

**Poliomyelitis Prevention  
in the United States:  
Introduction of a Sequential Vaccination  
Schedule of Inactivated Poliovirus  
Vaccine Followed by Oral  
Poliovirus Vaccine**

**Recommendations of the Advisory Committee on  
Immunization Practices (ACIP)**

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**

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# **Poliomyelitis Prevention in the United States: Introduction of A Sequential Vaccination Schedule of Inactivated Poliovirus Vaccine Followed by Oral Poliovirus Vaccine**

## **Recommendations of the Advisory Committee on Immunization Practices (ACIP)**

### **Summary**

*These revised recommendations of the Advisory Committee on Immunization Practices (ACIP) replace recommendations on poliomyelitis issued in 1982 and 1987, and present a new ACIP poliovirus vaccination policy that increases reliance on inactivated poliovirus vaccine (IPV). This change in policy is the most substantive since the introduction of oral poliovirus vaccine (OPV) in 1961. ACIP has determined that the risk-benefit ratio associated with the exclusive use of OPV for routine immunization has changed because of rapid progress in global polio eradication efforts. In particular, the relative benefits of OPV to the U.S. population have diminished because of the elimination of wild-virus-associated poliomyelitis in the Western Hemisphere and the reduced threat of poliovirus importation into the United States. The risk for vaccine-associated poliomyelitis caused by OPV is now judged less acceptable because of the diminished risk for wild-virus-associated disease (indigenous or imported). Consequently, ACIP recommends a transition policy that will increase use of IPV and decrease use of OPV during the next 3–5 years.*

*The revised recommendations include three options for poliovirus vaccination, all of which meet acceptable standards of care: sequential vaccination with IPV followed by OPV, OPV alone, or IPV alone. For overall public health benefit, ACIP recommends a sequential vaccination schedule of two doses of IPV followed by two doses of OPV for routine childhood vaccination. Vaccination schedules that include OPV alone or IPV alone are also acceptable and are preferred in some situations (e.g., IPV alone is recommended for children who are immunosuppressed; OPV alone is preferred for children who begin the primary vaccination schedule after 6 months of age). Implementation of these recommendations should reduce the risk for vaccine-associated paralytic poliomyelitis and facilitate a transition to exclusive use of IPV following further progress in global polio eradication.*

## **INTRODUCTION**

Since the introduction of poliovirus vaccines in the 1950s and 1960s, poliomyelitis control has been achieved in the United States, the Americas, and elsewhere (1,2). In the United States, the last indigenously acquired cases of poliomyelitis caused by wild poliovirus were detected in 1979 (3). In 1985, the countries of the Americas established a goal of regional elimination of wild poliovirus by the year 1990 (4), and in 1988, the World Health Assembly adopted the goal of global poliomyelitis eradication

by the year 2000 (5). In the Americas, the last case of poliomyelitis associated with isolation of wild poliovirus was detected in Peru in 1991 (6). The Western Hemisphere was certified to be free of indigenous wild poliovirus in 1994, an accomplishment achieved by the exclusive use of oral poliovirus vaccine (OPV) (7). The global poliomyelitis eradication initiative (PEI) has reduced the number of reported poliomyelitis cases worldwide by more than 80% since the mid-1980s, and worldwide eradication of the disease by the year 2000 appears feasible (8).

The United States can remain free of poliomyelitis only by reducing or eliminating the risk for poliovirus importation. ACIP strongly reaffirms its support of the global PEI, which relies on OPV in countries where the disease remains endemic or has recently been endemic. ACIP urges that continuing and adequate support be made available to the PEI to achieve the goal of global eradication by the year 2000.

Several factors have influenced the risk-benefit balance of the current immunization policy, including disease risk, risk for adverse vaccine reactions, and the cost of vaccines in the United States. Since 1980, an average of eight to nine cases of paralytic poliomyelitis associated with OPV has been reported annually in the United States. Vaccine-associated paralytic poliomyelitis (VAPP) has been the only indigenous form of the disease in the United States since 1979. Additional (unreported) cases of VAPP probably occur (9). The severity of these cases is similar to that of cases caused by wild virus.

Although the risk for VAPP is low (approximately one case to 2.4 million doses distributed, or one case to 750,000 children receiving their first dose of OPV), CDC estimates that 30–40 cases of vaccine-associated paralysis would have occurred in the United States during 1997–2000 if the previously recommended poliovirus vaccination practices had not changed. Adoption of a sequential vaccination schedule of inactivated poliovirus vaccine (IPV) followed by OPV will likely prevent at least half of these cases of VAPP. ACIP has reevaluated the national poliomyelitis prevention policy because a) the global PEI has substantially reduced the risk for reintroduction of wild poliovirus to the United States and b) IPV provides high levels of individual protection without a concomitant risk for paralytic disease among vaccine recipients or persons with whom they have contact.

After weighing the advantages and disadvantages of the various vaccines and schedules, ACIP concluded that three vaccination options offered essentially equal protection against poliomyelitis: a) sequential use of IPV and OPV, b) all OPV, and c) all IPV. ACIP considered the relevant scientific and programmatic issues and concluded that adoption of the sequential IPV-OPV vaccination schedule would yield the greatest overall public health benefit. This vaccination schedule includes doses of IPV administered at 2 and 4 months of age followed by doses of OPV administered at 12–18 months and 4–6 years of age. This strategy is intended to decrease the incidence of VAPP while maintaining high levels of population immunity to polioviruses to prevent poliomyelitis outbreaks should wild poliovirus be reintroduced to the United States. Nonetheless, the sequential vaccination schedule should be considered an interim recommendation. It is expected to remain in place 3–5 years until further progress toward global eradication is achieved. Such progress, along with the development and licensure of combination vaccines that reduce the need for multiple simultaneous vaccine injections, is expected to lead to adoption of an IPV-only vaccination schedule.



Ultimately, when worldwide eradication of wild-type polioviruses is certified, all poliovirus vaccination can be discontinued.

This statement summarizes the current recommendations for poliomyelitis prevention in the United States. It describes ACIP's rationale for selecting a sequential vaccination schedule of IPV followed by OPV as the preferred means to prevent both paralytic poliomyelitis caused by possible reintroduction of wild poliovirus and paralytic disease associated with OPV use.

## CHARACTERISTICS OF POLIOMYELITIS

### Acute Poliomyelitis

Poliomyelitis is a highly contagious infectious disease caused by poliovirus, an enterovirus. Most poliovirus infections are asymptomatic. Symptomatic cases are typically characterized by two phases—the first, a nonspecific febrile illness, is followed (in a small percentage of cases) by aseptic meningitis and/or paralytic disease. The ratio of cases of inapparent infection to paralytic disease ranges from 100:1 to 1,000:1.

After poliovirus exposure, the virus replicates in the oropharynx and the intestinal tract. Viremia follows, and may result in infection of the central nervous system. Replication of poliovirus in motor neurons of the anterior horn and brain stem results in cell destruction and causes the typical clinical manifestations of paralytic poliomyelitis. Depending on the sites of paralysis, poliomyelitis can be classified as spinal, bulbar, or spino-bulbar disease. Progression to maximum paralysis is rapid (i.e., 2–4 days), is usually associated with fever and muscle pain, and rarely continues after the patient's temperature has returned to normal. Spinal paralysis is typically asymmetric, and more severe proximally than distally. Deep tendon reflexes are absent or diminished. Bulbar paralysis may compromise respiration and swallowing. Paralytic poliomyelitis is fatal in 2%–10% of cases. After the acute episode, many patients recover at least some muscle function and prognosis for recovery can usually be established within 6 months after onset of paralytic manifestations.

### Post-Polio Syndrome

After an interval of 30–40 years, 25%–40% of persons who contract paralytic poliomyelitis in childhood may experience muscle pain and exacerbation of existing weakness or develop new weakness or paralysis. This disease entity, which is referred to as post-polio syndrome, has been reported only in persons infected during the era of wild poliovirus circulation. Risk factors for post-polio syndrome include a) increasing length of time since acute poliovirus infection, b) presence of permanent residual impairment after recovery from the acute illness, and c) female sex (10).

### Epidemiology

Poliomyelitis, which occurs worldwide, is caused by three serotypes of poliovirus (i.e., types 1, 2, and 3). In countries where poliovirus is still endemic, paralytic disease is most often caused by poliovirus type 1, less frequently by poliovirus type 3, and

least frequently by poliovirus type 2. The virus is transmitted from person to person primarily by direct fecal-oral contact. However, it also can be transmitted by indirect contact with infectious saliva or feces or by contaminated sewage or water.

The first paralytic manifestations of poliomyelitis usually occur 7–21 days from the time of initial infection (range: 4–30 days). The period of communicability begins after the virus replicates—and is excreted in the oral secretions and feces—and ends with the termination of viral replication and excretion, usually 4–6 weeks after infection. After household exposure to wild poliovirus, >90% of susceptible contacts become infected. Infection by poliovirus results in lifelong immunity specific to the infecting viral serotype.

Humans are the only reservoir for poliovirus. Long-term carrier states (i.e., excretion of virus by asymptomatic persons >6 months after infection) have been reported only in immunodeficient persons, among whom they are rare. Risk factors for paralytic disease include larger inocula of poliovirus, increasing age, pregnancy, strenuous exercise, tonsillectomy, and intramuscular injections administered while the patient is infected with poliovirus (11).

## **Poliomyelitis Eradication**

Following the widespread use of poliovirus vaccine in the mid-1950s, the incidence of poliomyelitis declined rapidly in many industrialized countries. In the United States, the number of cases of paralytic poliomyelitis reported each year declined from >20,000 cases in 1952 to <100 cases in the mid-1960s (3).

In 1985, the member countries of the Pan American Health Organization adopted the goal of eliminating poliomyelitis from the Western Hemisphere by 1990 (4). The strategy to achieve this goal included a) increasing vaccination coverage, b) enhancing surveillance for suspected cases (i.e., surveillance for acute flaccid paralysis), and c) using supplemental immunization strategies (e.g., national immunization days [NIDs], house-to-house vaccination, and containment activities) (12,13). Since 1991, when the last wild-virus-associated indigenous case was reported from Peru, no additional cases of poliomyelitis have been confirmed by isolation of wild virus despite intensive surveillance (6). In September 1994, an international commission certified the Western Hemisphere to be free of indigenous wild poliovirus. The commission based its judgment on detailed reports from national certification commissions that had been convened in every country in the region (8).

In 1988, the World Health Assembly (the governing body of the World Health Organization [WHO]) adopted the goal of global eradication of poliomyelitis by the year 2000 (5). Substantial progress toward meeting this objective already has been achieved in many WHO regions (7,14,15) including East Asia (16–18), the Middle East (19), Southern and Eastern Africa, and Europe (7,14–21). By the end of 1996, almost all polio-endemic countries outside the African region of WHO had conducted NIDs, as had >50% of African countries.

The PEI is supported by a coalition of international organizations that includes WHO, the United Nations Children's Fund (UNICEF), other bilateral and multilateral organizations, and Rotary International.

## Secular Trends in Disease and Vaccination Coverage in the United States

In the United States, poliovirus vaccines have eliminated poliomyelitis caused by wild poliovirus. The annual number of reported cases of paralytic disease declined from more than 20,000 in 1952 to an average of eight to nine cases annually during 1980–1991 (3,9). From 1980 through 1994, 133 cases of paralytic poliomyelitis were reported, including 125 cases of VAPP, six imported cases, and two indeterminate cases (CDC, unpublished data). Until worldwide poliomyelitis eradication is achieved, epidemics caused by importation of wild virus to the United States remain a possibility unless population immunity is maintained by vaccinating children early in their first year of life. In the United States, outbreaks of poliomyelitis occurred in 1970, 1972, and 1979 after wild poliovirus was introduced into susceptible populations that had low levels of vaccination coverage with OPV. Vaccination coverage among children in the United States is at the highest levels in history as a result of ongoing immunization initiatives. Assessments of the vaccination status of children entering kindergarten and first grade indicate that the percentage who had completed primary vaccination against poliomyelitis reached 95% in the 1980–81 school year and has since remained above that level.

Serologic surveys indicate that >90% of school-age children, adolescents, and young adults have detectable antibody to poliovirus types 1 and 2, and >85% have antibody to type 3 (22,23). Data from seroprevalence surveys conducted in two inner-city areas of the United States during 1990–1991 revealed that >80% of all children 12–47 months of age had antibodies to all three poliovirus serotypes. Of the children who had received at least three doses of OPV, 90% had antibody to all three serotypes (24).

Vaccination levels among preschool-age children are lower than the levels at school entry, but have increased substantially in recent years. Data from the National Immunization Survey conducted from April 1994 through June 1995 indicated that, among children 19–35 months of age, vaccination coverage with at least three doses of OPV increased from 83% in 1994 to 88% in April–June, 1995 (25).

Both laboratory surveillance for enteroviruses and poliomyelitis case surveillance suggest that endemic circulation of indigenous wild polioviruses ceased in the United States in the 1960s. In the 1970s, genotypic testing (e.g., molecular sequencing or oligonucleotide fingerprinting) of poliovirus isolates obtained from indigenous cases (both sporadically occurring and outbreak-associated) in the United States indicated that these viruses were imported (26). During the 1980s, five cases of poliomyelitis were classified as imported (9). The last imported case, reported in 1993, occurred in a child 2 years of age who was a resident of Nigeria; the child had been brought to New York for treatment of paralytic disease acquired in his home country. Laboratory investigations failed to isolate poliovirus in samples taken from this child.

Recent experience in Canada illustrates the continuing potential for importation of wild poliovirus into the United States until global eradication is achieved. In 1993 and 1996, health officials in Canada isolated wild poliovirus in stool samples from residents of Alberta and Ontario. No cases of paralytic polio occurred as a result of these wild-virus importations. The strain isolated in 1993 was linked epidemiologically and

by genomic sequencing to the 1992 poliomyelitis outbreak in the Netherlands (27). The isolate obtained in 1996 was from a child who had recently visited India (28).

Inapparent infection with wild poliovirus no longer contributes to establishing or maintaining poliovirus immunity in the United States because these viruses no longer circulate in the population. Thus, universal vaccination of infants and children is the only means of establishing and maintaining population immunity against poliomyelitis.

## Vaccine-Associated Paralytic Poliomyelitis

Cases of VAPP were observed almost immediately after the introduction of live, attenuated poliovirus vaccines (29,30). During 1980–1994, 125 cases of VAPP were reported. Forty-nine cases of paralysis occurred among otherwise healthy vaccine recipients, 40 cases among healthy close contacts of vaccine recipients, and six cases among persons classified as community contacts (i.e., persons from whom vaccine-related poliovirus was isolated although they had not been vaccinated recently or had direct contact with vaccine recipients). An additional 30 cases occurred in persons with abnormalities of the immune system who received OPV or who had direct contact with an OPV recipient (Table 1).

The overall risk for VAPP is approximately one case in 2.4 million doses distributed. However, among immunocompetent persons, 82% of cases among vaccine recipients and 65% of cases among contacts occur following administration of the first dose. The most current estimate of the risk for VAPP is one case to 750,000 first doses of OPV distributed, essentially unchanged from previous estimates (Table 1) (3,9). Among persons who are not immunodeficient, the risk for VAPP associated with the first dose of OPV is sevenfold to 21-fold higher than the risk for subsequent doses (9). Immunodeficient persons, particularly those who have B-lymphocyte disorders that inhibit synthesis of immune globulins (i.e., agammaglobulinemia and hypogammaglobulinemia), are at greatest risk for VAPP (3,200-fold to 6,800-fold greater than the risk for immunocompetent OPV recipients) (31).

**TABLE 1. Ratio of number of cases of vaccine-associated paralytic poliomyelitis (VAPP) to number of doses of trivalent OPV\* distributed—United States, 1980–1994**

Case category	Ratio of number of cases to millions of doses of OPV* distributed and number of cases reported (N) 1980–1994		
	All doses	First doses	Subsequent doses
Recipient	1:6.2 (49)	1:1.4 (40)	1:27.2 (9)
Contact	1:7.6 (40)	1:2.2 (26)	1:17.5 (14)
Community-acquired	1:50.5 (6)	NA	NA
Immunologically abnormal†	1:10.1 (30)	1:5.8 (11)	1:12.9 (19)
<b>Total</b>	<b>1:2.4 (125)</b>	<b>1:0.75 (77)</b>	<b>1:5.1 (42)</b>

\* Live, oral poliovirus vaccine (attenuated).

† 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 for VAPP in immunodeficient infants is 3,200-fold to 6,800-fold greater than in immunocompetent infants [31].

## POLIOVIRUS VACCINES

### Oral Poliovirus Vaccine

Trivalent OPV contains live attenuated strains of all three serotypes of poliovirus. The viruses are propagated in monkey kidney cell culture. Since it was licensed in the United States in 1963, OPV has been the nation's primary poliovirus vaccine. After complete primary vaccination with three doses of OPV,  $\geq 95\%$  of recipients develop long-lasting (probably life-long) immunity to all three poliovirus types. Approximately 50% of vaccine recipients develop antibody to all three serotypes after a single dose of OPV (32). OPV consistently induces immunity of the gastrointestinal tract that provides a substantial degree of resistance to reinfection with poliovirus. Administration of OPV interferes with subsequent infection by wild poliovirus, a property that is important in vaccination campaigns to control polio epidemics.

**Composition of OPV.** One dose of OPV\* (0.5 mL, administered orally from a single dose dispenser) contains a minimum of  $10^6$  TCID<sub>50</sub> (tissue culture infectious dose) Sabin strain of poliovirus type 1 (LSc 2ab),  $10^{5.1}$  TCID<sub>50</sub> Sabin strain of poliovirus type 2 (P712 Ch 2ab), and  $10^{5.8}$  TCID<sub>50</sub> Sabin strain of poliovirus type 3 (Leon 12a1b), balanced in a formulation of 10:1:3, respectively. The OPV manufactured in the United States contains approximately threefold to tenfold the minimum dose of virus necessary to meet these requirements consistently (33). Each dose of 0.5 mL also contains  $<25 \mu\text{G}$  each of streptomycin and neomycin.

### Inactivated Poliovirus Vaccine

Conventional IPV was introduced in the United States in 1955 and was used widely until OPV became available in the early 1960s. Thereafter, the use of IPV rapidly declined to a level of less than 2% of all poliovirus vaccine distributed annually in the United States.

A method of producing a more potent IPV with greater antigenic content was developed in 1978 (34). The first of these more immunogenic vaccines was licensed in the United States in 1987. Results of studies from several countries have indicated that the enhanced-potency IPV is more immunogenic for both children and adults than previous formulations of IPV (35).

A clinical trial of two preparations of enhanced-potency IPV was completed in the United States in 1984 (32). Among children who received three doses of one of the enhanced-potency IPV at 2, 4, and 18 months of age, 99%–100% had developed serum antibodies to all three poliovirus types at 6 months of age—2 months after administration of the second dose. The percentage of children who had antibodies to all three serotypes of poliovirus did not increase or decrease during the 14-month period following the second dose, confirming that seroconversion had occurred in almost all the children. Furthermore, geometric mean antibody titers increased fivefold to tenfold after both the second and third doses.

Data from subsequent studies have confirmed that 90%–100% of children develop protective antibody to all three types of poliovirus after administration of two doses of

\*Official name: Orimune™ (Poliovirus Vaccine, Live, Oral, Trivalent Types 1,2,3 [Sabin]). Manufactured by Lederle Laboratories, Pearl River, NY 10965.

the currently available IPV; 99%–100% develop protective antibody after three doses (32,36,37). Results of studies showing long-term antibody persistence after three doses of enhanced-potency IPV are not yet available in the United States. However, data from one study indicated that antibody persisted throughout a 4-year follow-up period (38). In Sweden, studies of persons who received four doses of IPV (a vaccine with lower antigen content than the IPVs currently licensed in the United States) indicated that >90% of vaccinated persons had serum antibodies to poliovirus 25 years after administration of the fourth dose (39).

Several European countries (e.g., Finland, Netherlands, and Sweden) have relied exclusively on enhanced-potency IPV for routine poliovirus vaccination to achieve elimination of poliomyelitis. More recently, most provinces of Canada have adopted vaccination schedules relying exclusively on IPV.

Although persons vaccinated with IPV can subsequently be infected with and excrete either wild-type strains or vaccine-virus (attenuated) strains in their feces, considerable evidence from epidemiologic studies has demonstrated that vaccinating with IPV diminishes circulation of wild poliovirus in the community. In the poliomyelitis outbreak in the Netherlands during 1992–1993, immunity induced by IPV apparently prevented circulation of wild poliovirus in the general population (40).

**Composition of IPV.** Two products are currently licensed in the United States\*:

- **IPOL™**: One dose (0.5 mL administered subcutaneously) consists of the sterile suspension of three types of poliovirus: Type 1 (Mahoney), type 2 (MEF-1), and type 3 (Saukett). The viruses are grown on Vero cells, a continuous line of monkey kidney cells, by the microcarrier method. After concentration, purification, and formaldehyde inactivation, each dose of vaccine contains 40 D antigen units of type 1, eight D antigen units of type 2, and 32 D antigen units of type 3. Each dose also contains 0.5% of 2-phenoxyethanol and up to 200 ppm of formaldehyde as preservatives, as well as trace amounts of neomycin, streptomycin, and polymyxin B used in vaccine production.
- **POLIOVAX™**: One dose (0.5 mL administered subcutaneously) consists of the sterile suspension of three types of poliovirus: Type 1 (Mahoney), type 2 (MEF-1), and type 3 (Saukett). The viruses are grown on human diploid (MRC-5) cell cultures, concentrated, purified, and formaldehyde inactivated. Each dose of vaccine contains 40 D antigen units of type 1, eight D antigen units of type 2, and 32 D antigen units of type 3, as well as 27 ppm formaldehyde, 0.5% 2-phenoxyethanol, 0.5% albumin (human), 20 ppm Tween 80™, and <1 ppm of bovine serum. Trace amounts of streptomycin and neomycin may be present as a result of the production process.

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\*Official names: Enhanced-Inactivated Poliomyelitis Vaccine (IPOL™), manufactured by Pasteur Mérieux Sérums & Vaccins S.A. Lyon, France; (POLIOVAX™), manufactured by Connaught Laboratories Limited, Willowdale, Ontario, Canada. Both vaccines are distributed by Connaught Laboratories, Inc., Swiftwater, PA 18370.

## SEQUENTIAL USE OF IPV FOLLOWED BY OPV

The sequential use of IPV and OPV has been proposed in the United States for more than a decade (41). In 1988, the Institute of Medicine reviewed poliomyelitis vaccination options for the United States and recommended adoption of a sequential schedule if a vaccine combining diphtheria and tetanus toxoids and pertussis vaccine and inactivated poliovirus vaccine (DTP-IPV) were licensed (42).

A sequential schedule of three doses of IPV followed by three doses of OPV has been used in Denmark since 1968 (43). More recently, Hungary and Lithuania have adopted vaccination schedules that include at least one dose of IPV followed by OPV (44). In North America, one province in Canada (Prince Edward Island) has also used a sequential vaccination schedule for many years.

### Immunogenicity

Investigators have evaluated different sequential vaccination schedules that use one to three doses of IPV followed by one to three doses of OPV. Most have concluded that two doses of IPV are necessary to induce levels of poliovirus antibody protective against VAPP before the first dose of OPV is administered (32,36,37).

In four of five studies, two doses of IPV induced development of protective antibodies to all three poliovirus serotypes in  $\geq 90\%$  of recipients (32,36,45,46). The fifth study indicated seroprevalence of antibodies to serotype 3 as low as 71% among recipients of an IPV produced in MRC-5 cells (POLIOVAX™) (37). In contrast, all studies using the IPV produced in Vero cells (the predominant IPV to be used in the United States) detected antibody to type 3 poliovirus among  $\geq 94\%$  of persons vaccinated. In each of four studies, investigators detected antibodies to poliovirus types 1 and 2 among  $>94\%$  of persons who had received two doses of IPV followed by one dose of OPV; 81%–100% of these persons had antibody to type 3. The timing of the dose of OPV did not influence the prevalence of antibody to poliovirus (Table 2) (36,37,45,46). With the addition of a second dose of OPV, all studies report seroconversion rates  $\geq 95\%$  to all three serotypes (37,45).

Both IPV and OPV induce immunity of the mucosa of the gastrointestinal tract, but the mucosal immunity induced by OPV is superior (47,48). Only one study has evaluated the improvement in this intestinal immunity when additional doses of OPV are administered after two doses of IPV. Among children who received three doses of IPV, the prevalence of viral shedding after administration of a challenge dose of OPV (i.e., a dose administered for purposes of measuring viral excretion) was 85%. In contrast, 66% of children who had received one previous dose of OPV and 25% of children who received two previous doses of OPV shed virus after the OPV challenge. No additional benefit was gained from a third dose (37). These data suggest that optimal gastrointestinal immunity is achieved after two doses of OPV in the sequential schedule. Both IPV and OPV are effective in reducing pharyngeal replication and subsequent transmission of poliovirus by the oral-oral route.

### Safety of a Sequential Schedule

The safety of sequential poliomyelitis vaccination schedules has been assessed among several hundred study participants (Table 2) and among infants residing in

**TABLE 2. Percent of vaccinated children seropositive\* following vaccination with IPV<sup>†</sup> alone, OPV<sup>§</sup> alone or IPV followed by OPV: Studies conducted in the United States**

Studies	Vaccine schedule				N <sup>¶</sup>	Poliovirus serotype								
	Type of vaccine administered					After dose 2			After dose 3			After dose 4		
	2 mos.	4 mos.	6 mos.	12-18 mos.		P1	P2	P3	P1	P2	P3	P1	P2	P3
McBean et al. [32]	I**†	I		I	331	99	99	99	99	100	100			
	I	I		I	332	99	100	100	100	100	100			
Faden et al. [36]	O <sup>§</sup>	O		O	337	92	100	96	97	100	100			
	I**	I		I	91	96	100	96	96	100	100			
	O	O		O	22	100	100	100	100	100	100			
	I**	O		O	29	94	100	94	100	100	100			
Modlin et al. [37]	I**	I		O	29	100	100	100	100	100	100			
	I <sup>§§</sup>	I		I	101	97	92	78	100	100	100			
	O	O		O	98	95	100	90	95	100	100			
	I <sup>§§</sup>	I		O	98	90	93	74	97	100	85			
Blatter & Starr [46]	I <sup>§§</sup>	I/O	O	O	106	89	96	71	94	100	81	95	100	95
	I <sup>§§</sup>	I/O	O	O	101	96	100	85 <sup>¶¶</sup>	93	99	97 <sup>***</sup>	98	100	100 <sup>†††</sup>
	I**	I		I	94	97	96	95	100	100	100			
	I††	I		I	68	98	100	98	100	100	100			
	I**	I		O	75	94	98	96	100	100	96			
Halsey et al. [45]	I††	I	I	O	99	99	99	95	100	100	99			
	I††	I		O	97	98	98	100	100	100	100	100	100	100
	I††	I	O	O	96	100	97	99	100	100	100	100	100	100
	I††	I	I/O	O	91	95	96	100	100	100	100 <sup>***</sup>	100	100	100 <sup>†††</sup>

\* Seropositivity defined as reciprocal antibody titers >8.

† Enhanced-potency inactivated poliovirus vaccine.

§ Live, oral poliovirus vaccine.

¶ Number of children enrolled at beginning of study.

\*\* IPV grown in Vero cells.

†† IPV grown in Vero cells and administered through double-barrelled syringe with DTP vaccine.

§§ IPV grown in MRC-5 cells.

¶¶ After second visit.

\*\*\* After third visit.

††† After fourth visit.



countries that routinely use sequential schedules. No serious adverse reactions have been reported from these studies. Over a 30-year period, approximately 1.5 million children in Denmark have been vaccinated with IPV followed by OPV. The only case of VAPP reported among these children occurred in 1969; it affected a child who had received only one dose of IPV (43). During the period of transition from IPV to OPV use in the United States (1961–1965), OPV was administered to millions of children who had previously received IPV. No serious adverse consequences were reported.

## VAPP

A sequential vaccination schedule is expected to reduce VAPP by  $\geq 50\%$ . Circulating antibody against poliovirus induced by IPV is expected to reduce the already minimal risk for VAPP among immunocompetent recipients (among whom approximately three cases occur annually) nearly to zero (9). Further reduction in VAPP may result from decreases in the overall use of OPV in the United States. Decreased community exposure to excreted poliovirus derived from OPV is expected to reduce the number of community-acquired cases of VAPP (3). IPV-induced immunity of the pharyngeal mucosa and (to a lesser degree) of the intestinal mucosa may also reduce the number of contact cases by preventing oral-oral and fecal-oral transmission.

Genetic sequencing studies suggest that reversion of Sabin poliovirus strains to potentially more neurovirulent phenotypes occurs commonly after OPV administration (49,50). Findings of two studies indicate that the use of a sequential vaccination schedule may not reduce the frequency of such reversions (51,52). However, findings from a third more systematic study designed to examine the issue of reversion suggest that, although administration of a dose of IPV before two or more doses of OPV may reduce shedding of type 3 virus (the most common cause of VAPP), the practice will not influence the shedding of types 1 or 2 or the extent of reversion (53). Thus, even if OPV is administered only to persons who have previously received one or more doses of IPV, reversion of vaccine poliovirus and excretion of revertant strains may still cause VAPP among susceptible contacts of OPV recipients.

In the United States, an average of two cases of VAPP among immunodeficient persons is reported annually. The recommended sequential IPV-OPV vaccination schedule may also reduce the occurrence of such cases (3,9,31,54,55). Although the use of OPV is contraindicated in this group (54–56), the diagnosis of immunodeficiency is frequently not established by 2 months of age, when the infant is scheduled to receive the first dose of OPV under the previous ACIP recommendations (55). The new recommendations delay the administration of the first dose of OPV to 12–18 months of age. This change will allow an additional 10 months for diagnosis of any immunodeficiency disorder that would contraindicate administration of OPV.

Some VAPP cases will likely occur despite the adoption of a sequential IPV-OPV vaccination schedule. Only the exclusive use of IPV or the discontinuation of all poliovirus vaccination efforts after achievement of global poliomyelitis eradication will completely eliminate VAPP.

## Programmatic Issues

Because no combination vaccine that includes IPV as a component is currently licensed in the United States, adoption of sequential IPV-OPV or all-IPV vaccination

schedules will require additional injections at 2 and 4 months of age. In addition, acellular pertussis vaccine for use among infants has been licensed as DTaP rather than as a combined vaccine (e.g., DTaP-*Haemophilus influenzae* type b conjugate vaccine [HbCV]) and is preferred for the pertussis vaccine series. DTP remains an acceptable alternative. Several licensed combination vaccines are available (e.g., DTP-HbCV, HbCV and hepatitis B combination vaccine [COMVAX™, Merck Co.]). Use of these vaccines during visits when IPV is administered will reduce the number of injections needed at a single visit.

For each infant, health-care providers and parents must decide which of the following alternatives is preferable: a) additional injections, b) use of licensed combination vaccines, c) polio vaccination with OPV only, or d) additional clinic visits for administration of vaccines. Health-care providers should select a vaccination schedule for which the likelihood of compliance will be high, thereby promoting optimal protection against all vaccine-preventable childhood diseases.

## RECOMMENDATIONS FOR POLIOVIRUS VACCINATION

### Routine Vaccination

#### *Rationale for Choice of Vaccine*

Parents of children who are to be vaccinated should be informed of the poliovirus vaccines available, the three alternative vaccination schedules, and the basis for poliovirus vaccination recommendations. The benefits and risks of the vaccines as well as the advantages and disadvantages of the three vaccination options for individuals and for the community, should be discussed (Table 3).

**TABLE 3. Advantages and disadvantages of three poliovirus vaccination options**

Attribute	OPV*	IPV†	IPV-OPV‡
Occurrence of VAPP¶	8–9 cases/year	None	2–5 cases/year**
Other serious adverse events	None known	None known	None known
Systemic immunity	High	High	High
Immunity of GI mucosa	High	Low	High
Secondary transmission of vaccine virus	Yes	No	Some
Extra injections or visits needed	No	Yes	Yes
Compliance with immunization schedule	High	Possibly reduced	Possibly reduced
Future combination vaccines	Unlikely	Likely	Likely (IPV)
Current cost	Low	Higher	Intermediate

\* Oral poliovirus vaccine.

† Inactivated poliovirus vaccine.

‡ Sequential vaccination with IPV and OPV.

¶ Vaccine-associated paralytic poliomyelitis.

\*\* Estimated.

Vaccination schedules using IPV alone or OPV alone are both effective; both are acceptable options for preventing poliomyelitis. However, ACIP recommends the use of IPV followed by OPV for primary poliovirus vaccination of children in the United States because a) high levels of individual protection from two doses of IPV should reduce by 95% the number of VAPP cases that occurs among OPV recipients; b) sequential administration of IPV and OPV also may reduce VAPP among household and community contacts of OPV recipients because IPV provides some degree of intestinal and pharyngeal immunity; c) continued use of OPV induces intestinal immunity among vaccine recipients, thereby enhancing community resistance to transmission of wild virus (should it be reintroduced); d) fewer injections are required in the second year of life than would be required if only IPV were used, facilitating compliance with the overall childhood vaccination schedule; and e) stocking of both poliovirus vaccines by health-care providers enhances parental choice. Licensure of additional combination products will reduce the number of injections needed to administer the complete series of recommended childhood vaccinations.

When the vaccination series is started after 6 months of age, OPV alone is preferred to enhance parent and provider compliance with the full childhood vaccination schedule. In this situation, the need to ensure administration of all recommended vaccines may require four or more simultaneous injections at each visit (see Accelerated Vaccination Schedule). OPV may be preferred if, during an initial visit, parents or providers decline the extra injections needed to administer all the recommended vaccines. OPV is preferred especially if there is concern that the child will not return on time for future vaccinations. OPV may also be preferred for children who are likely to travel to countries where polio is endemic. The superior gastrointestinal immunity conferred by OPV will reduce the risk that these children, should they be exposed during travel, might subsequently reintroduce wild poliovirus to the United States.

IPV is the only poliovirus vaccine recommended for immunocompromised persons and their family contacts (see Immunocompromised Persons). In addition, an all-IPV vaccination schedule may be used when the number of injections is not a concern and is not likely to decrease parent or provider compliance with the childhood immunization schedule. Some parents or providers may prefer an all-IPV option to minimize the risk for VAPP.

### ***Sequential Use of IPV and OPV***

For infants, children, and adolescents (i.e., persons <18 years of age), the primary sequential series of IPV and OPV consists of four doses. The primary series is administered at ages 2 months (IPV), 4 months (IPV), 12–18 months (OPV), and 4–6 years (OPV). For persons of any age, the first three doses should be separated by at least 4 weeks, although an interval of 6–8 weeks is preferred (see Accelerated Vaccination Schedule). Both IPV and OPV can be administered simultaneously with diphtheria and tetanus toxoids and whole-cell or acellular pertussis vaccine (DTP or DTaP), HbCV, hepatitis B vaccine, varicella vaccine, and measles-mumps-rubella (MMR) vaccine.

### ***OPV Alone***

The primary series consists of three doses of vaccine. For infants, the primary series is usually integrated with the other vaccines routinely administered at 2, 4, and 6–18 months of age (Table 4). For routine vaccination, the minimum recommended

interval between doses of OPV is 6–8 weeks. If the third dose of OPV is administered before the fourth birthday, a fourth dose of OPV should be provided before school entry (at 4–6 years of age). The fourth dose is not needed if the third dose is administered on or after the fourth birthday. OPV should not be used for the primary vaccination of persons  $\geq 18$  years of age (see Recommendations for Adults).

### ***IPV Alone***

The primary series consists of three doses of vaccine. In infancy, these primary doses are integrated with the administration of other routinely administered vaccines. The first two doses are administered at 2 and 4 months of age; the third dose should be administered at 12–18 months of age with an interval of 6–12 months between the second and third doses (Table 4). Whereas the first and second doses of IPV are necessary to induce a primary immune response, the third dose of IPV ensures “boosting” of antibody titers to high levels. If accelerated protection is needed, the minimum interval between doses of IPV is 4 weeks, although the preferred interval between the second and third doses is 6 months (see Recommendations for Adults). All children who have received three doses of IPV before their fourth birthdays should receive a fourth dose before or at school entry. The fourth dose is not needed if the third dose is administered on or after the fourth birthday.

### ***Interchangeability of Vaccines***

Completion of poliovirus vaccination with any of the three options (sequential IPV-OPV, OPV alone, or IPV alone) is preferred. However, if the vaccines are administered according to their licensed indications for minimum ages and intervals between doses, administration of four doses of IPV or OPV in any combination by 4–6 years of age is considered a complete poliovirus vaccination series. A minimum interval of 4 weeks should elapse if IPV is administered after OPV.

### ***Options for Reducing the Number of Injections***

The number of injections needed to administer all recommended childhood vaccines to children 2 and 4 months of age (i.e., IPV, DTP or DTaP, HbCV, and hepatitis B) can be reduced to three (if IPV and HbCV combined with hepatitis B vaccine are administered) or two (if OPV and HbCV combined with hepatitis B vaccine are administered). For parents concerned about the number of injections, the following options to decrease the number of injections at the 2- and 4-month visits may be helpful: a) schedule the hepatitis B vaccine series at 0, 1, and 6 months of age (so that no doses

**TABLE 4. Recommended poliovirus vaccination schedules for children**

Vaccination schedule	Child's age			
	2 mos.	4 mos.	12–18 mos.	4–6 yrs.
Sequential IPV*/OPV†	IPV	IPV	OPV	OPV
OPV*	OPV	OPV	OPV <sup>§</sup>	OPV
IPV†	IPV	IPV	IPV	IPV

\* Inactivated poliovirus vaccine.

† Live, oral poliovirus vaccine.

§ For children who receive only OPV, the third dose of OPV may be administered as early as 6 months of age.

of hepatitis B vaccine are needed during the 2- and 4-month visits); b) use licensed combination vaccines; c) schedule additional visits (if it can be ensured the child will be brought back for subsequent vaccinations at the recommended ages); and d) use OPV for the primary vaccination series. Development and licensure of additional combination products that contain the vaccine antigens recommended for children <1 year of age will make vaccination schedules that include IPV easier to implement.

### ***Supplementary Vaccination at School Entry***

The poliovirus vaccination status of all children should be checked at school entry. The requirements for supplementary poliovirus vaccination depend on the type of vaccination schedule and the child's age and vaccination history.

- *Sequential IPV-OPV vaccination schedule.* Children should receive a second dose of OPV to complete the four-dose sequential series, regardless of the age at which the series is initiated. Children who have previously received two doses of IPV followed by two doses of OPV do not require a supplementary dose at 4–6 years of age.
- *All-OPV vaccination schedule.* Children who have previously received three doses of OPV should receive a fourth dose. However, if the third primary dose was administered on or after the fourth birthday, the fourth dose is not required.
- *All-IPV vaccination schedule.* Children who have previously received three doses of IPV should receive a fourth dose. However, if the third primary dose was administered on or after the fourth birthday, the fourth dose is not required.

### ***Immunocompromised Persons***

IPV is the only poliovirus vaccine that should be administered to infants, adolescents, or adults if they have or are suspected to have a) an immunodeficiency disorder of any etiology (including infection with human immunodeficiency virus [HIV]), or if b) they are receiving immunosuppressive chemotherapy (e.g., cancer chemotherapy, or systemic steroid use). Because OPV virus can spread secondarily, OPV should not be administered to immunologically competent persons who live in a household with a person who has or is suspected to have any of these conditions; only IPV should be used.

### ***Incompletely Vaccinated Children***

Children's poliovirus vaccination status should be reevaluated periodically. Those who are inadequately protected should complete the recommended vaccination series:

- *Sequential IPV-OPV vaccination schedule.* The primary series of two doses of IPV followed by two doses of OPV is needed to ensure adequate humoral and intestinal immunity. Additional doses of vaccine are not needed if more than the recommended interval elapses between doses.
- *All-OPV vaccination schedule.* The primary series of three doses of OPV is needed to ensure development of antibody to all three serotypes of poliovirus.

Additional doses of vaccine are not needed if more than the recommended 6–8 weeks elapses between doses of OPV.

- *All-IPV vaccination schedule.* Three doses of enhanced-potency IPV administered after 1987 are considered a complete primary series. As with OPV, no additional doses are needed if more time than recommended elapses between doses (e.g., >6–8 weeks between the first two doses or >6–12 months between the second and third doses). For IPV administered before 1988, four doses were required to complete a primary series (three doses administered at an interval of 4–8 weeks with a fourth dose 6–12 months after the third) (46,47).

### ***Accelerated Vaccination Schedule***

For infants and children starting vaccination late (i.e., >6 months of age) or for whom accelerated protection against poliomyelitis is required, vaccination with OPV only is preferred (if not contraindicated). The minimum interval between doses of OPV under these circumstances is 4 weeks. A three-dose accelerated OPV series can be administered simultaneously with DTP or DTaP, HbCV, hepatitis B, MMR, and varicella vaccines. Limited data from the United States suggest that the rate of seroconversion among children vaccinated with three doses of OPV at 4-week intervals is similar to the rate among children who receive three doses of OPV at 8-week intervals (57). Children should be administered a supplemental dose of OPV at 4–6 years of age.

For infants and children for whom IPV is indicated, the accelerated schedule permits administration of the first two doses of IPV with a minimum interval of 4 weeks. An interval of 6 months between the second and third doses is preferred because it will provide optimal immune response. As with OPV, these children should receive an additional dose of IPV at 4–6 years of age.

For accelerated sequential IPV-OPV vaccination of infants and children, the first three doses (IPV, IPV, OPV) should be administered at 4-week intervals. The second dose of OPV should be administered at 4–6 years of age.

Incompletely vaccinated children who are at increased risk for exposure to poliovirus should be administered the remaining required doses. If time is a limiting factor, incompletely vaccinated children should be administered at least a single dose of either vaccine (see Recommendations for Adults).

## **RECOMMENDATIONS FOR ADULTS**

Routine poliovirus vaccination of adults (generally persons  $\geq 18$  years of age) residing in the United States is not necessary. Most adults have a minimal risk for exposure to polioviruses in the United States and most are immune as a result of vaccination during childhood.

Vaccination is recommended for certain adults who are at greater risk for exposure to polioviruses than the general population, including the following persons:

- travelers to areas or countries where poliomyelitis is epidemic or endemic,
- members of communities or specific population groups with disease caused by wild polioviruses,
- laboratory workers who handle specimens that may contain polioviruses,

- health-care workers who have close contact with patients who may be excreting wild polioviruses,
- unvaccinated adults whose children will be receiving oral poliovirus vaccine.

For unvaccinated adults, primary vaccination with IPV is recommended because the risk for vaccine-associated paralysis after administration of OPV is higher among adults than among children (29). Two doses of IPV should be administered at intervals of 4–8 weeks; a third dose should be administered 6–12 months after the second.

If three doses of IPV cannot be administered within the recommended intervals before protection is needed, the following alternatives are recommended:

- If  $\geq 8$  weeks are available before protection is needed, three doses of IPV should be administered at least 4 weeks apart.
- If  $< 8$  but  $> 4$  weeks are available before protection is needed, two doses of IPV should be administered at least 4 weeks apart.
- If  $< 4$  weeks are available before protection is needed, a single dose of OPV or IPV is recommended.

The remaining doses of vaccine should be administered later, at the recommended intervals, if the person remains at increased risk.

Adults who have had a primary series of OPV or IPV and who are at increased risk for exposure to poliovirus may receive another dose of either OPV or IPV. Persons who may be at increased risk include a) travelers to areas where poliomyelitis is endemic, b) certain laboratory personnel, and c) medical staff directly involved with the provision of care to patients who may be excreting poliovirus. These adults are not at increased risk for VAPP. The need for administration to adults of more than one supplementary dose of either IPV or OPV has not been established.

Adults who have not been adequately vaccinated against poliomyelitis with OPV or IPV have a minimal risk for developing OPV-associated paralytic poliomyelitis when OPV is administered to children in their households. Since 1980, approximately one–two cases of VAPP have occurred each year among adult household contacts of children who received OPV; during that time approximately 19 million doses of OPV were distributed yearly (see Adverse Reactions).

Because of the overriding importance of ensuring prompt and complete immunization, sequential IPV-OPV vaccination of children should begin regardless of the poliovirus vaccine status of adult household contacts. If unvaccinated or inadequately vaccinated persons are known to reside in the child's household, IPV alone should be used to complete the child's vaccination, thereby reducing the already minimal risk for VAPP among adult household contacts.

## **PRECAUTIONS AND CONTRAINDICATIONS**

### **Hypersensitivity or Anaphylactic Reactions to IPV, OPV, or the Antibiotics Contained in These Vaccines**

IPV should not be administered to persons who have experienced an anaphylactic reaction following a previous dose of IPV or an anaphylactic reaction to streptomycin, polymyxin B, or neomycin. OPV should not be administered to persons who have experienced an anaphylactic reaction to a previous dose of OPV.

### **Pregnancy**

Although no adverse effects of OPV or IPV have been documented among pregnant women or their fetuses, vaccination of pregnant women should be avoided. However, if a pregnant woman requires immediate protection against poliomyelitis, she may be administered OPV or IPV in accordance with the recommended schedules for adults. (See Recommendations for Adults.)

### **Immunodeficiency**

OPV should not be administered to persons who have immunodeficiency disorders (e.g., severe combined immunodeficiency syndrome, agammaglobulinemia, or hypogammaglobulinemia) because these persons are at substantially increased risk for VAPP. Similarly, OPV should not be administered to persons with altered immune states resulting from malignant disease (e.g., leukemia, lymphoma, or generalized malignancy), or to persons whose immune systems have been compromised (e.g., by therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation or by HIV infection). OPV should not be used to vaccinate household contacts of immunodeficient patients; IPV is recommended. Many immunosuppressed persons are immune to polioviruses as a result of previous vaccination or exposure to wild-type virus at a time when they were immunologically competent. Although their risk for paralytic disease is thought to be less than that for persons with congenital or acquired immunodeficiency disorders, these persons should not receive OPV. Administration of IPV to immunodeficient persons is safe. Although a protective immune response in these persons cannot be assured, IPV may confer some protection.

### **Inadvertent Administration of OPV to Members of Households with Immunocompromised Persons**

If OPV is inadvertently administered to a household contact of an immunodeficient patient, the patient and the recipient of OPV should avoid close contact for approximately 4–6 weeks after vaccination. If this is not feasible, rigorous hygiene and hand washing after contact with feces (e.g., after diaper changing) and avoidance of contact with saliva (e.g., sharing food or utensils) may be an acceptable but probably a less effective alternative. Maximum excretion of vaccine virus occurs within 4 weeks after oral vaccination.



## False Contraindications

Breastfeeding does not interfere with successful immunization against poliomyelitis with IPV or OPV. A dose of IPV may be administered to a child who has diarrhea. A dose of OPV may be administered to a child who has mild diarrhea. Minor upper respiratory illnesses with or without fever, mild to moderate local reactions to a previous dose of vaccine, current antimicrobial therapy, and the convalescent phase of an acute illness are not contraindications for vaccination with IPV or OPV (58).

## Regurgitation of OPV

Infants may not completely swallow OPV. If, in the judgment of the person administering the vaccine, a substantial amount of vaccine is regurgitated or vomited soon after administration (i.e., within 5–10 minutes) another dose can be administered during the same visit. If this repeat dose is not retained, neither dose should be counted and the vaccine should be readministered during a later visit (58).

## ADVERSE REACTIONS

### IPV

No serious side effects of enhanced-potency IPV have been documented. Because IPV contains trace amounts of streptomycin, polymyxin B, and neomycin, hypersensitivity reactions may occur among persons sensitive to these antibiotics.

### OPV

In rare instances, administration of OPV has been associated with paralysis in healthy recipients and their contacts. No procedures are currently available for identifying persons (other than those with immunodeficiency) who are at risk for such adverse reactions. Although the risk for vaccine-associated paralysis is minimal, vaccinees (or their parents) and their susceptible, close, personal contacts should be informed of this risk (Table 1). Administration of OPV may very rarely cause paralytic poliomyelitis that results in death (3,31).

## Guillain-Barré Syndrome

The available evidence indicates that administration of OPV or IPV does not measurably increase the risk for Guillain-Barré syndrome (GBS). Preliminary findings from two studies in Finland led to a contrary conclusion in a review conducted by the Institute of Medicine (IOM) in 1993 (59,60). The investigators in Finland reported an apparent increase in the incidence of GBS that was temporally associated with a mass vaccination campaign during which OPV was administered to children and adults who had previously been vaccinated with IPV. After the IOM review was completed, however, these data were reanalyzed and an observational study was completed in the United States. Neither the reanalysis nor the newly completed study provided evidence of a causal relationship between OPV administration and GBS (61).

## Reporting of Adverse Events Following Vaccination

The National Childhood Vaccine Injury Act of 1986 requires health-care providers to report serious adverse events following poliovirus vaccination (62). The events that must be reported are detailed in the Reportable Events Table within this Act, and include paralytic poliomyelitis and any acute complications or sequelae of paralytic poliomyelitis. Adverse reactions should be reported to the Vaccine Adverse Events Reporting System (VAERS). VAERS reporting forms and information are available 24 hours a day by calling (800) 822-7967.

## Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program, established by the National Childhood Vaccine Injury Act of 1986, provides a mechanism through which compensation can be paid on behalf of a person who died or was injured as a result of receiving vaccine.

A Vaccine Injury Table in the Act lists the vaccines covered by the program and the injuries, disabilities, illnesses, and conditions (including death) for which compensation may be paid. Development or onset of vaccine-associated paralytic poliomyelitis in an OPV recipient (within 30 days), or in a person in contact with an OPV vaccinee (not specified), or in an immunodeficient person (within 6 months) are potentially compensable under this law. Additional information is available (63).\*

## INVESTIGATION AND REPORTING OF SUSPECTED POLIOMYELITIS CASES

### Case Investigation

Each suspected case of poliomyelitis should prompt an immediate epidemiologic investigation. If evidence suggests the transmission of wild poliovirus, an active search for other cases that may initially have been misdiagnosed (e.g., as GBS, polyneuritis, or transverse myelitis) should be conducted. Control measures (including an OPV vaccination campaign designed to contain further transmission) should be instituted immediately. If evidence suggests vaccine-related poliovirus, no vaccination plan need be developed, because no outbreaks associated with live, attenuated vaccine-related poliovirus strains have been documented. Within an epidemic area, OPV should be provided for all immunocompetent persons, regardless of previous OPV vaccination status (see Immunodeficiency).

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\*National Vaccine Injury Compensation Program  
Health Resources and Services Administration  
Parklawn Building, Room 8-05  
5600 Fishers Lane  
Rockville, MD 20857  
Telephone: (800) 338-2382 (24-hour recording)

Persons wishing to file a claim for vaccine injury should call or write:  
U.S. Court of Federal Claims  
717 Madison Place, NW  
Washington, DC 20005  
Telephone: (202) 219-9657

The two most recent outbreaks of poliomyelitis reported in the United States affected members of religious groups who object to vaccination (i.e., outbreaks occurred in 1972 among Christian Scientists and in 1979 among members of an Amish community). Poliomyelitis should be suspected in any case of acute flaccid paralysis that affects an unvaccinated member of such a religious group. All such cases should be investigated promptly and followed up accordingly (see Surveillance).

## Surveillance

CDC conducts national surveillance for poliomyelitis in collaboration with state and local health departments. Suspected cases of poliomyelitis must be reported immediately to local or state health departments. CDC compiles and summarizes clinical, epidemiologic, and laboratory data concerning suspected cases. Three independent experts review the data and determine whether a suspected case meets the clinical case definition of paralytic poliomyelitis (i.e., a paralytic illness clinically and epidemiologically compatible with poliomyelitis in which a neurologic deficit is present 60 days after onset of symptoms [unless death has occurred or follow-up status is unknown]). On the basis of epidemiologic and laboratory criteria, CDC classifies confirmed cases of paralytic poliomyelitis as vaccine-associated or wild-type related and (based on OPV exposure data) as vaccine recipient or contact cases (9). For the recommended control measures to be undertaken in a timely manner, a preliminary assessment must ascertain as soon as possible whether a suspected case is likely vaccine-associated or caused by wild poliovirus (see Case Investigation and Laboratory Methods).

## Laboratory Methods

Specimens for virus isolation (e.g, stool, throat swab, and cerebrospinal fluid [CSF]) and serologic testing must be obtained in a timely fashion. The greatest yield for poliovirus is from stool culture, and timely collection of stool specimens increases the likelihood of case confirmation. At least two stool specimens and two throat swab specimens should be obtained from patients who are suspected to have poliomyelitis. Specimens should be obtained at least 24 hours apart as early in the course of illness as possible, ideally within 14 days of onset. Stool specimens collected  $\geq 2$  months after the onset of paralytic manifestations are unlikely to yield poliovirus. Throat swabs are less often positive than stool samples, and virus is rarely detected in CSF. In addition, an acute-phase serologic specimen should be obtained as early in the course of illness as possible, and a convalescent-phase specimen should be obtained at least 3 weeks later.

The following tests should be performed on appropriate specimens collected from persons who have suspected cases of poliomyelitis: a) isolation of poliovirus in tissue culture; b) serotyping of a poliovirus isolate as type 1, 2, or 3; and c) intratypic differentiation using DNA/RNA probe hybridization or polymerase chain reaction to determine whether a poliovirus isolate is vaccine-related or wild-type.

Acute-phase and convalescent-phase serum specimens should be tested for neutralizing antibody to each of the three poliovirus serotypes. A fourfold rise in antibody titer between appropriately timed acute-phase and convalescent-phase serum specimens is diagnostic for poliovirus infection. The recently revised standard protocol for

poliovirus serology should be used (64). Commercial laboratories usually perform complement fixation and other tests. However, assays other than neutralization are difficult to interpret because of inadequate standardization and relative insensitivity. Laboratory experts at CDC are available for consultation and will test specimens from patients who have suspected poliomyelitis (i.e., patients with acute paralytic manifestations); telephone (404) 639-2749.

## **RECOMMENDED SURVEILLANCE, RESEARCH, AND EDUCATION ACTIVITIES**

Several programmatic activities in disease surveillance, research, and education should be implemented in conjunction with the new poliovirus vaccination schedule. The recommended activities are:

- a) Enhance surveillance for paralytic poliomyelitis to facilitate early detection and control of outbreaks caused by imported wild virus and to evaluate the impact of the revised vaccination schedule on incidence of VAPP.
- b) Conduct expanded surveillance of potential adverse effects of IPV as the vaccine is administered to more children and adults.
- c) Assess the possible influence of the revised vaccination schedule on childhood vaccine coverage (particularly in populations in which coverage is suboptimal); continue development of vaccine registries.
- d) Expand surveillance of other vaccine-preventable childhood diseases as a means of detecting possible effects of the revised polio vaccination schedule (particularly the required additional injections) on coverage with all vaccines recommended for infants and children.
- e) Develop and evaluate materials to educate parents and health-care providers about poliovirus vaccines and vaccination schedules.
- f) Evaluate parent and provider acceptance of the additional injections required by the revised vaccination schedule at 2 and 4 months of age.
- g) Accelerate development of combination vaccines.

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