Polio vaccines. Grading tables

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

**Settings:** Global

**Question:** What is the evidence that oral poliovirus vaccine (OPV) protects against clinical poliomyelitis?

**Conclusion:** High scientific evidence that OPV protects against clinical poliomyelitis

<table>
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<th>Quality assessment</th>
<th>Summary of Findings</th>
<th>Importance</th>
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<tbody>
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¹ With observational studies, the level of scientific evidence will not normally exceed “low” according to the Grade system. However, as argued below, due to overwhelming historical evidence, the level of scientific evidence for the protective effectiveness of OPV was upgraded from “low” to “high”.

The success of the OPV in curtailing polio epidemics and reducing or even eliminating the disease in endemic countries provides overwhelming evidence of the effectiveness of polio vaccines, in particular OPV. Thus, following extensive immunization and other control measures three of the six WHO regions are already certified as free of indigenous wild poliovirus transmission (see Certifications of poliomyelitis eradication 1994, 2001, and 2002), wild poliovirus serotype 2 is eradicated, and the endemic circulation of wild polioviruses types 1 and 3 is now restricted to small geographic areas within 4 countries.

As examples of the vast literature in the field, 4 country-based reports are included that illustrate the dramatic overall impact of OPV on the incidence of poliomyelitis, but also illustrate that OPV-induced immunity may vary considerably between countries. The biological reasons for these geographic differences remain unclear.

Dong DX et al (1984) reported that 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.
Sutter RW et al (1991) conducted a case-control study of an outbreak in Oman where the incidence of paralytic disease in children aged < 2 years had reached 87/100,000, despite a coverage with 3 doses of OPV among 12-month-olds that recently had risen from 67% to 87%. It was found that 3 doses of OPV reduced the risk of paralysis by 91% against the imported outbreak strain.

Heymann DL et al (1987) provided proof of the considerable herd immunity effects of OPV in a study in Yaoundé, Cameroon, where the incidence of paralytic polio decreased by 85%, although only 35% of children 12-13 months of age had received 3 doses of the vaccine.

Deming MS et al (1992) conducted a case-control study in The Gambia. 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). 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).

Selected literature


**Polio vaccines. Grading tables**

**Table II: Birth dose of OPV**

**Settings:** Global

**Question:** What is the evidence that the immunological response to OPV schedules starting with a birth dose is at least as immunogenic as otherwise comparable OPV schedules starting at 6-8 weeks of age?

**Conclusion:** High scientific evidence that OPV schedules starting with a birth dose are at least as immunogenic as otherwise comparable OPV schedules starting at 6-8 weeks of age.

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1 Randomized controlled

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*Osei-Kwasi M et al (1995) conducted a randomized, controlled trial of antibody levels and seroconversion rates among 452 infants who received trivalent oral poliovirus vaccine at 6, 10, and 14 weeks of age, with or without a preceding birth dose. At 10, 14, and 18 weeks of age, the levels of poliovirus neutralizing antibodies as well as seroconversion rates were consistently higher among those who received the additional birth dose (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). Seroconversion rates as well as antibody levels were highest in infants with low maternal antibodies.

*Bhaskaram P et al (1997)* showed that administration of the additional dose in the newborn period significantly improved seropositivity and seroconversion rates compared to the conventional 3 or 5 dose schedules. (Exact figures not provided in summary).

*Sutter RW et al (1997)* studied the sequential use of inactivated polio vaccine followed by oral vaccine in Oman and found no difference in seroprevalence and geometric mean titers between those who had and those who had not received a birth dose.

*Jain PK et al (1997)* found that adding OPV (or IPV) at birth to the conventional schedule markedly increases the seroconversion rates, and that 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.
Khare S et al (1993) compared the sero-conversion rates among 87 infants (Group A) who were OPV-vaccinated on day 3 after birth in addition to receiving the conventional 3 OPV doses starting at 6 weeks of age, whereas 55 infants (Group B) received the conventional 3 OPV doses only. 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.

Weckx LY et al (1992) evaluated the neutralizing antibody response of trivalent OPV among 85 neonates in São Paulo, divided randomly into two groups. Group A received tOPV at birth and at 2, 4, and 9 months of age, and Group B received tOPV at 2, 4 and 6 months of age, only. Group A showed a superior response to poliovirus type 3. After 1 year, there were 3.7% susceptibles (lacking neutralizing antibody) in Group A and 25.9% in Group B. In Group A, excellent seroconversion rates were obtained from the third dose onward.

Literature


Polio vaccines. Grading tables

Table III: Persistence of protective antibodies* following immunization

With OPV or IPV

Settings: Global

Question: What is the level of scientific evidence for ≥80% long-term (>5-10 years) persistence of protective antibodies following ≥3-4 doses of OPV or IPV before school age, according to national schedules?

Conclusions: Low scientific evidence for ≥80% long-term (>5-10 years) persistence of protective antibodies following ≥3-4 doses of OPV or IPV.

*Presence of neutralizing antibodies against poliovirus is a reliable marker of protection against poliomyelitis

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¹With observational studies, the level of scientific evidence will not normally exceed “low”, according to the Grade system

1. Persistence of protective antibodies following ≥3-4 doses of OPV before school age

Nishio O et al (1984) investigated the persistence of neutralizing antibody (NA) against poliovirus after two doses of OPV in 67 children. After 5 years, more than 80% of them retained NA against all three types of poliovirus.

Kelley PW et al (1991) using micro-neutralization assay to investigate susceptibility to poliovirus types 1, 2, and 3 among young US Army recruits believed to have received polio vaccination (mainly OPV) 15-25 years earlier. The seronegativity rates for poliovirus types 1, 2, and 3 were 2.3%, 0.6%, and 14.6%, respectively; deviating trends by age, sex, and race-ethnicity were generally unremarkable.
Faden H et al (1993) found that immunization with OPV, eIPV, and combinations of the two vaccines confers long-term (>5 year) immunity.

Viviani S et al (2004) studied vaccine-induced antibody prevalences in representative samples of 8–9 year-olds as compared to 3–4 year olds (Fortuin M et al, 1995) in The Gambia. The geometric mean concentration of antibodies in children 8-9 years of age 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).

2. Persistence of protective antibodies following ≥3-4 doses of IPV before school age

Faden H et al (1993) found that all of the 86 children who by one year of age had received 3 doses of OPV and/or eIPV according to one of 4 different schedules (OPV-OPV-OPV, eIPV-eIPV-eIPV, eIPV-OPV-OPV, and eIPV-eIPV-OPV) 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.

Böttiger M (1990) found persisting neutralizing antibodies against polio in all of the 250 Swedish children who had received 3 doses of killed polio vaccine (IPV) 18 years earlier. Among 64 children who were tested more frequently, a marked fall of antibody titers was observed during the first few years after vaccination, then the decline leveled off to a mean decrease in titer of 0.05-0.10 log10 per year. Children who had a fourth dose of IPV at 10 years of age rather than at the scheduled age of 6 years had significantly higher antibody levels at 18 years of age.

Swartz TA et al (1986) showed adequate levels of neutralizing antibody persisting for five years after immunization with a 2 + 1 dose schedule of a combined DTP-IPV vaccine.

Carlsson RM et al (2002) found neutralizing antibodies against polioviruses in 96% - 99% of 180 vaccinees who 4.5 years earlier had received IPV-containing combination vaccines. There were no clinically relevant differences between children who had been vaccinated in their infancy according to a 3, 5 plus 13 months schedule versus a 2, 4, 6 plus 12 months schedule.

Langue J et al (2004) evaluated the persistence among 5-6 year old French children of antibodies against poliovirus types 1, 2, and 3 following primary immunization at 2 and 4 months and subsequent booster doses at 12-16 months and 5-6 years, using an IPV-containing tetravalent vaccine. Before the second booster, more than 90%, and 1 month after the second booster 100% of children had protective antibody titers.

1. Literature on duration of protection: OPV


2. Literature on duration of protection: IPV


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.

Polio vaccines. Grading tables

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

**Settings:** Global

**Question:** What is the evidence that inactivated poliovaccine (IPV) protects against clinical poliomyelitis?

**Conclusion:** High scientific evidence that IPV protects against clinical poliomyelitis.

<table>
<thead>
<tr>
<th>No of studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
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Francis T et al (1955, as cited by Plotkin S et al 2008) conducted a major field trial in the USA in 1954 that involved about 400,000 children, randomly assigned to IPV or placebo. A related, non-randomized study by the same authors involved another 200,000 children who were vaccinated and observed together with unvaccinated children. Altogether, 71 cases of paralytic polio occurred in vaccinated individuals versus 445 among unvaccinated individuals. In the placebo controlled trial, 11 cases of polio occurred among vaccines as compared to 70 cases in the control group. The calculated vaccine efficacy was 80%-90% against paralytic polio and 60%-70% against all types of polio.

Melnick JL et al (1961) calculated an efficacy of 96% through two polio seasons in Huston, Texas, whereas in a case-control analysis following a polio type 1 outbreak in Senegal, two doses of combined dTwP-IPV conferred 89% (96% CI 62-97) protection (MMWR 1988).

Stoeckel P et al (1984) studied the protective efficacy IPV among children in a rural area of Senegal. During the 3 year observation period following vaccination, no case of polio occurred in the vaccinated group. During the preceding 13 years an average of 3.9 cases of paralytic poliomyelitis (range, one to 13) were observed annually in the test region.
John T et al (1992) showed an IPV efficacy of 92% in a case-control study in India

Varughese PV et al (1989) found more than 90% vaccine efficacy following the introduction of this vaccine in Canada.

Literature:


Polio vaccines. Grading tables

Table V: Sequential administration IPV-OPV

**Settings:** Global

**Question:** What is the quality of scientific evidence that 1) sequential immunization schedules starting with two or more doses of IPV* and followed by two or more doses of OPV induce protective immune responses to all three poliovirus serotypes in ≥ 90% of vaccines, (i.e. responses comparable to those induced by the same number of doses of either OPV or IPV alone

* At least two doses of IPV are necessary to induce >90% protective antibody against polioviruses before the first dose of OPV is administered (McBean AM et al 1988; Faden H et al 1993; Asturias EJ et al (2007).

**Conclusion:** 1) Moderate level of scientific evidence that sequential immunization schedules starting with two or more doses of IPV and followed by two or more doses of OPV induce protective immunological responses to all three poliovirus serotypes in ≥ 90% of vaccines.

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<tr>
<td>5</td>
<td>Observational</td>
<td>No serious</td>
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</tbody>
</table>

¹ With observational studies, the level of scientific evidence will not normally exceed “low”, according to the Grade system

1. **Immunological impact of sequential administration:**

*Modlin JF et al (1997)* showed in a randomized controlled study of 510 infants, that for each of the 3 IPV-OPV experimental sequential schedules, the first OPV dose significantly enhanced seroconversion rates and geometric mean micro-neutralization 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. It was concluded that the optimal schedule consists of two IPV doses followed by two OPV doses.
Faden H et al (1990) showed that incorporation of at least one dose of IPV at the start of the immunization schedule tends to increase systemic as well as local antibody production.

Faden H et al (1993) showed that as compared to OPV-OPV-OPV, elIPV-elIPV-elIPV, elIPV-OPV-OPV, and elIPV-eIPV-OPV those receiving the elIPV-eIPV-OPV schedule maintained the highest antibody levels throughout the observation period, including the response to OPV challenge at 5 years of age.

Swartz TA et al (1998) assessing the effectiveness of an intercalated IPV-OPV vaccine programme in Israel concluded that the programme offered high individual protection throughout the first 5 years of life.

von Magnus H et al (1984) reported that in Denmark, where a sequential 3-dose IPV-3 dose OPV immunization programme had been practiced since 1968, greater than 95% of the population had antibodies to poliovirus, and the geometric mean titer of serum antibodies exceeded 10 IU for all three types.

Lu CY et al (2001) showed that protective antibodies were present in all infants at the age of 6 months, 2 months after the second IPV dose, and that the antibody titers were augmented at the age of 19 months, 1 month after the booster dose of OPV.

1. Literature: Immunogenicity of sequential IPV-OPV administration


