparisons). A priming immune response to poliovirus types 1, 2, and 3 occurred in 90.8%, 94.0%, and 89.6% of participants, respectively, in the group receiving the fractional dose as compared with 97.6%, 98.3%, and 98.1% in the group receiving the full dose (P=0.01 for the comparison with type 3). After the administration of the second dose of IPV in the group receiving fractional doses, cumulative two-dose seroconversion to poliovirus types 1, 2, and 3 occurred in 93.6%, 98.1%, and 93.0% of participants, respectively, as compared with 100.0%, 100.0%, and 99.4% in the group receiving the full dose (P<0.006 for the comparisons of types 1 and 3). The group receiving intradermal injections had the greatest number of adverse events, most of which were minor in intensity and none of which had serious consequences.

CONCLUSIONS: This evaluation shows that vaccinating infants with a single fractional dose of IPV can induce priming and seroconversion in more than 90% of immunized infants.


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%).


Enhanced potency inactivated poliovirus vaccine (EIPV), combined with diphtheria-tetanus-pertussis (DTP) vaccine, was compared with oral poliovirus vaccine (OPV) regarding immunogenicity in Thai infants, vaccinated at 2, 4 and 6 months of age. EIPV induced significantly higher seroconversion rates than OPV to all 3 poliovirus types after the second and third immunization. After 3 doses of each vaccine, at 7 months of age, all infants receiving EIPV proved seropositive for poliovirus type 1,
type 2 and type 3 neutralizing antibodies, whereas of those receiving OPV, 9% remained seronegative (titre < 1:4) for type 1 (p = 0.0042) and 11% for type 3 (p = 0.0013). All participating children were given an additional dose of OPV at the age of 9 months and tested again at 12 months of age. At that point, virtually all infants had poliovirus neutralizing antibodies, but the geometric mean titres to each poliovirus type were significantly higher in the vaccinees who had received EIPV. It is concluded that the greater immunogenicity of EIPV vis-à-vis 3 doses of OPV may be biologically significant for protection against poliovirus types 1 and 3 in countries where cases of poliomyelitis occur in young children. These findings warrant considering EIPV, alone or in combination with OPV, for an immunization programme in Thailand and similar countries in the future.

Seventy eight infants aged 6-8 weeks received either two doses of 0.1 ml of inactivated poliovirus vaccine (IPV) intradermally 8 weeks apart (group A) or three doses 4 weeks apart (group B). Pre- and 4 weeks post-immunization serum samples were tested for the presence and titer of neutralizing antibody to poliovirus types 1, 2 and 3. The seroconversion rates to poliovirus types 1, 2 and 3 were 90, 70 and 97%, respectively, among infants in group A and 90, 80 and 98%, respectively, in group B; in children without pre-existing maternal antibody, seroconversion rates were 100% to all three poliovirus serotypes in both groups. These rates were comparable to those in children receiving five doses of OPV or two doses of intramuscular IPV. Intradermal administration of fractional doses of IPV may be a less expensive alternative for use in developing countries.

Resik S et al. Randomized controlled clinical trial of fractional doses of inactivated poliovirus vaccine administered intradermally by needle-free device in Cuba. J Inf Dis. 2010;201(9):1344-52.
BACKGROUND: As part of an evaluation of strategies to make inactivated poliovirus vaccine (IPV) affordable for developing countries, we conducted a clinical trial of fractional doses of IPV in Cuba.
METHODS: We compared the immunogenicity and reactogenicity of fractional-dose IPV (0.1 ml, or 1/5 of a full dose) given intradermally using a needle-free jet injector device compared with full doses given intramuscularly. Subjects were randomized at birth to receive IPV at 6, 10, and 14 weeks.
RESULTS: A total of 471 subjects were randomized to the 2 study groups, and 364 subjects fulfilled the study requirements. No significant differences at baseline were detected. Thirty days after completing the 3-dose schedule of IPV, 52.9%, 85.0%, and 69.0% of subjects in the fractional-dose IPV arm seroconverted for poliovirus types 1, 2, and 3, respectively, whereas 89.3%, 95.5%, and 98.9% of subjects in the full-dose IPV arm seroconverted for poliovirus types 1, 2, and 3, respectively (all comparisons, P < .001). The median titers of each poliovirus serotype were significantly lower in the intradermal arm than in the intramuscular arm (P < .001). Only minor local adverse effects and no moderate or serious adverse events were reported.
CONCLUSIONS: This large-scale evaluation demonstrates the feasibility of fractional doses of IPV given intradermally as an antigen-sparing strategy but also shows that IPV given to infants at 6, 10, and 14 weeks of age results in suboptimal immunogenicity (especially for the fractional-dose arm).

BACKGROUND: We conducted a clinical trial of fractional doses of inactivated poliovirus vaccine administered to infants in Oman, in order to evaluate strategies for making the vaccine affordable for use in developing countries.

METHODS: We compared fractional doses of inactivated poliovirus vaccine (0.1 ml, representing one fifth of a full dose) given intradermally with the use of a needle-free jet injector device, with full doses of vaccine given intramuscularly, with respect to immunogenicity and reactogenicity. Infants were randomly assigned at birth to receive either a fractional dose or a full dose of inactivated poliovirus vaccine at 2, 4, and 6 months. We also administered a challenge dose of monovalent type 1 oral poliovirus vaccine at 7 months and collected stool samples before and 7 days after administration of the challenge dose.

RESULTS: A total of 400 infants were randomized, of whom 373 (93.2%) fulfilled the study requirements. No significant baseline differences between the groups were detected. Thirty days after completion of the three-dose schedule, the rates of seroconversion to types 1, 2, and 3 poliovirus were 97.3%, 95.7%, and 97.9%, respectively, in the fractional-dose group, as compared with 100% seroconversion to all serotypes in the full-dose group (P=0.01 for the comparison with respect to type 2 poliovirus; results with respect to types 1 and 3 poliovirus were not significant). The median titers were significantly lower in the fractional-dose group than in the full-dose group (P<0.001 for all three poliovirus serotypes). At 7 months, 74.8% of the infants in the fractional-dose group and 63.1% of those in full-dose group excreted type 1 poliovirus (P=0.03). Between birth and 7 months, 42 hospitalizations were reported, all related to infectious causes, anemia, or falls, with no significant difference between vaccination groups.

CONCLUSIONS: These data show that fractional doses of inactivated poliovirus vaccine administered intradermally at 2, 4, and 6 months, as compared with full doses of inactivated poliovirus vaccine given intramuscularly on the same schedule, induce similar levels of seroconversion but significantly lower titers.


OBJECTIVE: Comparison of a fractional inactivated poliovirus vaccine (IPV) dose administered intradermally (ID) to a full dose administered intramuscularly (IM).

METHODS: Healthy Filipino infants were randomized to receive IPV as either a fractional (1/5(th)) dose ID by needle injection or a full dose IM at 6, 10, and 14 weeks and a booster at 15-18 months of age. Pre- and post-vaccination anti-polio 1, 2, and 3 titers were estimated. Adverse events were monitored throughout the study.

RESULTS: Following primary series vaccination, anti-polio 1, 2, and 3 titers were ≥8 (1/dil) in 99-100% of participants, and the ID route was non-inferior to the IM route. Depending on the study group, antibody persistence was detected in 83-100% of participants, and the booster dose resulted in a strong anamnestic response in all groups. The incidence of adverse events in each group was similar, except for injection-site erythema (higher in the ID group).

CONCLUSIONS: Primary series and booster vaccination of a fractional IPV dose administered by the ID route was highly immunogenic and well tolerated. These data confirm the medical validity of using fractional ID doses of IPV. The programmatic feasibility of implementing affordable mass vaccination programs based on this delivery mode has yet to be established.

Oral polio vaccine (OPV) will likely be insufficient to completely eradicate polio due to its propensity to mutate into neurovirulent forms and its inability to produce adequate immunity in certain areas of the world. Inactivated polio vaccine (IPV), a killed vaccine which therefore cannot mutate, may be more effective than OPV in certain populations, and will likely be required for global polio eradication. However, the high cost of IPV is prohibitive in many areas of the world. Intradermal administration has the potential to lower the dose, and thus the cost, of IPV. This article reviews the clinical studies to date on intradermal fractional dose polio vaccination. We conclude that intradermal IPV vaccination shows potential as a means to reduce the cost and increase the ease of administration of IPV, but that additional research is needed to determine the optimal fractional dose, timing, and role of adjuvants in intradermal IPV vaccination as well as the clinical significance of different antibody titers above the threshold for seroconversion.


BACKGROUND: Antibody persistence was studied in 5.5-year-old Swedish children who in infancy completed a vaccine trial of a combined diphtheria toxoid, tetanus toxoid, acellular pertussis, inactivated polio and Haemophilus influenzae type b conjugate vaccine. Three priming doses at ages 2-4-6 months induced higher geometric mean concentrations of antibodies for all antigens than did two doses at 3-5 months, but there were no differences in proportions with protective antibody concentrations. After the booster dose administered at 13 or 12 months of age, respectively, there were no differences in concentrations or proportions between the groups. METHODS: In the present follow-up serum samples from 180 of the 228 vaccinees, 88 from the 4-dose and 92 from the 3-dose group, were 4.5 years later again tested for antibodies. RESULTS: The two groups did not differ significantly in antibody concentrations or proportions with antibodies above protective or other defined levels, with the exception of poliovirus type 3 (P < or = 0.01).

Langue J et al. Persistence of antibodies at 5-6 years of age for children who had received a primary series vaccination with a pentavalent whole-cell pertussis vaccine and a first booster with a pentavalent acellular pertussis vaccine. Vaccine, 2004;22(11-12):1406-14.

The main objective of this study was to assess in 5-6-year-old French children (n=162) the persistence of antibodies induced by a primary series vaccination (at 2-4 months of age) with a pentavalent whole-cell pertussis combined vaccine (DTwP-IPV-Hib; Pentacoq) and a first booster (at 12-16 months of age) with a pentavalent two-component acellular pertussis combined vaccine (DTacP-IPV-Hib; Pentavac). The second objective was to evaluate in these 5-6-year-old French children the safety and the immunogenicity of a tetravalent pertussis combined vaccine (DTacP-IPV, Tetravac) given as a second booster. RESULTS: before the 2nd booster, more than 90% of children had antibody titers above the defined threshold for polyribosyl ribitol phosphate (PRP), tetanus, diphtheria and poliomyelitis; antibody titers were very low for pertussis. One month after the second booster, all children had seroprotective post-booster titers for tetanus, diphtheria and poliomyelitis types 1-3; over 90% of children had a four-fold rise in titers against DTacP-IPV antigens. Adverse events were mostly solicited reactions, with no serious adverse event. A strong anamnestic response was also observed after the second booster injection with Tetravac, with a satisfactory safety
profile. CONCLUSION: Pentavac and Tetravac (acellular pertussis containing vaccines) may thus be administered as first and second boosters respectively, in children primed with Pentacoq (whole-cell pertussis containing vaccine).

Two hundred and fifty children born in 1967 and vaccinated with killed polio vaccine in Sweden were followed for 18 years and tested for neutralizing antibodies against polio. All of them had demonstrable antibodies at the age of 18. Sixty-four children were tested in samples collected throughout the years. After a more marked fall of antibody titres during the first few years after vaccination, the decline levelled off to a mean decrease in titre of 0.05-0.10 log10 per year. In half of them, the routine vaccination comprising a fourth dose at 6 years of age was changed and this booster was postponed to the age of ten. The children given the booster dose at ten had significantly higher antibody levels at 18 years of age than those given it at six.

In Denmark a polio vaccination program including both inactivated poliovirus vaccine (IPV) and oral poliovirus vaccine (OPV) has been in use since 1968. Three injections of IPV are given when the children are five, six, and 15 months of age. Subsequently, three vaccinations with trivalent OPV are administered at the age of three, four, and five years. The acceptance rate is high-93%-98%-and greater than 95% of the population has antibodies to poliovirus. The geometric mean titer of serum antibodies is much greater than 10 IU for all three types. The epidemiology of poliomyelitis and the background for the development of the present vaccination schedule are reviewed. The epidemiology of poliomyelitis and the background for the development of the present vaccination schedule are reviewed.

In order to evaluate the response to immunization of HIV-infected children we studied the humoral response to an enhanced potency inactivated poliovaccine (E-IPV) of 43 children born of HIV seropositive mothers. All these subjects have been followed for 32 (15-48) months in order to ascertain their infection status. After a course of 2 doses of E-IPV, 88% of children had neutralizing antibody (n.a.) titers greater than 1:4 to the 3 poliovirus serotypes and 100% to at least 2 polio strains. No statistically significant differences both as rates of n.a. positive subjects and as antibody levels were found between HIV infected children and those who lost HIV antibodies. The poorest response was observed in subjects with full-blown immunodeficiency (CD4 less than 1000/mm3, reduced response to PWM). Sixteen children also received a booster dose of vaccine one year after the completion of the primary cycle. Infected and non-infected subjects responded to the same extent with high levels of n.a. to this immunization. Interestingly, the recall dose was also able to induce high n.a. titers in those HIV infected children who showed significant decreases of n.a. titers in the months following the end of the primary cycle.

Hemophilic patients may present immunological dysfunctions resulting from either human immunodeficiency virus (HIV) infection, or other factors like impure factor VIII concentrate and other viral infections. We evaluated prospectively the serologic response to polio vaccination of Israeli hemophilic patients who were vaccinated during an outbreak of poliomyelitis. Eighty-two hemophilic patients, 43 seronegative and 39 seropositive for human immunodeficiency virus (HIV), were vaccinated with enhanced inactivated poliovirus (eIPV). Titers of antibodies for poliovirus types 1-3 were determined before and 4 weeks after immunization. T helper and suppressor lymphocytes (T4 and T8), B and T lymphocyte mitogenic response, and natural killer cells were tested and correlated with the response to vaccination. Both groups responded to vaccination with increased titers of antibodies to the three viral types, 4 weeks after immunization. HIV-seronegative patients, however, exhibited higher titers than the HIV-seropositive group. The same pattern was found when 21 patients were tested 1 year after the exposure to eIPV. HIV-seropositive patients were grouped according to their T4 count (between 16/microliter and 500/microliter). There was no statistically significant difference in the response of these different groups to vaccination. No correlation was found between the response to vaccination and other immune parameters. These results suggest that asymptomatic HIV-seropositive hemophilic patients respond well to eIPV, irrespective of their T4 count.


The outbreak of paralytic poliomyelitis in Finland in 1984 was halted by nationwide oral poliovirus vaccination campaign. Immunocompromised patients, including those with chronic uraemia and on continuous dialysis, were excluded from the oral vaccination group and instead were given a dose of the new enhanced-potency inactivated poliovirus vaccine before the campaign. We studied the antibody response to this vaccine in 49 patients on chronic dialysis, using conventional antigen of all three serotypes and two additional type 3 strains. It was observed that 86% (42 of 49) of patients either had a satisfactory concentration of neutralising poliovirus antibodies against all three serotypes prior to vaccination, or responded with at least a four-fold increase of antibodies. Fourteen of 21 patients originally seronegative to at least one of the five virus strains used showed a striking seroconversion. One patient remained seronegative to type 1 poliovirus while two and four other patients were left with low (less than 8) titres of type 1 and 3 antibodies respectively. The latter seven patients showed moderate or good responses to the other two serotypes. We conclude that the enhanced-potency inactivated poliovirus vaccine produces a good antibody response in uraemic patients.


Following a small outbreak of poliomyelitis which occurred in the summer of 1988 in Israel, two sequential doses of inactivated polio vaccine (IPV) were administered to 42 bone marrow transplant (BMT) recipients (aged 2-50 years) who were 6-96 months (median 16 months) after transplantation. Prior to vaccination, only 68-80% patients (n = 42) had protective (greater than or equal to 4) antibody levels against the three serotypes of poliovirus, compared with 92-96% (n = 25) before BMT (p = 0.02 for types 1 and 3). After the second dose of IPV, 89-98% (n = 27) of the recipients had protective antibody levels. The pre-vaccination antibody titers were lower than before BMT (p = 0.006, 0.0007 and 0.0008 for types 1,2 and 3, respectively). After the first dose of IPV, antibody titers
rose in the 42 patients (p = 0.002, 0.043 and 0.002 for types 1, 2 and 3, respectively) and following the second dose, a further increase in antibody levels was noted. Regression analysis revealed that graft-versus-host disease, pre-BMT polio antibody titers, age and type of transplantation (allogeneic versus autologous) were significant explanatory variables for the specific antibody levels, while the time lapse between BMT and vaccination, and primary disease proved of no significance. Vaccination against poliovirus after BMT is advocated, as it reinstates and raises the lost specific humoral immunity.

A controlled study was conducted in Karachi, Pakistan to compare humoral and mucosal immune responses against polioviruses in infants who received oral poliovirus vaccine (OPV) at birth and at 6, 10, and 14 weeks according to the Expanded Program on Immunization (EPI) with infants who received either three doses of inactivated poliovirus vaccine (IPV) at 6, 10, and 14 weeks together with OPV or one additional dose of IPV at 14 weeks together, with the last dose of OPV. A total of 1429 infants were enrolled; 24-week serum specimens were available for 898 infants (63%). They all received a challenge dose of OPV type 3 at 24 weeks of age. The addition of three doses of IPV to three doses of OPV induced a significantly higher percentage of seropositive children at 24 weeks of age for polio 1 (97% versus 89%, P<0.001) and polio 3 (98% versus 92%) compared to the EPI schedule. However, the one supplemental dose of IPV at 14 weeks did not increase the serological response at 24 weeks. Intestinal immunity against the challenge dose was similar in the three groups. Combined schedules of OPV and IPV in the form of diphtheria-pertussis-tetanus-IPV vaccine (DPT-IPV) may be useful to accelerate eradication of polio in developing countries.

CONTEXT: The last case of poliomyelitis in the United States due to indigenously acquired wild poliovirus occurred in 1979; however, as a consequence of oral poliovirus vaccine (OPV) use that began in 1961, an average of 9 cases of vaccine-associated paralytic poliomyelitis (VAPP) were confirmed each year from 1961 through 1989. To reduce the VAPP burden, national vaccination policy changed in 1997 from reliance on OPV to options for a sequential schedule of inactivated poliovirus vaccine (IPV) followed by OPV. In 2000, an exclusive IPV schedule was adopted. OBJECTIVE: To review the epidemiology of paralytic poliomyelitis and document the association between the vaccine schedule changes and VAPP in the United States. DESIGN AND SETTING: Review of national surveillance data from 1990 through 2003 for cases of confirmed paralytic poliomyelitis. MAIN OUTCOME MEASURES: Number of confirmed paralytic poliomyelitis cases, including VAPP, and ratio of VAPP cases to number of doses of OPV distributed that occurred before, during, and after implementation of policy changes. RESULTS: From 1990 through 1999, 61 cases of paralytic poliomyelitis were reported; 59 (97%) of these were VAPP (1 case per 2.9 million OPV doses distributed), 1 case was imported, and 1 case was indeterminate. Thirteen cases occurred during the 1997-1999 transitional policy period and were associated with the all-OPV schedule; none occurred with the IPV-OPV schedule. No cases occurred after the United States implemented the all-IPV policy in 2000. The last imported poliomyelitis case
occurred in 1993 and the last case of VAPP occurred in 1999. CONCLUSION: The change in polio vaccination policy from OPV to exclusive use of IPV was successfully implemented; this change led to the elimination of VAPP in the United States.


Moriniere BJ et al. Immunogenicity of a supplemental dose of oral versus inactivated poliovirus vaccine. Lancet. 1993;Jun 19;341(8860):1545-50. In many developing countries, the immunogenicity of three doses of live, attenuated, oral poliovirus vaccine (OPV) is lower than that in industrialised countries. We evaluated serum neutralising antibody responses in 368 children aged 6 months and 346 children aged 9 months in Côte d'Ivoire who had previously received three doses of OPV at 2, 3, and 4 months of age, and who were then randomised to receive a supplemental dose of OPV or enhanced-potency inactivated poliovirus vaccine (IPV) at the time of measles vaccination. Although both vaccines increased seroconversion to all three poliovirus types, antibody responses were greater in the IPV group. Among children with no detectable antibody at baseline, IPV was 2 to 14 times more likely than OPV to induce seroconversion (type 1, 80% vs 40% at 6 months [p < 0.001] and 81% vs 14% at 9 months [p < 0.001]; type 3, 76% vs 22% at 6 months [p < 0.001], and 67% vs 5% at 9 months [p < 0.001]. Among children with detectable antibody at baseline, IPV was 1.4 to 7 times more likely than OPV to elicit 4-fold or more rises in antibody titre (p < 0.01). Geometric mean titres (GMTs) to all three poliovirus types were also consistently higher among IPV recipients than in OPV recipients when measured 4-6 weeks and 13-17 months after vaccination. Administration of a supplemental dose of IPV or OPV, which requires no additional visits or changes in the existing immunisation schedule, might improve protection against paralytic poliomyelitis in communities with suboptimum seroconversion rates after three doses of OPV.


OBJECTIVE: To evaluate the economic consequences of introducing inactivated poliovirus vaccine (IPV) into the routine vaccination schedule in the United States to reduce vaccine-associated paralytic poliomyelitis (VAPP). DESIGN: Cost-benefit and cost-effectiveness models were formulated to compare the current national 4-dose live attenuated oral poliovirus vaccine (OPV) schedule with a 4-dose IPV schedule or a sequential schedule of 2 doses of IPV followed by 2 doses of OPV. Model assumptions were derived from the National Health Interview Survey (1994), current prices for OPV and IPV, a Delphi panel, compensatory awards by the National Vaccine Injury Compensation Program, and published and unpublished reports. MAIN OUTCOME MEASURES: Annual societal incremental cost relative to the current schedule for the cost-benefit model; cost per VAPP case prevented for the cost-effectiveness model. RESULTS: Changing to an IPV-only or a sequential schedule
would cost $28.1 million and $14.7 million, respectively. The costs per case of VAPP prevented were estimated as $3.0 million and $3.1 million for each option, respectively. Outcomes were most sensitive to the number of additional visits that may occur to avoid multiple injections. CONCLUSIONS: The introduction of IPV into the routine vaccination schedule would not be cost-beneficial at current vaccine prices and with the current compensation awards paid to VAPP cases. The analysis provides a range of costs that policymakers need to consider if they wish to prevent VAPP. Although these costs are higher than those of other public health prevention programs, they may be justified because VAPP continues to occur as a result of government-mandated vaccination policies in the absence of known wild poliovirus transmission in the United States.

The global polio eradication initiative (GPEI), which started in 1988, represents the single largest, internationally coordinated public health project to date. Completion remains within reach, with type 2 wild polioviruses apparently eradicated since 1999 and fewer than 2000 annual paralytic poliomyelitis cases of wild types 1 and 3 reported since then. This economic analysis of the GPEI reflects the status of the program as of February 2010, including full consideration of post-eradication policies. For the GPEI intervention, we consider the actual pre-eradication experience to date followed by two distinct potential future post-eradication vaccination policies. We estimate GPEI costs based on actual and projected expenditures and poliomyelitis incidence using reported numbers corrected for underreporting and model projections. For the comparator, which assumes only routine vaccination for polio historically and into the future (i.e., no GPEI), we estimate poliomyelitis incidence using a dynamic infection transmission model and costs based on numbers of vaccinated children. Cost-effectiveness ratios for the GPEI vs. only routine vaccination qualify as highly cost-effective based on standard criteria. We estimate incremental net benefits of the GPEI between 1988 and 2035 of approximately 40-50 billion dollars (2008 US dollars; 1988 net present values). Despite the high costs of achieving eradication in low-income countries, low-income countries account for approximately 85% of the total net benefits generated by the GPEI in the base case analysis. The total economic costs saved per prevented paralytic poliomyelitis case drive the incremental net benefits, which become positive even if we estimate the loss in productivity as a result of disability as below the recommended value of one year in average per-capita gross national income per disability-adjusted life year saved. Sensitivity analysis suggests that the finding of positive net benefits of the GPEI remains robust over a wide range of assumptions, and that consideration of the additional net benefits of externalities that occurred during polio campaigns to date, such as the mortality reduction associated with delivery of Vitamin A supplements, significantly increases the net benefits. This study finds a strong economic justification for the GPEI despite the rising costs of the initiative.

AIMS: To assess the cost-effectiveness of switching from oral polio vaccine (OPV) to inactivated poliovirus vaccine (IPV), or to cease polio vaccination in routine immunization services in South Africa at the time of OPV cessation globally following polio eradication.
METHODS: The cost-effectiveness of nine different polio immunization alternatives were evaluated. The costs of introducing IPV in a separate vial as well as in different combination vaccines were estimated, and IPV schedules with 2, 3 and 4 doses were compared with the current 6-dose OPV schedule. Assumptions about IPV prices were based on indications from vaccine manufacturers. The health impact of OPV cessation was measured in terms of vaccine associated paralytic paralysis (VAPP) cases and disability adjusted life years (DALYs) averted. CONCLUSIONS: The use of OPV in routine immunization services is predicted to result in 2.96 VAPP cases in the 2005 cohort. The cost-effectiveness of the different IPV alternatives varies between US$ 740,000 and US$ 7.2 million per VAPP case averted. The costs per discounted DALY averted amount to between US$ 61,000 and US$ 594,000. Among the IPV strategies evaluated, the 2-dose schedule in a 10-dose vial is the most costeffective option. At the assumed vaccine prices, all IPV options do not appear to be costeffective in the South African situation. OPV cessation without IPV replacement would result in cost savings of US$ 1.6 million per year compared to the current situation. This is approximately a 9% decrease in the budget for vaccine delivery in South Africa. However, with this option there is a risk (albeit small) of vaccine-derived poliovirus circulating in a progressively susceptible population. For IPV in a single dose vial, the break-even price, at which the costs of IPV delivery equal the current OPV delivery costs, is US$ 0.39.


OBJECTIVE: Estimate the economic impact of introducing inactivated poliovirus vaccine (IPV) into the Australian childhood immunisation schedule to eliminate vaccine-associated paralytic poliomyelitis (VAPP). METHODS: Cost-effectiveness of two different four-dose IPV schedules (monovalent vaccine and IPV-containing combination vaccine) compared with the current four-dose oral poliovirus vaccine (OPV) schedule for Australian children through age six years. Model used estimates of VAPP incidence, costs, and vaccine utilisation and price obtained from published and unpublished sources. Main outcome measures were total costs, outcomes prevented, and incremental cost-effectiveness, expressed as net cost per case of VAPP prevented. RESULTS: Changing to an IPV-based schedule would prevent 0.395 VAPP cases annually. At $20 per dose for monovalent vaccine and $14 per dose for the IPV component in a combination vaccine, the change would incur incremental, annual costs of $19.5 million ($49.3 million per VAPP case prevented) and $6.7 million ($17.0 million per VAPP case prevented), respectively. Threshold analysis identified break-even prices per dose of $1 for monovalent and $7 for combination vaccines. CONCLUSIONS: Introducing IPV into the Australian childhood immunisation schedule is not likely to be cost-effective unless it comes in a combined vaccine with the IPV-component price below $10. IMPLICATIONS: More precise estimates of VAPP incidence in Australia and IPV price are needed. However, poor cost-effectiveness will make the decision about switching from OPV to IPV in the childhood schedule difficult.