Position paper on Polio vaccines May 2010

Selected references

References inserted in the Position Paper and (from page 21) of the five Grading Tables with respective summaries, if available, listed in the order they occur in the respective documents. An extended list of references is provided separately (link).


Users of clinical practice guidelines and other recommendations need to know how much confidence they can place in the recommendations. Systematic and explicit methods of making judgments can reduce errors and improve communication. We have developed a system for grading the quality of evidence and the strength of recommendations that can be applied across a wide range of interventions and contexts. In this article we present a summary of our approach from the perspective of a guideline user. Judgments about the strength of a recommendation require consideration of the balance between benefits and harms, the quality of the evidence, translation of the evidence into specific circumstances, and the certainty of the baseline risk. It is also important to consider costs (resource utilisation) before making a recommendation. Inconsistencies among systems for grading the quality of evidence and the strength of recommendations reduce their potential to facilitate critical appraisal and improve communication of these judgments. Our system for guiding these complex judgments balances the need for simplicity with the need for full and transparent consideration of all important issues.


PIP: Infants should receive live trivalent oral poliovirus vaccine (TOPV) and DPT immunization as early in life as possible in order to minimize the time that they are at risk of contracting these vaccine-preventable diseases. Passively acquired circulating maternal antibodies provide protection in the 1st few weeks or months of life. Although these antibodies may modify or block the serum immune response during the 1st few weeks of life, the 1st or priming dose of DPT can be given effectively after 4 weeks of age. TOPV administered to infants during the 1st week of life results in intestinal infections and local immune responses in 50-100% of infants and serum antibody responses in 30-70% of infants. The serum antibody response following TOPV administration at 4-8 weeks of age is as effective as vaccine administered to older infants. The WHO Program on Immunization recommends initiating DPT and TOPV schedules at 6 weeks of age. In countries where
poliomyelitis has not been controlled, TOPV should be given at birth, or at 1st contact with the health services, then at 6 weeks of age, followed by 2 additional doses 4 weeks apart.


Co-administration of oral live-attenuated human rotavirus vaccine RIX4414 (Rotarix) and oral polio vaccine (OPV) was assessed. Healthy infants were randomised to receive 2-doses of either: RIX4414 or placebo co-administered with OPV (12 and 16 weeks of age); or RIX4414 or placebo given 15 days after OPV. After vaccination, 56.5-66.7% of RIX4414 and 18.6% of placebo recipients had seroconverted for rotavirus IgA. No significant differences between RIX4414 groups with or without OPV co-administration were observed. No statistically significant differences were observed between groups for polio seroprotection rates. RIX4414 vaccine was immunogenic when co-administered with OPV and did not interfere with OPV seroprotection rates.


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.
As the global eradication of wild poliovirus nears, the World Health Organization (WHO) is addressing challenges unprecedented in public health. The live, attenuated oral poliovirus vaccine (OPV), used for more than four decades to interrupt poliovirus transmission, and the vaccine of choice for developing countries, is genetically unstable. Reversion of the small number of substitutions conferring the attenuated phenotype frequently occurs during OPV replication in humans and is the underlying cause of the rare cases of vaccine-associated paralytic poliomyelitis (VAPP) in OPV recipients and their close contacts. Whereas VAPP has long been recognized, two other adverse events have been identified more recently: (a) long-term excretion of highly evolved vaccine-derived polioviruses (VDPVs) in persons with primary immunodeficiencies, and (b) polio outbreaks associated with circulating VDPVs in areas with low rates of OPV coverage. Developing a posteradication strategy to minimize the risks of VDPV emergence and spread has become an urgent WHO priority.


The authors investigated the possibility of an association between oral polio vaccine (OPV) and intussusception by linking Scottish vaccination and hospitalization data sets and performing self-controlled case series analysis. The issue was important because rotavirus vaccine, another live oral virus vaccine, was withdrawn from the market in 1999 after studies showed a strong association with intussusception. OPV was recommended for all infants in the United Kingdom at ages 2, 3, and 4 months until 2004, when new combination vaccines containing inactivated poliovirus were introduced. Analysis was carried out for 466 intussusception cases occurring in 1987-1999 for which linked records on OPV vaccination were available. Six possible risk periods for intussusception, ranging from 3 days after vaccination to 41 days after vaccination, were examined, with separate analysis for each of the three OPV doses and also for data on all three doses combined. Of the 24 possible risk periods examined, the relative incidence of intussusception after vaccination was unchanged for 18, significantly decreased for five, and significantly increased for only one. The authors conclude that overall, there is no evidence for an association between OPV and intussusception, even when each dose is considered separately.


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.


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.


In a simple study into the control of polio in the Third World a town was divided into 16 zones and pulses or oral polio vaccine given at one station in each zone, after extensive publicity about the campaign. Some 62% of children received three doses of the vaccine and the incidence of polio fell dramatically over the study period. It is suggested that this method is applicable to similar communities because it is cheap, effective, and able to be extended to unimmunised communities when resources allow.


BACKGROUND: The number of cases of paralytic poliomyelitis has declined in Nigeria since the introduction of newly licensed monovalent oral poliovirus vaccines and new techniques of vaccine delivery. Understanding the relative contribution of these vaccines and the improved coverage to the decline in incident cases is essential for future planning. METHODS: We estimated the field efficacies of monovalent type 1 oral poliovirus vaccine and trivalent oral poliovirus vaccine, using the reported number of doses received by people with poliomyelitis and by matched controls as identified in Nigeria's national surveillance database, in which 27,379 cases of acute flaccid paralysis were recorded between 2001 and 2007. Our estimates of vaccine coverage and vaccine-induced immunity were based on the number of doses received by children listed in the database who had paralysis that was not caused by poliovirus. RESULTS: The estimated efficacies per dose of monovalent type 1 oral poliovirus vaccine and trivalent oral poliovirus vaccine against type 1 paralytic poliomyelitis were 67% (95% confidence interval [CI], 39 to 82) and 16% (95% CI, 10 to 21), respectively, and the estimated efficacy per dose of trivalent oral poliovirus vaccine against type 3 paralytic poliomyelitis was 18% (95% CI, 9 to 26). In the northwestern region of Nigeria, which reported the majority of cases during the study period, coverage with at least one dose of vaccine increased from 59 to 78%. Between 2005 and 2007, vaccine-induced immunity levels among children under the age of 5 years more than doubled, to 56%. CONCLUSIONS: The higher efficacy of monovalent type 1 oral poliovirus vaccine (four times as effective as trivalent oral poliovirus vaccine) and the moderate gains in coverage dramatically increased
vaccine-induced immunity against serotype 1 in northern Nigeria. Further increases in coverage in Nigerian states with infected populations are required to achieve the levels of vaccine-induced immunity associated with the sustained elimination achieved in other parts of the country. 2008 Massachusetts Medical Society


BACKGROUND: In 1988, the World Health Assembly resolved to eradicate poliomyelitis. Although substantial progress toward this goal has been made, eradication remains elusive. In 2004, the World Health Organization called for the development of a potentially more immunogenic monovalent type 1 oral poliovirus vaccine. METHODS: We conducted a trial in Egypt to compare the immunogenicity of a newly licensed monovalent type 1 oral poliovirus vaccine with that of a trivalent oral poliovirus vaccine. Subjects were randomly assigned to receive one dose of monovalent type 1 oral poliovirus vaccine or trivalent oral poliovirus vaccine at birth. Thirty days after birth, a single challenge dose of monovalent type 1 oral poliovirus vaccine was administered in all subjects. Shedding of serotype 1 poliovirus was assessed through day 60. RESULTS: A total of 530 subjects were enrolled, and 421 fulfilled the study requirements. Thirty days after the study vaccines were administered, the rate of seroconversion to type 1 poliovirus was 55.4% in the monovalent-vaccine group, as compared with 32.1% in the trivalent-vaccine group (P<0.001). Among those with a high reciprocal titer of maternally derived antibodies against type 1 poliovirus (>64), 46.0% of the subjects in the monovalent-vaccine group underwent seroconversion, as compared with 21.3% in the trivalent-vaccine group (P<0.001). Seven days after administration of the challenge dose of monovalent type 1 vaccine, a significantly lower proportion of subjects in the monovalent-vaccine group than in the trivalent-vaccine group excreted type 1 poliovirus (25.9% vs. 41.5%, P=0.001). None of the serious adverse events reported were attributed to the trial interventions. CONCLUSIONS: When given at birth, monovalent type 1 oral poliovirus vaccine is superior to trivalent oral poliovirus vaccine in inducing humoral antibodies against type 1 poliovirus, overcoming high preexisting levels of maternally derived antibodies, and increasing the resistance to excretion of type 1 poliovirus after administration of a challenge dose.


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.


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


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.


This study was done to assess the response of newborns to trivalent oral polio vaccine and to study any efficacy of OPV if given to infants on third day of life. The study was conducted in two groups, A (87) and B (55) of infants in Delhi, India. In group A, the children received one birth dose or 'O' dose of TOPV, followed by 3 conventional doses started at 6 weeks, and in group B the children received only 3 doses of OPV. Pre and one month post immunization serum samples were tested for the presence of neutralising antibodies. In addition, in group A serum samples were collected at 6 weeks before the administration of 1st dose to see the sero response following 'O' dose of TOPV. It was found that administration of OPV on 3rd day of life leads to sero conversion in 15.3% of infants to all three polio virus types by the age of 6 weeks, and highest sero response was seen for polio virus type 1. Sero-conversion in group A
was significantly more than sero-conversion in group B after the administration of last dose. Thus the study has established that immunization of newborns with TOPV is a safe and effective means for improving protection against the disease.


The study was carried out to evaluate the efficacy of IPV in neonates and to study the additive effect of IPV or OPV at birth on seroconversion with three subsequent doses of OPV. Addition of IPV or OPV at birth to the conventional OPV schedule resulted in significantly higher seroconversion rates than in the controls, who received three doses of OPV. Three doses of IPV beginning from birth resulted in significantly better seroconversion rates than in the control group. Children receiving 3 doses of IPV showed significantly greater seroconversion rates against type III polio virus than those receiving IPV/OPV at birth followed by 3 doses of OPV. The difference in the seroconversion rates against the other virus types was not significant. A significantly greater number of children who received some vaccine at birth (IPV or OPV) were protected against poliomyelitis by 6 weeks age as compared to those who received no immunization at birth. The study recommends that seroconversion rates following three doses of IPV are satisfactory. Addition of IPV or OPV at birth to the conventional schedule markedly increases the seroconversion rates. Immunization can be started at birth to ensure early protection against poliomyelitis.


To evaluate the efficacy of the schedule currently recommended for immunization with trivalent oral poliovirus vaccine (TOPV) (i.e., at birth, 6 weeks, 10 weeks, and 14 weeks after birth), we randomly assigned 452 infants into test (231 infants) and control (221 infants) groups. The test group received TOPV as currently recommended, and the dose at birth was omitted for the control group. At 10, 14, and 18 weeks of age, the levels of poliovirus neutralizing antibodies as well as seroconversion rates were consistently higher for the test group than for the control group. The final seroconversion rates against poliovirus types 1, 2, and 3 were 83.5%, 91% and 83%, respectively, for the test group and 75%, 83.2%, and 79.1%, respectively, for the control group. The TOPV immunization schedule starting at birth therefore produced better results. Seroconversion rates as well as antibody levels were highest in infants with low maternal antibodies.


Described is the evaluation in Brazil of the immune response of early immunization with trivalent oral poliovirus vaccine (TOPV). A total of 85 normal neonates from São Paulo were
assigned one of the following immunization schedules: group A--one dose of TOPV at birth and subsequent doses at 2, 4, and 9 months of age; or group B--one dose of TOPV at 2, 4 and 6 months of age. Blood samples were collected sequentially from the mother at delivery, from the umbilical cord, and from the child at 2, 4, 6, 9 and 12 months of age for assay of poliovirus neutralizing antibodies. Administration of TOPV at birth, in addition to establishing immunity against poliomyelitis at an earlier stage, produced a superior immune response to poliovirus type 3. At the end of the first year, the proportion of susceptible individuals was 3.7% in group A and 25.9% in group B. When immunization against poliomyelitis is started at birth, excellent seroconversion rates are obtained from the third dose onward.


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-year-old 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 entrants to present evidence of having received at least two doses of measles vaccine, with one on or after entry into elementary school.


Summary objectives: We evaluated antibody prevalence to measles, polio 1 and 3, and tetanus toxoid antibodies in 8–9 year-old children in The Gambia within the framework of the Gambia Hepatitis Intervention Study (GHIS), a large vaccine trial aimed at evaluating vaccine efficacy against hepatitis B virus (HBV) infection, chronic carriage and primary liver cancer in a high risk population. The results of the present survey were compared with a previous
survey performed with the same objectives and same methodology but in different children at 3–4 years of age.

Methods: Four clusters of 200 children each were sampled as representative of the whole country. Children would have received BCG, diphtheria–pertussis–tetanus vaccine (DPT), poliovirus vaccine (OPV), measles and yellow fever immunization. The measles haemoagglutination inhibition test (HAI) was used to detect measles antibody. Antibodies to polioviruses 1 and 3 were tested using the standard polio neutralization assay described in the EPI manual (WHO 1990). An enzyme-linked immunosorbent assay (ELISA) was used to measure tetanus toxoid antibodies.

Results: A high proportion of children were fully vaccinated in both age groups. Measles antibody concentrations were £1 : 8 in 8.2% of 8–9 year-old vaccinated children. In the previous survey of 3–4 year-old children this was 11.3%. In the present survey, GMC was lower than in the 3–4 year-old children; 88% of 3–4 year-olds and 89% of 8–9 year-olds had detectable antibody levels against poliovirus type 1. Fewer children at 8–9 years of age had antibodies against poliovirus type 3 than 3–4 year-olds (78% vs. 89% P < 0.001). A significant overall lower proportion of 8–9 year-old children had detectable tetanus toxoid antibodies compared to 3–4 year-old children (87% vs. 95% P < 0.001), as well as those who received four doses of DPT (90% vs. 97% P < 0.001).

Conclusions: High vaccine coverage is achieved in The Gambia with EPI. With time the number of vaccinated children who are not protected against measles, poliovirus 3 and tetanus increases. Besides the maintenance of high vaccine coverage in infants and young children, booster doses of some of the EPI vaccines in adolescents should be considered.


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.

Phua KB, Quak SH, Lim FS, Goh P, Teoh YL, Datta SK, Han HH, Bock HL. Immunogenicity, reactogenicity and safety of a diphtheria-tetanus-acellular pertussis-

INTRODUCTION: In recent years, acellular pertussis combination vaccines have facilitated compliance with and coverage of the national immunisation programme in Singapore. This phase-II study (Rota-007) evaluated the immunogenicity, reactogenicity and safety of a DTPa-IPV/Hib combined vaccine when co-administered with a rotavirus vaccine.

MATERIALS AND METHODS: A total of 2464 children aged 3 months were vaccinated with DTPa-IPV/Hib together with a randomised 1:3 ratio of either placebo (n=653) or 1 of 3 different formulations of a rotavirus vaccine. Blood samples were collected for immunogenicity analysis 1 month after the third DTPa-IPV/Hib vaccine dose in a subset of subjects (n = 640). Local and general reactogenicity and unsolicited adverse events were recorded during the follow-up after each vaccination. RESULTS: Serological analysis showed >95% response for all antigens in the co-administered DTPa-IPV/Hib vaccine, with no difference between the rotavirus vaccine and placebo groups. No differences in adverse events and reactogenicity were reported in the rotavirus vaccine and placebo groups. Only 0.2% of the subjects reported Grade 3 adverse events. Three subjects (from the vaccine groups) died during the study, which were assessed by the investigators as unrelated to vaccination. No deaths were reported in the placebo group. CONCLUSION: The combined DTPa-IPV/Hib vaccine is safe, well tolerated and highly immunogenic when given alone or coadministered with the rotavirus vaccine for infants in Singapore.


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%).


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.


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 samples were collected before vaccination and at least 4 weeks after the last dose. Stool samples were obtained before and 7 days after challenge with OPV. RESULTS: The seroconversion rates in group A were 94%, 83%, and 100% for types 1, 2, and 3 poliovirus, respectively. 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. (ClinicalTrials.gov number, NCT00260312 [ClinicalTrials.gov]). Copyright 2007 Massachusetts Medical Society.

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 ≤ 0.01).

Langue J, Matisse N, Pacoret P, Undreiner F, Boisnard F, Soubeyrand B; Pentavac study group. 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: immunogenicity and tolerance of second booster with a tetravalent acellular vaccine at 5-6 years of age. Vaccine. 2004 Mar 29;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 (DTwcP-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 sero-protective 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.


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.

The relative immunity induced by sequential administration of inactivated poliovirus vaccine (IPV) produced in human diploid cells and live attenuated oral poliovirus vaccine (OPV) was evaluated by randomization of 510 infants to receive IPV and OPV sequentially according to one of three experimental schedules, IPV only, or OPV only. The antibody response to two IPV doses was lower than expected. However, for each of the IPV-OPV sequential schedules, the first OPV dose significantly enhanced seroconversion rates and geometric mean microneutralization antibody titers. Three months after the final dose, 96%-99%, 99%-100%, and 81%-100% of infants had antibodies to poliovirus types 1, 2, and 3, respectively, and subjects with two or more prior OPV doses were significantly less likely than those with none or one prior OPV dose to excrete virus in feces after an OPV challenge. Sequential IPV-OPV immunization is now recommended for routine use in the United States. The optimal schedule consists of two IPV doses followed by two OPV doses.


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.


The Gaza Strip is an area in transition which in the 1960's had a high prevalence of malnutrition and infectious diseases. The infant mortality was approximatively 140 per 1000 live births. Pediatric Services were almost non-existant. Trivalent oral poliovaccine (TOPV) has been used since 1967. Coverage however did not exceed 70%. From 1973 a network of comprehensive Child Health Centers was spread throughout the area, a set of laws was passed which made vaccination obligatory and the community became heavily involved in health education. These measures resulted in a vaccination coverage, from fixed centers, of over 90% of the susceptible infant population. Though infant mortality decreased rapidly, poliomyelitis was less affected and the mean annual incidence of the paralytic disease until
1977 continued to be 10 per 100,000 inhabitants. Two outbreaks caused by poliovirus Type 1 were registered in 1974 and 1976 with an incidence of 18 per 100,000 inhabitants. In these outbreaks 34% and 50% of the affected children, respectively, had received 3-4 doses of (TOPV). A new vaccination schedule was implemented in 1978 combining TOPV and inactivated polio vaccine in the form of an injectable quadruple vaccine. In the first three years following this change the annual incidence of the paralytic disease dropped from 10 to 2.2 per 100,000 inhabitants. In the following 5 years (1981-1985) only 4 cases of paralytic poliomyelitis were discovered, an annual incidence of 0.16 per 100,000 inhabitants. A serosurvey was done in 1980 on 117 immunized children age 6 months to three years.(ABSTRACT TRUNCATED AT 250 WORDS)


The history of polio vaccination in the United States spans 50 years and includes different phases of the disease, multiple vaccines, and a sustained significant commitment of resources. We estimated cost-effectiveness ratios and assessed the net benefits of polio vaccination applicable at various points in time from the societal perspective and we discounted these back to appropriate points in time. We reconstructed vaccine price data from available sources and used these to retrospectively estimate the total costs of the U.S. historical polio vaccination strategies (all costs reported in year 2002 dollars). We estimate that the United States invested approximately US dollars 35 billion (1955 net present value, discount rate of 3%) in polio vaccines between 1955 and 2005 and will invest approximately US dollars 1.4 billion (1955 net present value, or US dollars 6.3 billion in 2006 net present value) between 2006 and 2015 assuming a policy of continued use of inactivated poliovirus vaccine (IPV) for routine vaccination. The historical and future investments translate into over 1.7 billion vaccinations that prevent approximately 1.1 million cases of paralytic polio and over 160,000 deaths (1955 net present values of approximately 480,000 cases and 73,000 deaths). Due to treatment cost savings, the investment implies net benefits of approximately US dollars 180 billion (1955 net present value), even without incorporating the intangible costs of suffering and death and of averted fear. Retrospectively, the U.S. investment in polio vaccination represents a highly valuable, cost-saving public health program. Observed changes in the cost-effectiveness ratio estimates over time suggest the need for living economic models for interventions that appropriately change with time. This article also demonstrates that estimates of cost-effectiveness ratios at any single time point may fail to adequately consider the context of the investment made to date and the importance of population and other dynamics, and shows the importance of dynamic modeling.


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 cost-effective option. At the assumed vaccine prices, all IPV options do not appear to be cost-effective 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: 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.

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.


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

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


Oral polio vaccine (OPV) is recommended for routine immunization in the United States in part because of its ability to induce intestinal and pharyngeal immunity to reinfection. Mucosal immunity produced by OPV and enhanced-potency inactivated polio vaccine (E-IPV) was compared by challenging vaccines with type 1 OPV. Fewer OPV (25%) than E-IPV (63%) vaccinees excreted OPV virus in stool after challenge. The mean stool virus titer was higher and the duration of shedding longer among E-IPV excreters. Only one E-IPV and three OPV vaccinees shed virus in the pharynx after challenge. Prechallenge serum neutralizing antibody levels were not statistically different among E-IPV vaccinees who did and did not shed virus; these levels were much higher than those of OPV vaccinees. Poliovirus-specific IgA levels in stool did not correlate with viral excretion. E-IPV was less effective than OPV in preventing and limiting intestinal infection, even though it induced higher postvaccination serum antibody levels.


BACKGROUND: Although the risk of vaccine-associated paralytic poliomyelitis (VAPP) has remained relatively constant during the past 30 years, estimates of VAPP depend largely on the completeness of reporting to the existing passive surveillance system. The National Vaccine Injury Compensation Program constitutes an alternative system for reporting VAPP, and data available from this system permitted us to evaluate the completeness of the national poliomyelitis surveillance system. METHODS: We compared cases of paralytic poliomyelitis reported to the national surveillance system (maintained by the Centers for Disease Control and Prevention, Atlanta, Ga) with cases recommended for compensation by the National Vaccine Injury Compensation Program, Rockville, Md, and we calculated the observed completeness of reporting to the national system for 1980 through 1991. A capture-recapture method was also used to estimate completeness of reporting, ie, to account for cases potentially missed by both systems. In addition, we reviewed the epidemiology and updated the risk of VAPP based on the most current information on cases of VAPP. RESULTS: From 1980 through 1991, 105 cases of paralytic poliomyelitis were identified by the Centers for Disease Control and Prevention and National Vaccine Injury Compensation Program systems, 98 (93%) of which were VAPP (average, 8.2 cases per year). The observed completeness of reporting to the Centers for Disease Control and Prevention was 94%, and the estimated
completeness of reporting (capture-recapture method) was 81%. The overall risk of VAPP was one case per 2.5 million doses of oral poliovirus vaccine distributed. In the sensitivity analysis, the risk estimates of VAPP remained relatively stable throughout a wide range of assumptions regarding underreporting and specificity of the case definition for paralytic poliomyelitis. CONCLUSION: The risk of VAPP remains virtually unchanged from previous estimates despite the inclusion of previously unidentified VAPP cases. Despite the potential for both underreporting and misclassification of cases, our risk estimates were relatively insensitive to either of these biases. Since both of these biases were in opposite directions, and both probably occurred with low frequency, the risk estimates provided in this report appear valid and approximate the "true" risk of VAPP in the United States.

References for Grading Tables

Table I: Efficacy/effectiveness of oral poliovirus vaccine (OPV) against clinical poliomyelitis


In May 1985, the Pan American Health Organization (PAHO) proposed the goal of interruption of wild poliovirus transmission in the Western Hemisphere by 1990 (1). This proposal was endorsed by all member governments and was supported by several agencies and organizations, including Rotary International, the U.S. Agency for International Development, the United Nations Children's Fund, the Inter-American Development Bank, and the Canadian Public Health Association. On August 20, 1994, PAHO reported that 3 years had passed since the occurrence of the last case of poliomyelitis associated with wild poliovirus isolation in the Americas (Peru, August 1991) (2). This report summarizes the steps to certify eradication of polio in the Americas.


On October 29, 2000, the Regional Commission for the Certification of Poliomyelitis Eradication certified that the Western Pacific Region (WPR) of the World Health Organization (WHO) is free of indigenous wild poliovirus transmission. The last known case of indigenous poliovirus transmission occurred in Cambodia in March 1997 in a 15-month-old girl. WPR is the second of the six WHO regions to be certified as poliomyelitis-free; the first was the Region of the Americas in 1994. WPR comprises 37 countries and territories (Figure 1) with an estimated 1.6 billion persons (27% of the world's population).
Certification of poliomyelitis eradication. Wkly Epidemiol Rec. 2002 Jul 5;77(27):221-3. (No summary)


China began to produce oral, live poliovirus vaccine (OPV) in 1960. During 1960-1964, OPV was introduced in major cities only and subsequently was used throughout the country. Since that time the incidence of poliomyelitis has dropped dramatically, and the percentage of the healthy population with antibody has clearly risen. Data from many observations showed a high rate of isolation of other enteroviruses in the healthy population and in individuals with poliomyelitis. These findings indicate that some paralytic cases may be caused by other enteroviruses. Localized outbreaks of poliomyelitis still occur, however, and their elimination will require a campaign to ensure that greater than 90% of susceptible individuals are immunized.

PIP: Available only in major cities in China during 1960-64, oral, poliovirus vaccine (OPV) now is used throughout the country. Prior to the vaccination program in 1960-64, the average annual incidence of poliomyelitis was 3.18 cases/100,000 population. The incidence dropped to 0.80/100,000 population in 1976-80 and to 0.47/100,000 population in 1981. The incidence of poliomyelitis was reduced markedly in those areas where an expanded immunization program was well administered. The data from a large investigation of poliovirus neutralizing antibody in health populations in Shanghai, Hunan, Henan, and other cities and provinces showed clear elevation of antibody levels as well as good immunologic effectiveness for OPV. The high rate of isolation of other enteroviruses in the health population (16.1% compared with 3.2% for poliovirus) and in persons with poliomyelitis (rate of isolation of poliovirus, 29.5%; other enteroviruses, 13.9%) indicates that some paralytic cases may be caused by other enteroviruses. The eradication of poliomyelitis has not yet been realized in China. Outbreaks in local areas, reported on occasion, influence the national incidence rates. Investigations conducted in several such areas showed that 93% of the affected individuals had not been vaccinated previously. An expanded immunization program is needed.


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.


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.

An epidemic of poliomyelitis caused by poliovirus type 1 occurred in The Gambia from May to November 1986. Descriptive findings and vaccination coverage levels are reported in part I. This article (part II) describes a case-control study to estimate the clinical efficacy of three or more doses of trivalent oral polio vaccine compared with zero doses. "Cases" were 1- to 7-year-old children paralyzed during the epidemic who were diagnosed as having poliomyelitis by designated referral physicians. They were identified by reports from referral physicians during the epidemic and by a nationwide village-to-village search after the epidemic. Up to five controls were randomly selected for each case from among children of the same age and sex living in neighboring households. In a matched analysis of 195 cases and 839 controls, the efficacy of three or more doses of trivalent oral polio vaccine was 72% (95% confidence interval 57-82) when children without vaccination cards were considered unvaccinated. The efficacy of three or more doses in 1- to 2-year-old children, in whom the determination of vaccination status was considered to be more accurate than in older children, was 81% (95% confidence interval 66-90). Vaccine failure was not associated with short intervals between doses. Higher levels of vaccination coverage and efficacy than those achieved in The Gambia may be needed in African countries to prevent the return of poliomyelitis as an epidemic disease after it has been controlled as an endemic disease.

Table II: Birth dose of OPV


To evaluate the efficacy of the schedule currently recommended for immunization with trivalent oral poliovirus vaccine (TOPV) (i.e., at birth, 6 weeks, 10 weeks, and 14 weeks after birth), we randomly assigned 452 infants into test (231 infants) and control (221 infants) groups. The test group received TOPV as currently recommended, and the dose at birth was omitted for the control group. At 10, 14, and 18 weeks of age, the levels of poliovirus neutralizing antibodies as well as seroconversion rates were consistently higher for the test group than for the control group. The final seroconversion rates against poliovirus types 1, 2, and 3 were 83.5%, 91% and 83%, respectively, for the test group and 75%, 83.2%, and 79.1%, respectively, for the control group. The TOPV immunization schedule starting at birth therefore produced better results. Seroconversion rates as well as antibody levels were highest in infants with low maternal antibodies.


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.


Seroprevalence and geometric mean titters (GMTs) were compared at 6 and 10 months after vaccination with monovalent type 1 oral poliovirus vaccine (OPV) at 6 months and trivalent OPV at 7 and 9 months. Group 1 had received 4 doses of OPV, group 2 OPV at birth and 3 doses of OPV and inactivated poliovirus vaccine (IPV), and group 3 placebo at birth and 3 doses of IPV. A total of 547 infants completed the study. At 10 months, seroprevalence to poliovirus type 1 was 98%, 99%, and 98% in groups 1, 2, and 3; 100%, 100%, and 98% to poliovirus type 2; and 80%, 96%, and 91% to poliovirus type 3. Differences in seroprevalence among the groups were significant for poliovirus type 3 (P < .001). Between 6 and 10 months, significant increases in seroprevalence and GMTs occurred for poliovirus type 1 but not for types 2 and 3. Two OPV doses following 3 IPV doses did not significantly increase seroprevalence or raise GMTs for poliovirus types 2 and 3; however, significant increases were found for poliovirus type 1, which may have benefitted from monovalent type 1 administration.


The study was carried out to evaluate the efficacy of IPV in neonates and to study the additive effect of IPV or OPV at birth on seroconversion with three subsequent doses of OPV. Addition of IPV or OPV at birth to the conventional OPV schedule resulted in significantly higher seroconversion rates than in the controls, who received three doses of OPV. Three doses of IPV beginning from birth resulted in significantly better seroconversion rates than in the control group. Children receiving 3 doses of IPV showed significantly greater seroconversion rates against type III poliovirus than those receiving IPV/OPV at birth followed by 3 doses of OPV. The difference in the seroconversion rates against the other virus types was not significant. A significantly greater number of children who received some vaccine at birth (IPV or OPV) were protected against poliomyelitis by 6 weeks age as compared to those who received no immunization at birth. The study recommends that seroconversion rates following three doses of IPV are satisfactory. Addition of IPV or OPV at birth to the conventional schedule markedly increases the seroconversion rates. Immunization can be started at birth to ensure early protection against poliomyelitis.

This study was done to assess the response of newborns to trivalent oral polio vaccine and to study any efficacy of OPV if given to infants on third day of life. The study was conducted in two groups, A (87) and B (55) of infants in Delhi, India. In group A, the children received one birth dose or 'O' dose of TOPV, followed by 3 conventional doses started at 6 weeks, and in group B the children received only 3 doses of OPV. Pre and one month post immunization serum samples were tested for the presence of neutralising antibodies. In addition, in group A serum samples were collected at 6 weeks before the administration of 1st dose to see the sero response following 'O' dose of TOPV. It was found that administration of OPV on 3rd day of life leads to sero conversion in 15.3% of infants to all three polio virus types by the age of 6 weeks, and highest sero response was seen for polio virus type 1. Sero-conversion in group A was significantly more than sero-conversion in group B after the administration of last dose. Thus the study has established that immunization of newborns with TOPV is a safe and effective means for improving protection against the disease.


Described is the evaluation in Brazil of the immune response of early immunization with trivalent oral poliovirus vaccine (TOPV). A total of 85 normal neonates from São Paulo were assigned one of the following immunization schedules: group A--one dose of TOPV at birth and subsequent doses at 2, 4, and 9 months of age; or group B--one dose of TOPV at 2, 4 and 6 months of age. Blood samples were collected sequentially from the mother at delivery, from the umbilical cord, and from the child at 2, 4, 6, 9 and 12 months of age for assay of poliovirus neutralizing antibodies. Administration of TOPV at birth, in addition to establishing immunity against poliomyelitis at an earlier stage, produced a superior immune response to poliovirus type 3. At the end of the first year, the proportion of susceptible individuals was 3.7% in group A and 25.9% in group B. When immunization against poliomyelitis is started at birth, excellent seroconversion rates are obtained from the third dose onward.

Table III: Persistence of protective antibodies following immunization with OPV or IPV

*Literature on duration of protection: OPV*

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.


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-year-old 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 entrants to present evidence of having received at least two doses of measles vaccine, with one on or after entry into elementary school.

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


Summary objectives: We evaluated antibody prevalence to measles, polio 1 and 3, and tetanus toxoid antibodies in 8–9 year-old children in The Gambia within the framework of the Gambia Hepatitis Intervention Study (GHIS), a large vaccine trial aimed at evaluating vaccine efficacy against hepatitis B virus (HBV) infection, chronic carriage and primary liver cancer in a high risk population. The results of the present survey were compared with a previous survey performed with the same objectives and same methodology but in different children at 3–4 years of age.

Methods: Four clusters of 200 children each were sampled as representative of the whole country. Children would have received BCG, diphtheria–pertussis–tetanus vaccine (DPT), poliovirus vaccine (OPV), measles and yellow fever immunization. The measles haemoagglutination inhibition test (HAI) was used to detect measles antibody. Antibodies to polioviruses 1 and 3 were tested using the standard polio neutralization assay described in the EPI manual (WHO 1990). An enzyme-linked immunosorbent assay (ELISA) was used to measure tetanus toxoid antibodies.

Results A high proportion of children were fully vaccinated in both age groups. Measles antibody concentrations were ≤ 1:8 in 8.2% of 8–9 year-old vaccinated children. In the previous survey of 3–4 year-old children this was 11.3%. In the present survey, GMC was lower than in the 3–4 year-old children; 88% of 3–4 year-olds and 89% of 8–9 year-olds had detectable antibody levels against poliovirus type 1. Fewer children at 8–9 years of age had antibodies against poliovirus type 3 than 3–4 year-olds (78% vs. 89% P < 0.001). A significant overall lower proportion of 8–9 year-old children had detectable tetanus toxoid antibodies compared to 3–4 year-old children (87% vs. 95% P < 0.001), as well as those who received four doses of DPT (90% vs. 97% P < 0.001).

Conclusions: High vaccine coverage is achieved in The Gambia with EPI. With time the number of vaccinated children who are not protected against measles, poliovirus 3 and tetanus increases. Besides the maintenance of high vaccine coverage in infants and young children, booster doses of some of the EPI vaccines in adolescents should be considered.

A nation-wide cross-sectional survey of 816 children 3-4 years old was carried out in The Gambia between September 1990 and July 1991 to assess the seroprevalence of antibodies against 3 diseases included in the expanded programme on immunization: measles, poliomyelitis and tetanus. Among 689 children whose records were available, 94.5% were fully immunized. Measles vaccine was administered to 97% of the children and 91% of these had detectable antibodies at the time of the survey. Antibodies against type 1 and type 3 polioviruses, after up to 6 doses of oral polio vaccine, were present in 88.1% and 89.3% of the children respectively. Ninety-seven percent of the children who had received 4 doses of diphtheria-pertussis-tetanus vaccine (DPT) and 91% of those who received 3 doses had detectable tetanus toxoid antibodies at the age of 3-4 years. This study shows that serological responses to EPI vaccines given in infancy persist at very satisfactory levels throughout early childhood.

Literature on duration of protection: IPV


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


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.


A five-year serologic follow-up and a four-year monitoring of the polio and pertussis morbidity in an area immunized with a 2 + 1 dose schedule of a combined DTP-Po vaccine have shown that: the individual protection against polio measured by the presence of neutralizing antibody persists at a very adequate level five years after the first booster; after three years of a steady high proportion of children with pertussis antibody, a considerable drop is observed and in about 28% of individuals agglutinin levels of less than 1:20 were found five years after booster; the community protection against paralytic poliomyelitis and pertussis is satisfactory up to four years after the introduction of the program. Continuation of immunization with a 2 + 1 dose schedule at a maximal coverage and close seroepidemiologic surveillance are necessary in order to draw definite conclusions, because of the potentially strong impact of very dynamic ecological factors present in our geopolitical area upon the agent-host interrelationship.


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, Matisse N, Pacoret P, Undreiner F, Boisnard F, Soubeyrand B; Pentavac study group. 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: immunogenicity and tolerance of second booster with a tetravalent acellular vaccine at 5-6 years of age. Vaccine. 2004 Mar 29;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 (DTwcP-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).

Table IV: Efficacy/effectiveness of inactivated polio vaccine (IPV) against clinical poliomyelitis


Combined diphtheria-tetanus-pertussis (DTP)-killed poliovirus vaccine was used (along with bacille Calmette-Guérin, measles, yellow fever, and smallpox vaccines) in a routine immunization program in a rural area of Senegal. A control group in a neighboring region received DTP vaccine without poliovirus vaccine. All immunizations were given at two
sessions six months apart by a small mobile health team led by a nurse. Six months after the second dose of DTP-polio vaccine, 97.4%, 97.7%, and 90% of subjects two to eight months old at the start had detectable antibody to poliovirus types 1, 2, and 3, respectively. In the control group, 50%, 38%, and 80% of such subjects had antibody to poliovirus types 1, 2, and 3, respectively, acquired by natural infection during the study year. An average of 3.9 cases of paralytic poliomyelitis (range, one to 13) were observed annually at one dispensary in the test region from 1966 through 1979. From 1980 through 1982, since the immunization program has been in effect, only one case has been observed (in a nonimmunized child).


During the period 1950-1954, surveillance for paralytic poliomyelitis in Canada revealed an average of 1,914 cases (13.2 cases per 100,000) annually. The licensing and widespread use of inactivated poliovirus vaccine (IPV) in 1955 coincided with a marked decline in disease rates. Due to incomplete vaccine coverage of the population, a resurgence began in 1958 and peaked in 1959, despite an observed vaccine efficacy of 96% for 3 doses of IPV. The introduction and widespread use of oral poliovirus vaccine (OPV) started in 1960 and coincided with a decline in disease rates. Virtual elimination of the natural disease was achieved in the 1970s in all provinces regardless of the specific immunization program chosen (IPV or OPV alone or combined). From 1965 to 1988, 51 cases of paralytic poliomyelitis were reported in Canada. Thirty-five of these cases, all but one occurring before 1980, were attributed to wild virus infection, (14 caused by imported virus and 21 assumed to be endemic). Sixteen cases were OPV-associated: 4 in vaccine recipients and 12 in contacts of OPV recipients. Vaccine-associated paralysis in recipients and contacts occurred at the rate of one case per 9.5 million and 3.2 million vaccine doses distributed, respectively. The risk of paralysis attributable to OPV therefore is small compared to the overall benefit of the vaccine. Both IPV and OPV appear equally effective, and theoretically, a combination of the two (IPV followed by OPV) provides the best risk benefit ratio. Occasional exposure of the Canadian population to imported wild virus requires that high levels of population immunity be maintained.

Table V: Sequential administration IPV-OPV

Literature on the necessity of two doses

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.


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


BACKGROUND: The immunogenicity of inactivated poliovirus vaccine (IPV) in developing countries is not well documented. This study compared the immune response to IPV with that to oral polio vaccine (OPV) in Guatemalan infants. METHODS: This was an open-label, randomized comparison of IPV only, OPV only, or IPV followed by OPV in Guatemalan public health clinics. Serum samples were tested for neutralizing antibodies, and stool samples were tested for Sabin strain polioviruses. RESULTS: Seropositivity rates 2 months
after 2 doses of IPV were 98%-100% for polio types 1, 2, and 3 and were 97.1%, 99.3%, and 92.1% for OPV-only recipients (P<.001 for the response to type 3). One month after the third dose, 100% of IPV-only recipients had protective antibodies against all 3 types, compared with 99%, 100%, and 97% against polio types 1, 2, and 3 respectively, among recipients of OPV only. Infants who received IPV only had higher geometric mean titers than infants who received OPV only. Maternal antibodies lowered the final antibody responses to IPV but did not prevent the development of protective levels of antibody. Of 191 stool samples from infants who received IPV only, 5 (2.6%) were positive for poliovirus vaccine strains.

CONCLUSIONS: IPV alone and IPV followed by OPV are safe and effective for Guatemalan infants.

*Literature on immunogenicity of sequential IPV-OPV administration*


The relative immunity induced by sequential administration of inactivated poliovirus vaccine (IPV) produced in human diploid cells and live attenuated oral poliovirus vaccine (OPV) was evaluated by randomization of 510 infants to receive IPV and OPV sequentially according to one of three experimental schedules, IPV only, or OPV only. The antibody response to two IPV doses was lower than expected. However, for each of the IPV-OPV sequential schedules, the first OPV dose significantly enhanced seroconversion rates and geometric mean microneutralization antibody titers. Three months after the final dose, 96%-99%, 99%-100%, and 81%-100% of infants had antibodies to poliovirus types 1, 2, and 3, respectively, and subjects with two or more prior OPV doses were significantly less likely than those with none or one prior OPV dose to excrete virus in feces after an OPV challenge. Sequential IPV-OPV immunization is now recommended for routine use in the United States. The optimal schedule consists of two IPV doses followed by two OPV doses.


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.

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


A combined enhanced inactivated polio vaccine (EIPV) and oral polio vaccine (OPV) programme was introduced in Israel in 1990, with the purpose of providing a solution to the persistent polio morbidity in spite of a 30 year long OPV programme. The schedule comprised two doses of EIPV administered at the age of 2 and 4 months, intercalated with two doses of OPV at 4 and 6 months, followed by a reinforcing dose with the two vaccines simultaneously administered at 12 months. The 5-year evaluation of the programme included: the assessment of clinical suspicions of polio, early immune response in successive cohorts administered the new schedule, dynamics of the immune profile in a cohort followed up to the age of 5, and monitoring of wild poliovirus excretion in sewage specimens collected in 25 permanent sites throughout Israel as well as from the Palestinian Authority. No paralytic polio cases associated with a wild or vaccinal poliovirus strain were detected since the introduction of the programme. At the age of 4 months, one week after administration of the second EIPV and first OPV dose, 100% seropositivity and high geometric mean titres (GMTs) of neutralizing antibody (NA) to the three vaccinal and to the wild poliovirus type 1, responsible for the 1988 polio outbreak, were observed. No change in percent of seropositivity occurred between the age of 6 and 12 months. Thirty days after the IPV and OPV reinforcing doses, GMTs to each of the four poliovirus strains were > or = 3037. Up to the age of 5, the seropositivity was unchanged. After a 2.5-10-fold decline in the first year following the completion of the programme, GMTs to the three vaccinal and the wild poliovirus strain levelled off at rather high values, considered protective. Between 1990 and 1995, 16 wild poliovirus type 1 strains were isolated in three separate episodes in Gaza Strip sewage and once only in one Israeli site very close to Gaza City. The rapidly established, high and persistent NA titre to the vaccinal and wild poliovirus strains and the presence of immunological memory are indicative of high individual protection throughout the first 5 years of life. The only one-time introduction, without circulation, of a wild poliovirus strain in a single Israeli settlement suggests community protection. The intercalated programme offers a contribution to polio eradication by providing a solution to the primary and secondary
failure associated with OPV, as well as to the control of vaccine-associated paralytic poliomyelitis.


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.


BACKGROUND AND PURPOSE: Though inoculation with inactivated poliovirus vaccine (IPV) is advocated, sequential use of IPV and live oral poliovirus vaccines (OPV) has many advantages. This study aimed to define the immunogenicities of IPV and OPV in Taiwanese children after the use of a sequential schedule of IPV-OPV and also to determine whether prior IPV inoculation hampers the fecal passage of OPV. METHODS: Fifty-nine infants were recruited to receive IPV-OPV sequential vaccinations consisting of IPV given at the ages of 2 and 4 months and OPV given at the ages of 6 and 18 months. Blood samples were taken at ages 2, 6, 18, and 19 months for antibody determination, and stool samples were collected to isolate vaccine strains of poliovirus after the second dose of OPV, at the age of 18 months. RESULTS: None of the children had severe systemic or local reactions. Protective antibodies were detected in all infants at the age of 6 months, 2 months after the second IPV dose. The antibody titers were augmented at the age of 19 months, 1 month after the booster dose of OPV. Stool samples collected 7 days after the second dose of OPV yielded at least one type of poliovirus in 9 of 18 children. Analysis of stool samples revealed that poliovirus was excreted by the 28th day in only two of the children. CONCLUSIONS: Our study showed that both IPV and OPV exhibit immunogenicity in Taiwanese children. Side effects of an IPV-OPV sequential schedule were mild and infrequent. Viral shedding in stools after OPV vaccination was preserved in a substantial proportion of subjects. These findings suggest that this sequential vaccination schedule can maintain herd immunity.