Inactivated poliovirus vaccine (IPV) is efficacious against paralytic disease, but its effect on mucosal immunity is debated. We assessed the efficacy of IPV in boosting mucosal immunity. Participants received IPV, bivalent 1 and 3 oral poliovirus vaccine (bOPV), or no vaccine. A bOPV challenge was administered 4 weeks later, and excretion was assessed 3, 7, and 14 days later. Nine hundred and fifty-four participants completed the study. Any fecal shedding of poliovirus type 1 was 8.8, 9.1, and 13.5% in the IPV group and 14.4, 24.1, and 52.4% in the control group by 6- to 11-month, 5-year, and 10-year groups, respectively (IPV versus control: Fisher’s exact test P < 0.001). IPV reduced excretion for poliovirus types 1 and 3 between 38.9 and 74.2% and 52.8 and 75.7%, respectively. Thus, IPV in OPV-vaccinated individuals boosts intestinal mucosal immunity.

![Image](http://science.sciencemag.org/content/345/6199/922/f1.large.jpg)

**Table 1. Demographic characteristics and baseline prevalence of poliovirus antibodies (n = 954).**

<table>
<thead>
<tr>
<th>Study group/age group</th>
<th>Median age (years) (IQR)*</th>
<th>Gender</th>
<th>Father’s education</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>[% male (95% CI)]</td>
<td>[% illiterate (95% CI)]</td>
</tr>
<tr>
<td>IPV</td>
<td>5.4 (0.9–10.2)</td>
<td>45.9 (40.3–51.6)</td>
<td>45.1 (39.5–50.8)</td>
</tr>
<tr>
<td>bOPV</td>
<td>5.5 (0.9–10.2)</td>
<td>47.7 (42.1–53.3)</td>
<td>44.9 (39.3–50.8)</td>
</tr>
<tr>
<td>Control</td>
<td>5.5 (0.9–10.2)</td>
<td>49.2 (43.6–54.9)</td>
<td>43.5 (37.9–49.2)</td>
</tr>
<tr>
<td>6–11 months</td>
<td>0.8 (0.7–0.9)</td>
<td>45.8 (40.1–51.5)</td>
<td>44.2 (38.5–49.9)</td>
</tr>
<tr>
<td>5 years</td>
<td>5.4 (5.2–5.7)</td>
<td>48.8 (43.2–54.3)</td>
<td>44.3 (38.8–49.9)</td>
</tr>
<tr>
<td>10 years</td>
<td>10.4 (10.2–10.6)</td>
<td>48.1 (42.5–53.8)</td>
<td>45.0 (39.4–50.6)</td>
</tr>
</tbody>
</table>

**Table 2. Seroprevalence.**

<table>
<thead>
<tr>
<th>Type</th>
<th>Overall</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPV</td>
<td>99.6 (98.9–99.9)</td>
<td>99.7 (98.2–100)</td>
<td>99.4 (97.9–99.9)</td>
<td>99.7 (98.3–100)</td>
</tr>
<tr>
<td>bOPV</td>
<td>91.6 (89.7–93.3)</td>
<td>92.1 (88.5–94.8)</td>
<td>89.1 (85.2–92.3)</td>
<td>93.7 (90.4–96.1)</td>
</tr>
<tr>
<td>Control</td>
<td>93.3 (91.5–94.8)</td>
<td>94.6 (91.9–96.8)</td>
<td>91.0 (87.3–93.9)</td>
<td>94.3 (91.2–96.6)</td>
</tr>
</tbody>
</table>

| Type 1 | 99.7 (97.2–99.9) | 99.7 (97.9–99.9) | 99.6 (98.2–100) |
| Type 2 | 99.4 (97.9–99.9) | 99.4 (97.3–100) | 99.4 (98.3–100) |
| Type 3 | 99.7 (98.3–100) | 99.7 (98.3–100) | 99.7 (98.3–100) |

**Corresponding author:** E-mail: sutterr@who.int

---

1World Health Organization, India-National Polio Surveillance Project, R. K. Khanna Stadium, Africa Avenue, Safdarjung Enclave, New Delhi 110029, India. 2EnteroVirus Research Center, Hafkine Institute Compound, Parel, Mumbai, India. 3World Health Organization, Ave Appia, Geneva, Switzerland. 4Panacea Biotec Ltd., New Delhi, India. 5Centers for Disease Control and Prevention, Atlanta, GA, USA. 6Department of Infectious Disease Epidemiology, Imperial College London, London, UK. 7Division of Polio Eradication, World Health Organization, CH-1211 Geneva 19, Switzerland. 8Present address: Biological E Ltd., Hyderabad, India.
gender, father’s education, or baseline sero-
prevalence levels, which was high (≥99%) for type 1 and somewhat lower for types 2 and 3, particularly in the youngest age group (Table 1).

The prevalence of poliovirus excretion for type 1 and 3 after challenge with bOPV is shown in table S1. For poliovirus type 1, the highest prevalence was 43.8% [95% confidence interval (CI) 34.1–53.8] in 10-year-olds in the control group compared to 7.7% (95% CI 3.4–14.6) in the IPV group (Fig. 1). Excluding participants excreting virus on day 0 (n = 17) produced similar results.

The relative reduction in excretion between IPV group and control group was markedly consistent across the poliovirus types. For poliovirus type 1, the decrease in excretion in any stool sample after challenge in the IPV group compared to the control group was 38.9% (8.8% versus 14.4%) in the 6- to 11-month, 62.2% (9.1% versus 24.1%) in the 5-year, and 74.2% (13.5% versus 52.4%) in the 10-year age group; the corresponding decreases for poliovirus type 3 were 71.1% (3.9% versus 15.4%) in the 10-year age group (table S1).

bOPV significantly decreased excretion of type 1 by 51.9% and type 3 by 40.5% only in the 10-year age group (Fisher’s exact test P < 0.001 for type 1; P = 0.002 for type 3).

For poliovirus type 1, the median duration of excretion was estimated to be 7.6 days (95% CI 6.0–10.1 days) for the IPV group, 8.7 days (95% CI 7.3–10.5) in the control group, and 9.1 days (95% CI 7.4–11.4) in the bOPV group. For poliovirus type 3, the median duration was 10.4 days (95% CI 7.4–15.4) for the IPV group, 13.1 days (95% CI 10.1–17.4) in the control group, and 11.6 days (95% CI 9.0–15.4) in the bOPV group. None of these differences were statistically significant (table S2).

The median virus titers among participants excreting poliovirus type 1 were highest 7 days after challenge, ranging from 4.1 log_{10} CCID_{50} (50% cell culture infectious dose) per gram of stool (95% CI 3.5–4.7) in the control group to 3.8 log_{10} CCID_{50} (95% CI 2.1–5.4) in the IPV group, a decrease of 49.9% (Wilcoxon rank-sum test P = 0.872). The median titers to poliovirus type 3 were 4.1 log_{10} CCID_{50} (95% CI 3.6–4.5) in the control group compared to 3.4 log_{10} CCID_{50} (95% CI 2.6–4.2) in the IPV group, a decrease of 80.0% (P = 0.043) (table S3). The relative reduction in the prevalence of excretion in the IPV group compared to the control group was between 38.9 and 75.7%, the absolute decrease in median titer of virus in stool specimens was between 0.3 and 0.7 log_{10} CCID_{50} (at day 7 after challenge), and the absolute decline in length of excretion was between 1.1 and 2.7 days (Fig. 2).

Four weeks after vaccination, an IPV dose induced a humoral immune response (i.e., seroconversion or fourfold increase in antibody titer) to poliovirus type 1 in 82.9% (95% CI 67.9–92.8), 98.2% (95% CI 90.6–100), and 95.6% (89.1–98.8) of participants in the 6- to 11-month, 5-year, and 10-year age groups, respectively, compared to 2.9% (95% CI 0–15.3), 3.1% (95% CI 0.3–10.8), and 0% (95% CI 0–4.2) in the control group (Fisher’s exact test P < 0.001 for all age groups). A bOPV dose induced a humoral immune response in 14.3% (95% CI 4.8–30.3), 12.9% (95% CI 5.7–23.9), and 42.4% (32.1–53.1) of participants (P = 0.198 for the 6- to 11-month group, P = 0.052 for the 5-year group, and P < 0.001 for 10-year group, compared to control group; significantly lower than the IPV group, P < 0.001 for all age groups). Similar levels in humoral response were noted against poliovirus type 3 (Table 2).

We divided the antibody titers into quartiles and assessed the excretion prevalence in each quartile. Because the antibody titers were high, we collapsed quartiles 3 and 4 (where the median titers were at the final dilution tested, ≥1:1448). The overall excretion of poliovirus type 1 was 0 (n = 1), 18.2, and 9.9% in quartiles 1, 2, and 3-4, respectively, in the IPV group compared to 40.8, 26.5, and 12.9% in the control group and 30.7, 28.4, and 13.0% in the bOPV group, respectively (test for overall trend: Fisher’s exact test P < 0.001). Similar trends were found for poliovirus type 3.

Our trial provides the following insights: (i) A single dose of IPV boosts intestinal mucosal
immunity against polioviruses in infants and children with a history of multiple doses of OPV; (ii) the magnitude of this effect is substantially larger after IPV compared to bOPV; and (iii) the oldest age group displayed the highest degree of waning intestinal mucosal immunity manifested by highest prevalence of excretion after challenge.

Although IPV reliably induces humoral immunity (18–20) that is highly efficacious in preventing paralytic poliomyelitis (21, 22), the ability of IPV alone to induce intestinal mucosal immunity is limited (23, 24). Studies in countries that do not use OPV show that >90% of IPV-vaccinated children excrete challenge poliovirus (25, 26). Limited data are available on IPV effectiveness in boosting intestinal mucosal immunity in children with a history of multiple doses of OPV (19, 27, 28). Live virus contact to mucosal surfaces appears necessary to induce a specific secretory immunoglobulin A response (29, 30).

The most important comparisons are between the IPV and the control group, where a decrease in the prevalence of excretion of 39 to 76% was found in the IPV group compared to the control group. The decrease after a dose of bOPV was considerably lower, not significant in the 6- to 11-month and 5-year age groups, but 41 to 52% among 10-year-olds.

The study also demonstrated that higher humoral antibody titers are associated with decreased challenge virus excretion, as has been shown previously (4, 19, 27). bOPV increased antibody titers to poliovirus type 2, presumably because of boosting of cross-reacting neutralizing antibodies (31), since we did not isolate poliovirus type 2 from any stool samples. The data support the use of IPV (or OPV) to boost intestinal immunity for travelers to and from polio-infected countries.

Our study had a limitation. We conducted the study in Moradabad district in Uttar Pradesh State of India where the immunogenicity of OPV is low (11, 12). Therefore, extrapolation or generalization of these findings to other areas in India or elsewhere must be done with caution.

The Strategic Advisory Group of Experts (SAGE) recommended in 2012 the introduction of ≥1 dose of IPV in all routine immunization programs for risk mitigation before OPV2 withdrawal (32). A dose of IPV is expected to induce seroconversion or priming in close to 100% of naive infants (33). Should poliovirus type 2 be reintroduced, a second IPV dose would rapidly boost antibody titers and prevent, or decrease the magnitude of, an outbreak. Furthermore, IPV would be expected to close the remaining type-specific immunity gaps.

Our study provides strong evidence that IPV boosts intestinal immunity among children with a history of multiple OPV doses more effectively than an additional OPV dose. These data provided the scientific foundation for the development of the new polio endgame plan (34) and are guiding the development of strategies to hasten the elimination of the final poliovirus reservoirs and to decrease the vulnerability of polio-free areas to epidemic transmission after poliovirus importations.

Thus, more than 25 years after the World Health Assembly resolution to eradicate poliomyelitis, the answer to the vaccine controversy is...
Table 2. Seroconversion or fourfold increase in poliovirus antibody titer between days 0 and 28.

| Intervention groups | Type 1 | | Type 2 | | Type 3 | |
|---------------------|--------|----------------|--------|----------------|--------|
|                     | n      | % (95% CI) | P value | n              | % (95% CI) | P value |
| 6–11 months         |        |            |         |                |            |         |
| Control             | 1/34   | 2.9 (0–15.3) | Ref     | 3/73           | 4.1 (0.9–11.5) | Ref     |
| IPV                 | 34/41  | 82.9 (67.9–92.8) | <0.001 | 55/67          | 82.1 (70.8–90.4) | <0.001 |
| bOPV                | 5/35   | 14.3 (4.8–30.3) | 0.198   | 5/74           | 6.8 (2.2–15.1) | 0.719   |
| 5 years             |        |            |         |                |            |         |
| Control             | 2/64   | 3.1 (0.3–10.8) | Ref     | 1/103          | 1.0 (0.0–5.5) | Ref     |
| IPV                 | 56/57  | 98.2 (90.6–100) | <0.001 | 90/95          | 94.7 (88.1–98.3) | <0.001 |
| bOPV                | 8/62   | 12.9 (5.7–23.9) | 0.052   | 7/101          | 6.9 (2.8–13.8) | 0.034   |
| 10 years            |        |            |         |                |            |         |
| Control             | 0/87   | 0.0 (0.0–4.2) | Ref     | 2/101          | 2.0 (0.2–7.0) | Ref     |
| IPV                 | 87/91  | 95.6 (89.1–98.8) | <0.001 | 99/103         | 96.1 (90.4–98.9) | <0.001 |
| bOPV                | 39/92  | 42.4 (32.1–53.1) | <0.001 | 36/105         | 34.3 (25.3–44.2) | <0.001 |

P values calculated with Fisher’s exact (two-tailed) test. 95% confidence intervals calculated with Clopper-Pearson method.

REFERENCES AND NOTES

3. World Health Organization, World Health Assembly (WHA) resolution, 1988 (resolution 41.8).


ACKNOWLEDGMENTS

Funding was provided by Rotary International Polio Plus Program (through a grant approved by the Polio Research Committee of the World Health Organization). The study was approved by the Drugs Controller General (India), the Indian Council of Medical Research, and the Ethics Review Committees of the WHO. The trial was registered with the Indian Clinical Trials Registry (www.ctri.nic.in) (registration number CTRI/2011/09/ 002018). We acknowledge the contributions of Uttar Pradesh State Government health staff, social mobilization network of the United Nations Children’s Fund and CORE, and the operations team from WHO India-National Polio Surveillance Project who were instrumental in the setup and implementation of the study. We also acknowledge the extensive work performed by the laboratory staff at ERC Mumbai. Finally, we express our sincere thanks to the Government of India, Ministry of Health and Family Welfare and the GPEI partners. The data set is available in the supplementary materials. The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, or other participating organizations.

SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/345/6199/922/suppl/DC1
Materials and Methods
Figs. S1 and S2
Tables S1 to S3
Data set
References (36–40)
21 April 2014; accepted 15 July 2014
10.1126/science.1255006

CARBON CYCLE

Sunlight controls water column processing of carbon in arctic fresh waters

Rose M. Cory,1* Collin P. Ward,1 Byron C. Crump,2 George W. Klings3

Carbon in thawing permafrost soils may have global impacts on climate change; however, the factors that control its processing and fate are poorly understood. The dominant fate of dissolved organic carbon (DOC) released from soils to inland waters is either complete oxidation to CO2 or partial oxidation and river export to oceans. Although both processes are most often attributed to bacterial respiration, we found that photochemical oxidation exceeds rates of respiration and accounts for 70 to 95% of total DOC processed in the water column of arctic lakes and rivers. At the basin scale, photochemical processing of DOC is about one-third of the total CO2 released from surface waters and is thus an important component of the arctic carbon budget.

Carbon dioxide emissions from inland surface waters to the atmosphere are as large as the net carbon transfer from the atmosphere to Earth’s surface (~2 Pg C year–1; 1 Pg = 1015 g) (1–5). This large flux is affected by the movement of dissolved organic carbon (DOC) from land (1, 2) and its subsequent oxidation to CO2 in fresh waters (3–5). The remaining DOC may be unprocessed, flocculated, or partially oxidized and exported in rivers to

Downloaded from http://science.sciencemag.org/ on August 6, 2017
Efficacy of inactivated poliovirus vaccine in India

Hamid Jafari, Jagadish M. Deshpande, Roland W. Sutter, Sunil Bahl, Harish Verma, Mohammad Ahmad, Abhishek Kunwar, Rakesh Vishwakarma, Ashutosh Agarwal, Shilpi Jain, Concepcion Estivariz, Raman Sethi, Natalie A. Molodecky, Nicholas C. Grassly, Mark A. Pallansch, Arani Chatterjee and R. Bruce Aylward

Science 345 (6199), 922-925.
DOI: 10.1126/science.1255006

Two vaccines together are better than one alone

Polio is proving difficult to eradicate. Making the choice between administering a live attenuated vaccine orally (Sabin) or an inactivated vaccine (Salk) by injection has been highly controversial. Patients prefer the Sabin vaccine, but it requires many doses to offer immunity. Jafari et al. tested the two vaccines together in northern India. The injected vaccine significantly reduced virus shedding and boosted intestinal mucosal immunity in children already given the oral vaccine. Thus, using both vaccines could help speed the eventual global demise of polio.

Science, this issue p. 922