



## AMERICAN ACADEMY OF PEDIATRICS

Committee on Infectious Diseases

### POLICY STATEMENT

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of All Children

#### **Prevention of Rotavirus Disease: Updated Guidelines for Use of Rotavirus Vaccine**

**ABSTRACT.** This statement updates and replaces the 2007 American Academy of Pediatrics (AAP) statement for prevention of rotavirus gastroenteritis. In February 2006, a live, oral human-bovine reassortant rotavirus vaccine (RV5 [RotaTeq]) was licensed as a 3-dose series for use in infants in the United States. The AAP recommended routine use of RV5 in infants in the United States. In April 2008, a live, oral human attenuated rotavirus vaccine (RV1 [Rotarix]) was licensed as a 2-dose series for use in infants in the United States. The AAP recommends routine immunization of infants in the United States with rotavirus vaccine. The AAP does not express a preference for either RV5 or RV1. RV5 is to be administered orally in a 3-dose series with doses administered at 2, 4, and 6 months of age. RV1 is to be administered orally in a 2-dose series with doses administered at 2 and 4 months of age. The first dose of rotavirus vaccine should be administered from 6 weeks through 14 weeks, 6 days of age. The minimum interval between doses of rotavirus vaccine is 4 weeks. All doses should be administered by 8 months, 0 days of age. Recommendations in this statement also address the maximum ages for doses, contraindications, precautions, and special situations for administration of rotavirus vaccine.

*Key words: rotavirus vaccine, rotavirus gastroenteritis.*

## **Prevention of Rotavirus Disease: Updated Guidelines for Use of Rotavirus Vaccine, *continued***

ABBREVIATIONS: RV1, live, oral human attenuated rotavirus vaccine; RV5, live, oral human-bovine reassortant rotavirus vaccine; AAP, American Academy of Pediatrics; DTaP, diphtheria and tetanus toxoids and acellular pertussis; Hib, *Haemophilus influenzae* type b; IPV, inactivated poliovirus vaccine; HBV, hepatitis B vaccine.

### **SUMMARY OF CHANGES TO THE RECOMMENDATIONS FROM THE 2007**

#### **STATEMENT**

1. Recommendations now include a second rotavirus vaccine, live, oral human attenuated rotavirus vaccine (RV1 [Rotarix, GlaxoSmithKline, [Rixensart, Belgium]], administered in a 2-dose series at 2 and 4 months of age.
2. Maximum ages for doses
  - a. Maximum age for dose 1 of rotavirus vaccine is now 14 weeks, 6 days of age (previous recommendation: 12 weeks of age).
  - b. Maximum age for last dose of rotavirus vaccine is now 8 months, 0 days of age (previous recommendation: 32 weeks of age).
3. The minimum interval between doses of rotavirus vaccine is 4 weeks (previous recommendation: 4 through 10 weeks between doses).
4. The rationale to consider rotavirus immunization of HIV-exposed or HIV-infected infants is described.
5. Rotavirus vaccine may be administered at any time before, concurrent with, or after administration of any blood product, including antibody-containing blood products. The previous recommendation was to defer immunization for 42 days following receipt of an antibody-containing product, if possible.

#### **PURPOSE OF REVISED RECOMMENDATIONS AND RATIONALE**

The purpose of this statement is to update recommendations of the American Academy of Pediatrics (AAP) for routine use of rotavirus vaccine in infants, which originally were published in

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*Pediatrics* in January 2007.<sup>1</sup> Updated recommendations are needed because a second rotavirus vaccine has been licensed, and the 2 licensed rotavirus vaccines differ in composition and US Food and Drug Administration (FDA)-licensed schedule of administration (Table 1).

### **INTRODUCTION**

Rotavirus is the most common cause of severe gastroenteritis in infants and young children worldwide. Before initiation of the rotavirus immunization program, it was estimated that nearly every child in the United States was infected with rotavirus by 5 years of age, and most infected children developed gastroenteritis. Each year, rotavirus caused more than 400 000 physician visits, more than 200 000 emergency department visits, 55 000 to 70 000 hospitalizations, 20 to 70 childhood deaths, and direct and indirect costs in excess of \$1 billion.<sup>2-5</sup>

### **VACCINES**

#### **Pentavalent Human-Bovine Reassortant Rotavirus Vaccine**

In February 2006, a live, oral human-bovine reassortant rotavirus vaccine (RV5 [RotaTeq, Merck and Co, Whitehouse Station, NJ]) was licensed for use in the United States. RV5 contains 5 live reassortant rotavirus strains. The rotavirus parent strains of the reassortants were isolated from human and bovine hosts. Four reassortant rotaviruses express 1 of the outer capsid proteins (G1, G2, G3, or G4) from the human rotavirus parent strain and the attachment protein (P7[5]) from the bovine rotavirus parent strain. The fifth reassortant virus expresses the attachment protein (P1A[8]) from the human rotavirus parent strain and the outer capsid protein G6 from the bovine rotavirus parent strain. RV5 is given to infants as 3 oral doses.

#### **Monovalent Human Rotavirus Vaccine**

A second rotavirus vaccine (RV1) was licensed on April 3, 2008 for use in the United States. The vaccine contains the RIX4414 strain of the human rotavirus G1P[8]. The RIX4414 strain was

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developed further from rotavirus strain 89–12, which originally was derived from a young boy in Cincinnati, OH. RV1 is administered to infants as 2 oral doses.

The safety and efficacy of RV5 and RV1 for prevention of rotavirus gastroenteritis in healthy infants have been evaluated in 11 randomized controlled trials involving more than 146 000 infants worldwide (Table 2). This includes 3 randomized controlled trials for RV5<sup>6-8</sup> and 7 randomized controlled trials for RV1.<sup>9-15</sup>

### **SAFETY**

#### **Reactogenicity**

Both vaccines are well tolerated with a low reactogenicity profile when given alone. They do not cause clinically significant increases in reactogenicity when coadministered with other routine childhood vaccines.<sup>16,17</sup>

For both vaccines the incidence of fever, vomiting, diarrhea, and irritability were measured in the clinical trials. For RV5, no significant difference versus placebo was observed in the incidence of fever or severe fever and irritability or severe irritability. A 3% increase in the incidence of diarrhea and vomiting was observed with RV5, but these symptoms were mild and did not require treatment.<sup>6,8,18</sup> For RV1, no difference versus placebo was observed in the incidence of diarrhea, fever or severe fever, vomiting or severe vomiting, and irritability or severe irritability within 14 days of immunization with any dose.<sup>9,10,13,15</sup> There was no statistically significant increased risk for death or other serious adverse events noted with either vaccine compared with placebo.

#### **Intussusception**

Two trials were designed specifically to evaluate the risk of intussusception after vaccine administration.<sup>8,11</sup> The risk of intussusception was no greater for either rotavirus vaccine than that observed in placebo recipients. For RV5, during the 42 days after each dose of vaccine, 6 cases of

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intussusception were reported among 28 038 vaccine recipients, and 5 cases were reported in 27 965 placebo recipients (relative risk [RR], 1.2; 95% confidence interval [95% CI], 0.3–5.0). During the 12 months after each dose of RV5, 12 cases of intussusception were reported among vaccine recipients and 15 in placebo recipients ([RR], 0.8; 95% CI, 0.3–1.8).<sup>8</sup> For RV1, during the 31 days after each dose of vaccine, 6 cases of intussusception were reported in 31 673 vaccine recipients, and 7 cases were reported in 31 552 placebo recipients (RR, 0.9; 95% CI, 0.3–2.4). In a subset of infants, during the 12 months after each dose of RV1, 4 cases of intussusception were reported among vaccine recipients and 14 in placebo recipients (RR, 0.3; 95% CI, 0.1–0.8).<sup>11</sup>

Even though neither RV5 nor RV1 has been associated with intussusception in large prelicensure trials, rigorous postlicensure monitoring for safety endpoints is necessary because of possible differences in the characteristics of infants receiving the vaccine in routine use compared with the clinical trials and the large numbers of infants being immunized. In addition, background cases of intussusception that are unrelated to vaccine are expected to occur in the weeks after immunization by chance alone.

With more than 14 million doses of RV5 distributed in the United States since 2006, the Centers for Disease Control and Prevention (CDC) Immunization Safety Office summary of postlicensure safety monitoring of RV5 does not indicate that immunization with RV5 is associated with intussusception.<sup>19</sup> Further monitoring is ongoing. Rigorous postlicensure monitoring for safety endpoints has also been initiated for RV1.

### **Shedding and Transmission**

Vaccine virus shedding in stool has been documented with both rotavirus vaccines. Rotavirus shedding occurs in approximately 9% of RV5 recipients after dose 1 but rarely after subsequent doses.<sup>18</sup> No cases of transmission of RV5 have been documented. Shedding and transmission are not

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considered significant safety concerns because of the attenuated nature of the rotavirus vaccine strains. For RV1, live rotavirus shedding in stool occurs in approximately 25% of recipients, with peak excretion occurring around day 7 after dose 1. Transmission of virus has not been evaluated. There have been a few cases of documented transmission to contacts. The rate of transmission is unknown, but no known cases have developed symptoms of rotavirus gastroenteritis.<sup>10</sup>

### **EFFICACY**

The efficacy of rotavirus vaccines was evaluated against the following endpoints in healthy infants: rotavirus gastroenteritis of any severity (RV5 and RV1), severe rotavirus gastroenteritis (RV5 and RV1), rotavirus gastroenteritis requiring an office visit (RV5) or medically attended visit (RV1), rotavirus gastroenteritis requiring hospitalization (RV5 and RV1) or an emergency department visit (RV5), and rotavirus gastroenteritis caused by different rotavirus serotypes (G1P[8], G2P[4], G3P[8], G4P[8], G9P[8]; RV5 and RV1).

Efficacy was demonstrated for each vaccine in prelicensure clinical trials. Vaccine efficacy studies demonstrated 85% to 98% protection against severe rotavirus disease and 74% to 87% protection against any rotavirus disease. The efficacy of RV5 after completion of a 3-dose regimen against rotavirus gastroenteritis of any severity was 74%.<sup>8</sup> In European infants, the efficacy of RV1 against rotavirus gastroenteritis of any severity was 87%.<sup>14</sup> The efficacy against rotavirus gastroenteritis of any severity was not measured in the Latin American trial of RV1.<sup>11</sup>

The severity of rotavirus gastroenteritis in these clinical trials was assessed using different clinical scales (Vesikari scale for RV1 and Clark scale for RV5). A recent study comparing the clinical scales found the 2 scales differ primarily in their definition of severe cases.<sup>20</sup> The authors of this study concluded that the use of different evaluation scales affects the ability to compare the effectiveness of rotavirus vaccines.

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Efficacy of RV5 against severe rotavirus gastroenteritis was 98%.<sup>8</sup> Data indicate that efficacy of RV1 against severe rotavirus gastroenteritis over the first rotavirus season in Europe was 96%, and efficacy against severe disease in Latin America was 85%.<sup>11,14</sup>

Efficacy against rotavirus gastroenteritis hospitalizations for RV5 was 96%.<sup>8</sup> For rotavirus gastroenteritis-associated emergency department visits, efficacy after the third dose of RV5 was 94%.<sup>8</sup> Efficacy of RV1 against any rotavirus gastroenteritis hospitalization in Europe was 96%, and efficacy against hospitalizations in Latin America was 85%.<sup>11,14</sup>

Rotavirus immunization reduced the need for any medical attention attributable to rotavirus gastroenteritis. For RV5, data indicate that immunization reduced the number of office visits by 86%.<sup>8</sup> Data available for RV1 from Europe indicate that efficacy in prevention of acute rotavirus gastroenteritis requiring medical attention (from a visit to a doctor to hospitalization) is 84% through the end of the second season of follow-up.<sup>14</sup>

Efficacy has been established for both vaccines against clinically important outcomes for the most prevalent circulating serotypes (G1P[8], G3P[8], G4P[8], G9P[8], and G2P[4]).<sup>8,11,14</sup> Efficacy of RV5 against rotavirus gastroenteritis-associated hospitalization or emergency department visits was demonstrated against G1 (95%), G2 (88%), G3 (93%), G4 (89%), and G9 (100%) serotypes, although relatively few non-G1 rotavirus cases were reported.<sup>8</sup> In Latin America, efficacy of RV1 against severe rotavirus episodes caused by serotype G1 strains, homologous to the vaccine strain, was 91%, and efficacy against strains sharing only the P[8] antigen (G3, G4, and G9) was 87%.<sup>11</sup> For serotype G2P[4] rotavirus, which does not share either the G or the P antigen with the RV1 vaccine strain, efficacy was 41%. In the European trial, efficacy of RV1 against severe rotavirus episodes caused by serotype G1 strains was 96%; efficacy was also demonstrated against G3 (94%), G4 (95%), and G9 (85%) serotype strains.<sup>14</sup> For serotype G2P[4] rotavirus efficacy was 86%.

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Data for efficacy of fewer than 3 doses of RV5 and fewer than 2 doses of RV1 are limited. The protective effect of RV1 against any grade of severity of rotavirus gastroenteritis observed immediately after receipt of dose 1 and before receipt of dose 2 was 90%.<sup>14</sup> Published data on the efficacy of fewer than 3 doses of RV5 are not available.

### **Interchangeability of Rotavirus Vaccines**

No studies address the interchangeability of the rotavirus vaccines. However, there is no theoretical reason to expect that risk of adverse events would be increased if the series included more than one product, compared with the risk of adverse events of a series containing only one product. Further, although it is possible that effectiveness of a series that contained both products could be reduced compared with a complete series with one product, the effectiveness of a series that contained both products is likely to be greater than an incomplete series with one product.

### **Postlicensure Vaccine Effectiveness of RV5 in the United States**

To summarize rotavirus activity during the 2007-08 rotavirus season, the CDC analyzed data from the National Respiratory and Enteric Virus Surveillance System and the New Vaccine Surveillance Network.<sup>21</sup> Compared with the 15 previous seasons (1991–2006), rotavirus activity during the 2007-08 rotavirus season was delayed in onset by 2 to 4 months and reduced in magnitude by greater than 50%. Additional surveillance and epidemiologic studies are needed to confirm the impact of rotavirus immunization on the 2007-08 rotavirus season and to monitor the impact of the vaccine on the disease incidence, geographical distribution, and timing of rotavirus disease during future seasons. Studies also are needed to monitor serotype distribution and possible strain replacement in future seasons.

### **Efficacy in Special Populations**

Studies have shown that either rotavirus vaccine can be administered to infants who are being

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breastfed without the efficacy of the vaccines being affected.<sup>9,11,22</sup> An uninterrupted schedule of breastfeeding was permitted in infants participating in prelicensure clinical trials of both vaccines.

Coadministration of each rotavirus vaccine with commonly administered pediatric vaccines has been evaluated. Both RV1 and RV5 can be coadministered with diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP), *Haemophilus influenzae* type b vaccine (Hib), inactivated poliovirus vaccine (IPV), hepatitis B vaccine (HPV), and pneumococcal conjugate vaccine, with no observed immune interference.<sup>16,17</sup>

Little data are available on the efficacy, safety, and reactogenicity of rotavirus vaccine in infants with underlying conditions. Studies in HIV-infected infants are ongoing for RV1 and are planned for RV5.

Evidence indicates that RV5 can be given safely to otherwise healthy preterm infants born at greater than 32 weeks of gestation (median, 34 weeks of gestation), according to postnatal age, on the same schedule as for infants born at term.<sup>23</sup> Overall, 3 doses of RV5 reduced the rate of hospitalizations and emergency department visits in preterm infants attributable to rotavirus gastroenteritis by 100%. The vaccine also prevented 73% of rotavirus gastroenteritis cases of any severity. Studies examining administration of RV1 in preterm infants are ongoing.

### **COST-BENEFIT ANALYSIS**

In a published analysis using estimates of rotavirus disease burden, vaccine efficacy, vaccine coverage rates, and health care costs in the late 1990s, investigators estimated that a national rotavirus immunization program for the United States in which 3 doses of RV5 are administered at 2, 4, and 6 months of age to a single birth cohort of 4 million infants would result in 255 000 fewer physician visits, 137 000 fewer emergency department visits, 44 000 fewer hospitalizations, and 13 fewer deaths per year in children younger than 5 years of age.<sup>5</sup> At a manufacturers price of \$62.50 (2006 dollars) per

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dose, a 3-dose RV5 immunization series would cost \$138 per case averted, \$3024 per serious case averted, and \$197 190 per life-year saved. In 2008, the CDC conducted an updated analysis of a rotavirus immunization program in the United States and concluded that the cost-effectiveness of a 3-dose RV5 vaccine program and a 2-dose RV1 vaccine program would be similar (CDC unpublished data, 2008). The cohort model employed in the study by Widdowson et al was used.<sup>5</sup> At an estimated total immunization cost per child for 3 doses of RV5 of \$218 and 2 doses of RV1 of \$208, immunization cost per case averted was \$139 for RV5 and \$94 for RV1. The cost per life-year saved was \$198 546 for RV5 and \$128 400 for RV1. Although the median estimates in this model suggest small increased cost-effectiveness of 2-dose RV1 vaccine over 3-dose RV5 vaccine, the CDC concluded that these differences in median estimates might not translate into a true difference for a program because of variation in the actual cost of vaccine to providers, possible differences in the costs for administration and shipping of each product, and the field vaccine effectiveness of a product's full or partial series.<sup>24</sup> For example, if there is as high a vaccine efficacy after dose 1 for the 3-dose RV5 vaccine as reported following the first dose of RV1, the difference between the 2 vaccines will be much smaller.

Rotavirus vaccine may be more cost-effective than calculations to date, if immunization provides indirect protection to unimmunized children and children who failed to have an adequate immune response to vaccine.

## **CONTRAINDICATIONS AND PRECAUTIONS**

### **Contraindications**

- Rotavirus vaccine should not be administered to infants who have a history of a severe allergic reaction (eg, anaphylaxis) after a previous dose of rotavirus vaccine or to a vaccine component (AIII).

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- Latex rubber is contained in the RV1 oral applicator, so infants with a severe (anaphylactic) allergy to latex should not receive RV1 (AIII). The RV5 dosing tube is latex free.

### Precautions

- **Altered Immunocompetence**

Practitioners should consider the potential risks and benefits of administering rotavirus vaccine to infants with known or suspected altered immunocompetence; consultation with an immunologist or infectious diseases specialist is advised (CIII).

Children and adults who are immunocompromised because of congenital immunodeficiency, hematopoietic stem cell transplantation, or solid organ transplantation sometimes experience severe or prolonged rotavirus gastroenteritis. However, no published safety or efficacy data are available for administration of rotavirus vaccine to infants who are immunocompromised or potentially immunocompromised, including infants:

- with primary and acquired immunodeficiency states, including cellular immunodeficiencies, and hypogammaglobulinemic and dysgammaglobulinemic states;
- with blood dyscrasias, leukemia, lymphomas, or other malignant neoplasms affecting the bone marrow or lymphatic system;
- on immunosuppressive therapy (including high-dose systemic corticosteroids ( $\geq 2$  mg/kg per day of prednisone or equivalent)); or
- who are HIV-exposed or HIV-infected. However, the decision whether to immunize HIV-exposed or HIV-infected infants should be made on the basis of the following considerations:

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- HIV infection may be presumptively excluded by 4 to 8 weeks of age, before the first rotavirus vaccine dose is given, in infants born to HIV-infected mothers in the United States who are not breastfeeding (infants in the United States born to HIV-infected mothers should not be breastfed);
- HIV-exposed infants in the United States who are not breastfeeding can be identified as HIV-infected by 4 to 8 weeks of age;
- preliminary data with one of the licensed vaccines has shown the vaccine to be safe when given to HIV-infected infants in Africa; and
- vaccine strains of rotavirus are considerably attenuated.

- **Moderate-to-Severe Acute Gastroenteritis**

Rotavirus vaccine should not be administered to infants with acute, moderate-to-severe gastroenteritis until the condition improves. However, infants with mild acute gastroenteritis may be immunized, particularly if the delay in immunization might be substantial and might make the child ineligible to receive vaccine (eg, 15 weeks, 0 days of age or older before the vaccine series is started or older than 8 months, 0 days at the time of the last dose) (CIII).

- Rotavirus vaccine has not been studied in infants with concurrent acute gastroenteritis. In these infants, the immunogenicity and efficacy of rotavirus vaccine theoretically can be compromised. For example, infants who receive oral poliovirus vaccine (OPV) during an episode of acute gastroenteritis, in some circumstances, have diminished poliovirus antibody responses.

- **Moderate-to-Severe Acute Illness**

Immunization should not be delayed because of mild respiratory tract illness or other mild acute illness with or without fever. In contrast, as with all other vaccines, the presence of a

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moderate or severe acute illness with or without fever is a precaution to administration of rotavirus vaccine. Infants with a moderate-to-severe acute illness should be immunized as soon as they have recovered from the acute phase of the illness (BIII).

- This precaution avoids superimposing any potential adverse effects of the vaccine on the underlying illness or mistakenly attributing a manifestation of the underlying illness to the vaccine.

### **• Preexisting Chronic Gastrointestinal Diseases**

Infants with preexisting gastrointestinal tract conditions (eg, congenital malabsorption syndromes, Hirschsprung disease, short-gut syndrome) who are not undergoing immunosuppressive therapy should benefit from receiving rotavirus vaccine, and the AAP believes the benefits outweigh the theoretical risks (CIII).

- No data are available on the safety and efficacy of rotavirus vaccine for infants with preexisting chronic gastrointestinal tract disease.

### **• Previous History of Intussusception**

Practitioners should consider the potential risks and benefits of administering rotavirus vaccine to infants with a previous history of intussusception (BIII).

- Compared with infants who have never had intussusception, infants with a history of intussusception are at higher risk of a repeat episode of intussusception. No data are available on the administration of rotavirus vaccine to infants with a previous history of intussusception. Available data do not indicate that RV5 or RV1 are associated with intussusception. A previously licensed rotavirus vaccine that is no longer available (Rotashield [Wyeth-

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Lederle Vaccines and Pediatrics]) was associated with an increased risk of intussusception.

- **Infants With Spina Bifida or Bladder Exstrophy**

Latex rubber is contained in the RV1 oral applicator. The RV5 dosing tube is latex free. Some experts, therefore, prefer that infants with spina bifida or bladder exstrophy, who are at high risk of acquiring latex allergy, receive RV5 instead of RV1 to minimize latex exposure in these children (CIII). However, if RV1 is the only rotavirus vaccine available, it should be given, because the benefit of immunization is considered to be greater than the risk of sensitization.

### **RECOMMENDATIONS**

#### **Routine Administration**

- The AAP recommends routine immunization of infants in the United States with rotavirus vaccine. The AAP does not express a preference for either of the 2 licensed rotavirus vaccines, RV5 and RV1, for use in infants in the United States (AI).
- RV5 is to be administered orally in a 3-dose series with doses administered at 2, 4, and 6 months of age. RV1 is to be administered orally in a 2-dose series with doses administered at 2 and 4 months of age (Table 3) (AI).
- The first dose of rotavirus vaccine should be administered from 6 weeks, 0 days of age through 14 weeks, 6 days of age. Immunization should not be initiated for infants 15 weeks, 0 days of age or older because of insufficient data on safety of the first dose of rotavirus vaccine in older infants (CIII).
- The minimum interval between doses of rotavirus vaccine is 4 weeks. All doses should be administered by 8 months, 0 days of age (RV5, AI; RV1, CIII).

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- For infants to whom the first dose of rotavirus vaccine is inadvertently administered at 15 weeks, 0 days of age or older, the remainder of the rotavirus immunization series should be completed according to the schedule, because timing of the first dose should not affect the safety and efficacy of the subsequent dose(s) (BIII).
- Infants who have had rotavirus gastroenteritis before receiving the full series of rotavirus immunization should begin or complete the schedule following the age and interval recommendations, because the initial rotavirus infection provides only partial protection against subsequent rotavirus disease (AII).
- Breastfeeding before or after receipt of rotavirus vaccine is encouraged. Breastfed infants should be immunized according to the same schedule as nonbreastfed infants (AI).
- As with all other vaccines, rotavirus vaccine may be administered to infants with minor acute illness (eg, mild gastroenteritis or mild upper-respiratory tract infection, with or without fever) (AIII).

### **Simultaneous Administration**

- Rotavirus vaccine may be administered concurrently with DTaP, Hib, IPV, HBV, and PCV7 (AI).
- Rotavirus vaccine may be administered concurrently with trivalent inactivated influenza vaccine (TIV) for infants older than 6 months of age. Live-attenuated influenza vaccine (LAIV) is not licensed for immunization of children younger than 2 years of age (BIII).
  - The infant's immune response to TIV administered at the same time as rotavirus vaccine has not been studied. However, the General Recommendations issued by the Advisory Committee on Immunization Practices (ACIP) of the CDC note that an inactivated vaccine (eg, inactivated influenza vaccine) may be administered either

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simultaneously or at any time before or after a different inactivated vaccine or live vaccine (eg, rotavirus vaccine).

### **Interchangeability of Rotavirus Vaccines**

- The AAP recommends that the rotavirus vaccine series be completed with the same product whenever possible (AIII).
- Rotavirus immunization should not be deferred because the product used for a previous dose(s) is unknown or is not available. In such a circumstance, the health care professional should continue or complete the series with the product available. If any dose in the series was RV5 or the vaccine product is unknown for any dose in the series, a total of 3 doses of rotavirus vaccine should be administered (CIII). All doses should be given by 8 months, 0 days of age.

### **Special Situations**

- **Preterm Infants (Those Born at Less Than 37 Weeks' Gestation)**

Preterm infants should be immunized on the same schedule and with the same precautions as for full-term infants and under the following conditions: the infant's postnatal age meets the age requirements for rotavirus vaccine (eg, from 6 weeks through 14 weeks, 6 days of age for the first dose) and the infant is clinically stable (RV5, AI; RV1, BIII).

- Data suggest that preterm infants are at increased risk of hospitalization from rotavirus or other viral pathogens associated with gastroenteritis during their first year of life. In clinical trials, rotavirus vaccine appeared to be generally well tolerated in a relatively small number of preterm infants. Although the lower level of maternal antibody against prevalent rotavirus genotypes in very preterm infants theoretically could increase the risk of adverse events from

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rotavirus vaccine, the AAP believes the benefit of immunizing the infant when age-eligible and clinically stable outweighs the theoretical risks.

- **Preterm Infants in the Neonatal Intensive Care Unit or Nursery**

Preterm infants who are age eligible and clinically stable may be immunized at the time of discharge from the neonatal intensive care unit (NICU) or nursery (BIII).

- Vaccine strains of rotavirus are shed in stools of immunized infants, so if an infant were to be immunized with a rotavirus vaccine while still needing care in the NICU or nursery, at least a theoretical risk exists for vaccine virus being transmitted to infants in the same unit who are acutely ill (moderate-to-severe illness is a precaution for immunization) and preterm infants who are not age eligible for vaccine. The AAP believes that, in usual circumstances, the risk from shedding outweighs the benefit of immunizing infants who are age eligible for vaccine but who will remain in the NICU or nursery following immunization.

- **Readmission of an Immunized Preterm Infant to the NICU or Nursery**

If an infant immunized with a rotavirus vaccine requires readmission to the NICU or nursery within 2 weeks after receipt of vaccine, contact precautions should be instituted for the readmitted infant and should be maintained for 2 to 3 weeks after vaccine administration (BIII).

- **Exposure of Immunocompromised People to Immunized Infants**

Infants living in households with people who have or are suspected of having an immunodeficiency disorder or impaired immune status can be immunized (BIII).

- Vaccine virus (attenuated rotavirus) is shed in the stool of infants after rotavirus immunization. However, no data are available on risk of transmission of vaccine

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virus to household contacts and the risk for any subsequent disease. Vaccine virus is shed more commonly and for longer periods after receipt of RV1 than after receipt of RV5. The majority of experts believe the protection of immunocompromised household member afforded by immunizing the infant in the household and preventing wild-type rotavirus disease outweighs the small risk for transmitting vaccine virus to an immunocompromised household member and any subsequent risk of vaccine virus-associated disease. Vaccine virus is shed during the first weeks after administration of rotavirus vaccine; hand washing after diaper changing is always recommended.

- **Exposure of Pregnant Women to Immunized Infants**

Infants living in households with pregnant women should be immunized according to the same schedule as infants in households without pregnant women (BIII).

- The majority of women of childbearing age have preexisting immunity to rotavirus, and therefore, the risk of infection and any subsequent theoretical risk of disease from potential exposure to the attenuated vaccine virus are believed to be very low.

- **Regurgitation of Vaccine**

The practitioner should not readminister a second dose of rotavirus vaccine to an infant who regurgitates, spits out, or vomits during or after administration of vaccine (BIII).

- No data exist on the benefits or risks associated with readministering a dose. The infant should receive the remaining recommended doses of rotavirus vaccine following the routine schedule (with a 4-week minimum interval between doses).

- **Hospitalization After Immunization**

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If a recently immunized infant is hospitalized for any reason, no precautions other than standard precautions need to be taken to prevent the spread of vaccine-virus in the hospital setting (BIII).

- **Infants Who Have Recently Received or Will Receive an Antibody-Containing Blood Product**

Rotavirus vaccine may be administered at any time before, concurrent with, or after administration of any blood product, including antibody-containing products, according to the routinely recommended schedule for rotavirus vaccine among infants who are eligible for immunization (BIII).

- In theory, infants who have recently received an antibody-containing blood product might have an attenuated immune response to a dose of rotavirus vaccine. However, 2 or 3 doses of vaccine are administered in the full rotavirus vaccine series, so adequate protection is anticipated and no increased risk of adverse events is expected.

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National Institute for Allergy and Infectious Disease

Lucia Lee, MD

Food and Drug Administration

Jennifer S. Read, MD, MS, MPH, DTM&H

National Institutes of Health

Benjamin Schwartz, MD

National Vaccine Program Office

Jeffrey R. Starke, MD

American Thoracic Society

### **CONSULTANTS**

Edgar O. Ledbetter, MD

H. Cody Meissner, MD

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*Red Book* Associate Editor

## **Prevention of Rotavirus Disease: Updated Guidelines for Use of Rotavirus Vaccine, *continued***

### **STAFF**

Jennifer Frantz, MPH

Hope Hurley, Interim Manager

### **ACKNOWLEDGEMENTS**

This AAP policy statement was prepared in parallel with CDC recommendations and reports. Much of this statement is based on literature reviews, analyses of unpublished data, and deliberations of CDC staff in collaboration with the Advisory Committee on Immunization Practices Rotavirus Working Group, with liaison from the AAP.

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**Prevention of Rotavirus Disease: Updated Guidelines for Use of Rotavirus Vaccine, *continued***

**Table 1. Profiles of Rotavirus Vaccines Licensed in United States**

<b>Profile</b>	<b>RV5 (RotaTeq)</b>	<b>RV1 (Rotarix)</b>
Type of vaccine	Live attenuated oral	Live attenuated oral
Parent rotavirus strain	Bovine strain WC3	Human strain 89–12
Composition	Five human-bovine reassortant strains	Single human strain RIX4414
G and P types	G1P[5] G2P[5] G3P[5] G4P[5] G6P[8]	G1P[8]
Labeled indication	Immunization against rotavirus gastroenteritis caused by G1, G2, G3, G4	Immunization against rotavirus gastroenteritis caused by G1, G3, G4, G9
Labeled age of administration	6 through 32 wk <sup>a</sup>	6 through 24 wk <sup>a</sup>
Dosing	Given at 2, 4, and 6 mo	Given at 2 and 4 mo
Formulation	Liquid requiring no reconstitution	Vial of lyophilized vaccine with a prefilled oral applicator of liquid diluent
How supplied	Single dose squeezable plastic tube	Tip cap and rubber plunger of the oral applicator contain dry natural latex rubber. The vial stopper and transfer adapter are latex-free.
Volume per dose	2 mL	1 mL
Preservatives	None	None
Shelf life	24 mo	24 mo
Storage	Store refrigerated at 2° to 8°C (36°–46°F), protect from light, and administer as soon as possible after being removed from refrigeration.	<u>Storage before reconstitution:</u> Refrigerate vials of lyophilized vaccine at 2° to 8°C (36–46°F), protect from light. Store diluent at 20° to 25°C (68–77°F). <u>Storage after reconstitution:</u> Administer within 24 hours of reconstitution. May be stored refrigerated at 2° to 8°C (36–46°F) or at room temperature up to 25°C (77°F).

<sup>a</sup> The AAP recommends 8 months 0 days as maximum age for the last dose of vaccine.

**Prevention of Rotavirus Disease: Updated Guidelines for Use of Rotavirus Vaccine, *continued***

**Table 2. Performance of Rotavirus Vaccines Licensed in United States in Clinical Trials<sup>a</sup>**

<b>Profile</b>	<b>RV5 (RotaTeq)</b>	<b>RV1 (Rotarix)</b>
Safety profile	No increase in fever or irritability Slight increase in mild diarrhea and vomiting	No increase in fever, irritability, diarrhea or vomiting
Intussusception	Not associated	Not associated
Shedding	9% of recipients after dose 1, rarely after subsequent doses	25% after first dose peak excretion around day 7
Efficacy against any rotavirus gastroenteritis	74%	87%
Efficacy against severe rotavirus gastroenteritis	98%	85% to 96%
Efficacy against health care encounters	Significantly reduced hospitalizations, physician office visits, emergency department visits	Significantly reduced hospitalizations and need for medical attention
Efficacy by serotype against severe rotavirus gastroenteritis	G1 (95%), G2 (88%), G3 (93%), G4 (89%), and G9 (100%)	In Latin America: G1 (91%), G2 (41%), G3, G4, and G9 (87%) In Europe: G1 (96%), G2 (86%), G3 (94%), G4 (95%), G9 (85%)

<sup>a</sup> Efficacy cannot be compared between vaccines, because 2 different severity scales were used in the clinical trials.

**Prevention of Rotavirus Disease: Updated Guidelines for Use of Rotavirus Vaccine, *continued***

**Table 3. Recommended Schedule for Administration of Rotavirus Vaccine**

<b>Recommendations</b>	<b>RV5 (RotaTeq)</b>	<b>RV1 (Rotarix)</b>
Number of doses in series	3	2
Recommended ages for doses	2, 4, and 6 mo	2 and 4 mo
Minimum age for first dose	6 wk	
Maximum age for first dose	14 wk 6 days	
Minimum interval between doses	4 wk	
Maximum age for last dose	8 mo, 0 days	

**Appendix 1. Infectious Diseases Society of America–US Public Health Service Grading System for Ranking Recommendations in Clinical Guidelines**

<b>Category, Grade</b>	<b>Definition</b>
<b>Strength of Recommendation</b>	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
<b>Quality of Evidence</b>	
I	Evidence from $\geq 1$ properly randomized, controlled trial
II	Evidence from $\geq 1$ well-designed clinical trial, without randomization; from cohort or case-controlled analytical studies (preferably from $>1$ center); from multiple time-series; or from dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Adapted from Canadian Task Force on the Periodic Health Examination. The periodic health examination. *Can Med Assoc J.* 1979;121(9):1193–1254