Poliomyelitis Prevention: Recommendations for Use of Inactivated Poliovirus Vaccine and Live Oral Poliovirus Vaccine

ABSTRACT. A change in the recommendations for routine immunization of children is indicated because of the reduced risk of exposure to wild-type polioviruses and the continued occurrence of vaccine-associated paralytic poliomyelitis after oral polio vaccine (OPV). All children should receive four doses of vaccine before the child enters school. Regimens of sequential inactivated polio vaccine (IPV) and OPV, IPV only, or OPV only are acceptable. Each regimen has advantages and disadvantages. In special circumstances, one of the regimens is preferred or recommended. Because logistical problems with the current childhood immunization schedule may make these new recommendations difficult to implement immediately, their adoption likely will be gradual. Nevertheless, assuming continued progress toward global eradication and the development of new combination products, the routine use of an IPV-only regimen is likely to become desirable and feasible in future years.

VACCINE EFFECTIVENESS

Since the introduction of poliovirus vaccines in the 1950s and early 1960s, their effectiveness in the prevention of poliomyelitis has been amply demonstrated. The last reported case in the United States of indigenously acquired poliomyelitis caused by wild poliovirus was in 1979.1 No cases have occurred in the western hemisphere since August 1991.2 These and other findings from national surveillance in countries of the Americas led to the certification in 1994 by an international commission that wild-type poliovirus transmission has been interrupted in this hemisphere, thus achieving a goal established by the Pan American Health Organization in 1985.3 Concurrently, the global poliomyelitis eradication initiative of the World Health Organization (WHO) has resulted in a more than 80% reduction in the incidence of reported poliomyelitis cases worldwide since 1988 and demonstrated that the goal of global eradication is achievable.4,5

These successes are attributable primarily to the widespread use of oral polio vaccine (OPV), which is the vaccine recommended by the WHO. Continued progress in poliomyelitis elimination clearly necessitates the use of OPV in those countries in which wild poliovirus remains or recently has been endemic. In the United States, the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) has strongly reaffirmed its support of the eradication program and the use of OPV for this purpose.6

In the United States, the evolving national and international epidemiology of poliomyelitis in the past two decades has prompted reexamination of current vaccination recommendations for the routine use of OPV. Earlier reevaluation by the Institute of Medicine in 1977 and again in 1988 had reaffirmed the use of OPV for national poliomyelitis control at those times.7,8 Since 1979, however, nearly all cases of paralytic poliomyelitis in the United States have been vaccine associated.

Between 1980 and 1994, a total of 125 cases of vaccine-associated paralytic poliomyelitis (VAPP) were reported, whereas only 6 imported and 2 indeterminate cases have occurred.6 The number of imported cases in recent years has decreased markedly, especially from Latin America, where the majority of imported cases to the United States formerly originated. The only reported importation in the 1990s was a 30-month-old Nigerian brought to this country for treatment of the disease. Thus, the current risk of exposure to wild poliovirus in the United States is not only very low but also of diminishing magnitude as global elimination proceeds. In comparison, the risk of VAPP from OPV, albeit low, for both recipients of the vaccine and their susceptible contacts is significantly greater, as evidenced by the 8 to 9 cases of VAPP reported each year, than the risk of paralytic poliomyelitis from wild-type poliovirus. This substantial alteration in the relative benefits and risks of OPV in comparison to those of inactivated polio vaccine (IPV) during the past two decades led to the ACIP resolution in June 1995 to recommend the development of a new poliomyelitis vaccine policy with a greatly enhanced role for IPV to decrease the occurrence of VAPP.9

The Committee on Infectious Diseases concurs with the ACIP recommendation for expanded use of IPV.9 Continued use of OPV for primary immunization in the United States, even assuming global eradication is achieved by the year 2000, would likely result in as many as 100 or more cases of VAPP. Routine immunization against poliomyelitis will need to be continued until worldwide certification of the eradication of wild-type poliovirus. This interval is likely to be at least 10 years from now and strongly supports a change in policy now rather than after global eradication is achieved. In the resulting deliberations of both the ACIP and Committee on Infectious Diseases, multiple other issues have been considered, including efficacy and safety of the two...
types of polio vaccine, options for immunization schedules, possible impact on the immunization rates in children, and the importance of informing parents and physicians of the benefits and risks of these schedules and involving them in the selection of vaccine. These considerations have resulted in revised recommendations for poliomyelitis vaccination in this country.

OPV

Trivalent OPV, the live-attenuated vaccine, in a three-dose series results in sustained, probably lifelong protection against paralytic disease caused by each of three poliovirus serotypes in more than 95% of recipients. OPV induces intestinal immunity against poliovirus reinfection, which explains its effectiveness in controlling wild virus circulation. In addition, OPV persists in the pharynx for 1 to 2 weeks and is excreted in the feces for several weeks or longer after administration. Consequently, vaccine virus can be transmitted to contacts and results in their immunization. In rare cases, however, VAPP can occur in these contacts as well as in those vaccinated.

In addition to intestinal immunity, advantageous properties of OPV are ease of administration and lower costs than those of IPV. The only well-documented adverse event associated with OPV is VAPP. Although an Institute of Medicine committee noted an increased risk of Guillain-Barré syndrome after OPV administration in two studies in Finland, reanalysis of these data and a subsequent study in the United States did not demonstrate an increased risk of Guillain-Barré syndrome after OPV administration.

VAPP

The rate of VAPP after the first dose of OPV is approximately 1 case per 760,000 doses of OPV distributed, including recipient and contact cases. The risk of a recipient case after the first OPV dose is estimated to be 1 per 1.5 million doses; for a contact case resulting from exposure to a first-dose recipient it is 1 per 2.2 million doses. For subsequent doses, the risk is substantially lower for both recipients and contacts (Table). For immunodeficient persons, the risk is 3200- to 6800-fold higher than in immunologically healthy OPV recipients.

Of the 125 cases of VAPP reported from 1980 to 1994, 49 (39%) occurred in otherwise healthy recipients, 78% of which were associated with the first dose, and 93% occurred in the first year of life. Cases in healthy contacts accounted for 40 (32%), approximately three fourths of which occurred in adults. In 30 cases (24%), which includes recipients and contacts, the patients had immunologic abnormalities, the majority of which were disorders of humoral immunity, ie, antibody deficiency syndromes. Six cases from which vaccine-related virus was isolated occurred in community contacts with no history of recent vaccination or contact with a vaccine recipient.

IPV

The original inactivated viral vaccines against polio were replaced in the late 1980s by those of greater antigentic content and have been denoted as enhanced-potency IPV. Administration of enhanced-potency vaccine in most studies has resulted in seroconversion to the three poliovirus types in 94% to 100% of vaccinees after two doses and high titers of serum-neutralizing antibody in 99% to 100% of recipients after three doses. In the one study in which lower seroconversion to serotype 3 after two doses of vaccine occurred, the seroconversion rate was 100% after a third dose of IPV and 94% after two doses of OPV. The limited data on antibody persistence suggest that immunity is prolonged and perhaps lifelong.

Mucosal immunity is induced by enhanced-potency IPV but to a lesser extent than that with OPV, IPV inhibits pharyngeal acquisition of poliovirus and to a lesser extent intestinal acquisition.

The effectiveness of IPV has been demonstrated by its use in several countries in Western Europe that controlled and now eliminated poliomyelitis. These countries include Finland, France, the Netherlands, Norway, and Sweden. Recently in Canada, where a pentavalent vaccine of diphtheria and tetanus toxoids and pertussis, IPV, and Haemophilus influenzae conjugate vaccine is used, the exclusive use of IPV has been adopted by most provinces. IPV use in the United States requires additional injections (until new combination vaccine products become available), does not provide optimal mucosal immunity to maintain community resistance to introduction of wild polio virus, and costs more than OPV. However, the cost of this vaccine likely will decrease with greater use and the resulting increase in volume of sales. No serious adverse events have been associated with the use of the currently available enhanced-potency IPV products in which the three types of poliovirus (1, 2, and 3) are completely inactivated with formaldehyde after viral concentration and purification. As with any vaccine, rare adverse reactions cannot be excluded until IPV has been used in large populations. To date, however,

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**TABLE. Ratio of Number of Cases of Vaccine-associated Paralytic Poliomyelitis to Number of Doses of Trivalent OPV Distributed, United States, 1980 Through 1994**

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<th>Case Category</th>
<th>Ratio (No. of Cases to Millions of Doses of OPV Distributed)</th>
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<tbody>
<tr>
<td></td>
<td>All doses</td>
</tr>
<tr>
<td>Recipient</td>
<td>1:6.2 (49)</td>
</tr>
<tr>
<td>Contact</td>
<td>1:7.6 (40)</td>
</tr>
<tr>
<td>Community acquired</td>
<td>1:50.5 (6)</td>
</tr>
<tr>
<td>Immunologically abnormal‡</td>
<td>1:101.30 (30)</td>
</tr>
<tr>
<td>Total</td>
<td>1:2.4 (125)</td>
</tr>
</tbody>
</table>

* Live, oral poliovirus vaccine (attenuated).
† NA indicates not applicable.
‡ Because the denominator is doses of OPV distributed, the calculated ratio is low. However, if the denominator is the number of immunodeficient infants born each year, the risk of VAPP in immunodeficient infants is 3200 to 6800-fold higher than in immunocompetent infants.27
Sequential Use of IPV Followed by OPV

The sequential use of IPV and OPV for primary immunization in the United States was proposed in 1987 to reduce the risk of VAPP. The expert panel convened in 1988 by the Institute of Medicine recommended consideration of this schedule after a combination product of IPV and a vaccine of diphtheria and tetanus toxoids and pertussis became available, which at the time was anticipated in 3 to 5 years.

Although the experience with sequential schedules is limited, they have been used in Denmark and in one Canadian province for more than two decades and more recently have been adopted in Israel, Hungary, and Lithuania.

The rationale for the sequential schedule is that two doses of IPV induce sufficient humoral immunity in most recipients to prevent VAPP from subsequent administration of OPV, which will induce optimal intestinal immunity as well as sustain humoral immunity.

In studies of the immunogenicity of the sequential use of IPV and OPV, seroconversion after two doses of IPV and one dose of OPV was 94% or greater to serotypes 1 and 2 and 78% to 100% for serotype 3. After the second dose of OPV, humoral immunity was greater than 95% to all serotypes. Two doses of OPV seem necessary for optimal intestinal immunity, and no additional benefit is gained from a third dose.

Based on the epidemiologic characteristics of VAPP, universal application of a sequential schedule would be expected to reduce the number of cases by 50% to 75%. The sequential schedule should eliminate most cases of VAPP in vaccine recipients and prevent some cases in unimmunized contacts, because IPV provides some degree of mucosal immunity, resulting in reduced excretion of the vaccine virus after OPV administration. Although the use of OPV in a sequential schedule would mean continued circulation of vaccine virus and some contact cases of VAPP, this circulation would be reduced by the decreased usage of OPV in the sequential schedule, because only two doses rather than four would be given to each child.

In almost all OPV recipients, reversion of attenuated vaccine viruses to more virulent strains by reverse mutation after replication in the intestine seems to occur. Although the proportion of viruses reverting to more virulent strains might not be reduced in OPV recipients who previously received two doses of IPV, the balance of the evidence indicates that the rate of excretion and frequency of revertants is not increased in persons who previously received IPV.

RECOMMENDATIONS OF THE CDC (ACIP)

The ACIP, in considering the three strategy options for polio vaccination, concluded that although OPV-only and IPV-only schedules are acceptable, the sequential schedule of two doses of IPV followed by two doses of OPV is recommended as the current public health strategy. This decision is based on the reduced risk of VAPP, optimal mucosal immunity from OPV to maintain community resistance to introduction of wild poliovirus, and the necessity for only two additional injections in comparison to four in an IPV-only regimen. The ACIP also notes that a sequential schedule is likely to be an interim recommendation until further progress in global eradication is achieved and combination vaccines are licensed, at which time an IPV-only schedule probably would be recommended. Ultimately, after worldwide certification of eradication of wild-type poliovirus, vaccination against polio infection can be discontinued, because humans are the only natural reservoir for wild-type polioviruses.

CONSIDERATIONS AND CONCLUSIONS IN THE CHOICE OF VACCINE

The goal of poliomyelitis vaccination programs is the worldwide eradication of both the disease and wild-type poliovirus circulation. In the United States, where eradication has been achieved and the western hemisphere has been certified as free of indigenous wild-type poliovirus since 1994, an additional goal is to reduce and eventually eliminate VAPP by the expanded use of IPV. Although prevention of VAPP can be most rapidly achieved by an IPV-only regimen, the number of injections in the current childhood immunization schedule, limited availability of combination vaccine products, and local practice constraints related to costs and other factors could prevent the immediate routine implementation of this option. In addition, many experts support the continuing need for optimal intestinal immunity as induced by OPV to limit further circulation of wild-type polio virus if importation were to occur.

Each of the three poliomyelitis vaccine schedules—sequential IPV and OPV, IPV only, and OPV only—are highly effective in protecting against poliomyelitis from wild-type polioviruses and are acceptable. Physicians, thus, have three options for immunizing their patients. Major factors in the selection of the most appropriate options are the following:

1. Risk of VAPP;
2. Need for optimal intestinal immunity;
3. Number of injections required at scheduled visits to administer the recommended vaccines;
4. Possible increased number of visits resulting from parental or provider preference to avoid additional injections at one or more visits;
5. Possible decreased vaccination rates in infants and young children as a result of the increased number of vaccine injections and visits to complete sequential or IPV-only regimens;
6. Vaccine costs;
7. Parent and/or provider choice; and
8. Introduction of new combination vaccines.

When these factors are considered, the choice of schedule should be based on the goal of reducing VAPP without compromising poliomyelitis immu-
nity or the delivery of other recommended childhood immunizations in both the public and private sectors. Accordingly, the American Academy of Pediatrics (AAP) recommends expanded use of IPV but recognizes that OPV only may be indicated for some children to ensure timely completion of the routine childhood immunization schedule against other vaccine-preventable diseases. Once additional combination vaccines are widely available, an IPV-only schedule should be feasible for all children in the United States, assuming global progress toward elimination of poliovirus circulation continues. Eventually, assuming confirmation of worldwide eradication, poliovirus vaccination would be discontinued.

The considerations that support expanded use of IPV apply primarily to countries where wild-type poliovirus transmission has been interrupted for at least seven years. OPV remains the vaccine of choice for global eradication in the following areas: (1) areas where wild poliovirus has recently been or is currently circulating; (2) most developing countries, where the higher cost of IPV prohibits its use; and (3) areas where inadequate sanitation necessitates an optimal mucosal barrier to wild-type virus circulation.

On the basis of these considerations, the AAP concludes that regimens of sequential IPV and OPV (eg IPV followed by OPV), IPV only, and OPV only are acceptable. The choice of schedule for most children will depend on one or more of the following factors:

1. Parent-provider choice;
2. Cost;
3. Local public health recommendations;
4. Practice preference;
5. Product availability; and
6. Expected completion of the entire immunization schedule, concerns regarding injections and the need for additional visits, and the likelihood of return for these visits.

Depending on circumstances, the ACIP-recommended sequential IPV and OPV regimen, the IPV-only regimen, or the OPV-only regimen may be preferred. In the sequential regimen, two doses of OPV are necessary for optimal intestinal immunity.

To implement these guidelines for these three acceptable regimens, a single schedule for the recommended ages for administration of poliovirus vaccine, irrespective of which vaccine is to be given, has been developed. Accordingly, IPV and OPV in many circumstances are considered interchangeable; the exception is in the sequential regimen, in which two doses of OPV are necessary for optimal intestinal immunity.

Children who have received one or more doses of OPV can complete the four-dose series with IPV if desired.

Issues in Scheduling IPV Administration

Until new combination vaccines are widely available, the administration of IPV necessitates additional injections. In scheduling IPV administration, the following options should be considered to decrease the number of injections at the 2- and 4-month visits:

1. Hepatitis B vaccine can be administered at birth and ages 1 and 6 months.
2. Additional visits can be scheduled, assuming that the child is likely to return.
3. Available licensed combination products that reduce the number of injections required to administer recommended vaccines can be used.

Alternatively, OPV can be given in place of IPV until the combination vaccines become widely available.

**RECOMMENDATIONS FOR POLIOMYELITIS IMMUNIZATION OF INFANTS AND CHILDREN IN THE UNITED STATES**

Expanded use of IPV is indicated during the transition period of global eradication of poliomyelitis to reduce the risk of VAPP and to maintain immunity against wild-type poliovirus infection. The CDC ACIP has recommended the sequential use of two doses of IPV followed by two doses of OPV as the current public health strategy for prevention of poliomyelitis. Because logistic problems with the current childhood immunization schedule may make these new recommendations for the use of IPV difficult to implement immediately, their adoption likely will be gradual. Nevertheless, assuming continued progress toward global eradication and the availability of additional combination vaccine products, the routine use of an IPV-only regimen is likely to become more feasible in future years. The AAP recommends the following:

1. Poliomyelitis vaccine should be given at 2, 4, and 12 to 18 months and 4 to 6 years of age, for a total of four doses at or before school entry. For children who receive OPV only, the third dose may be given as early as 6 months of age in accordance with prior recommendations. An additional dose at school entry is not indicated for children who received the third dose of any licensed polio vaccine on or after their fourth birthdays.
2. Physicians have three options for immunizing their patients. Regimens of sequential IPV and OPV, IPV only, and OPV only are acceptable. Each regimen has advantages and disadvantages, and in the circumstances described in recommendations 3 through 5, one may be preferred or recommended. Parents or other care givers should be informed of the advantages and disadvantages of the three acceptable regimens.
3. Immunization with IPV only is recommended:
   - For immunocompromised persons and their household contacts, because OPV is contraindicated. The poliovirus is found in respiratory secretions for several days and in the stool for several weeks after vaccination and transmission to household contacts occurs frequently.
   - For the infants and children for whom adult household members are identified as being inadequately vaccinated against poliomyelitis,
because unimmunized adults are at increased risk of VAPP.6
• When the number of injections is not likely to decrease compliance and when IPV is preferred by health care providers and parents or other care givers.

4. Immunization with OPV only is recommended:
• When parents or providers who prefer not to have the child receive the additional injections needed if IPV were to be used.
• For infants and children starting a vaccination regimen after 6 months of age in whom an accelerated schedule is necessary to complete immunizations, an OPV-only regimen will minimize the number of injections required at each visit. For similar reasons, in populations with low vaccination rates, OPV may be preferred to expedite implementation of the routine childhood immunization schedule.

5. The sequential IPV and OPV schedule is recommended:
• To reduce the total number of injections required to reduce the risk of VAPP while maintaining optimal intestinal immunity, especially for travelers to areas where poliovirus is still endemic.

6. The AAP supports the WHO recommendations for the use of OPV to achieve global eradication of poliomyelitis, especially for countries with continued or recent circulation of wild-type poliovirus and occurrence of paralytic poliomyelitis and for those in which the increased cost of IPV and its administration makes its use impractical.

7. Precautions and contraindications to administration of IPV and OPV remain unchanged from prior recommendations and are given in the current edition of the Red Book: Report of the Committee on Infectious Diseases.29

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