Rotavirus

Diarrheal disease has been recognized in humans since antiquity. Until the early 1970s, a bacterial, viral, or parasitic etiology of diarrheal disease in children could be detected in fewer than 30% of cases. In 1973, Bishop and colleagues observed a virus particle in the intestinal tissue of children with diarrhea by using electron micrography. This virus was subsequently called "rotavirus" because of its similarity in appearance to a wheel (rota is Latin for wheel). By 1980, rotavirus was recognized as the most common cause of severe gastroenteritis in infants and young children in the United States. It is now known that infection with rotavirus is nearly universal, with almost all children infected by 5 years of age. Rotavirus is responsible for 20–60 deaths per year in the United States and up to 500,000 deaths from diarrhea worldwide. A vaccine to prevent rotavirus gastroenteritis was first licensed in August 1998 but was withdrawn in 1999 because of its association with intussusception. A second-generation vaccine was licensed in 2006.

Rotavirus

- First identified as cause of diarrhea in 1973
- Most common cause of severe diarrhea in infants and children
- Nearly universal infection by age 5 years
- Responsible for up to 500,000 diarrheal deaths each year worldwide

Rotavirus

Rotavirus is a double-stranded RNA virus of the family *Reoviridae*. The virus is composed of three concentric shells that enclose 11 gene segments. The outermost shell contains two important proteins—VP7, or G-protein, and VP4, or P-protein. VP7 and VP4 define the serotype of the virus and induce neutralizing antibody that is probably involved in immune protection. Five strains of rotavirus (G1–4, G9) account for 90% of isolates from children younger than 5 years in the United States. Of these, the G1 strain accounts for more than 80% of isolates.

Rotavirus is very stable and may remain viable in the environment for weeks or months if not disinfected.

Rotaviruses cause infection in many species of mammals, including cows and monkeys. These animal strains are antigenically distinct from those causing human infection, and they rarely cause infection in humans.

Rotavirus

- Reovirus (RNA)
- VP7 and VP4 antigens define virus serotype and induce neutralizing antibody
- 5 predominant strains in U.S. (G1-G4, G9)
- Strain G1 accounts for 50% of infections

Pathogenesis

The virus enters the body through the mouth. Viral replication occurs in the villous epithelium of the small intestine. Replication outside the small intestine and systemic spread of the virus (viremia) are believed to be uncommon in immunocompetent persons. Infection may result in decreased intestinal absorption of sodium, glucose, and water, and decreased levels of intestinal lactase, alkaline phosphatase, and sucrase activity, and may lead to isotonic diarrhea.

Rotavirus Pathogenesis

- Entry through mouth
- Replication in epithelium of small intestine
- Replication outside intestine and viremia uncommon
- Infection leads to isotonic diarrhea

Rotavirus Immunity

- Antibody against VP7 and VP4 probably important for protection
- First infection usually does not lead to permanent immunity
- Reinfection can occur at any age
- Subsequent infections generally less severe

The immune correlates of protection from rotavirus are poorly understood. Serum and mucosal antibodies against VP7 and VP4 are probably important for protection from disease. Cell-mediated immunity probably plays a role in recovery from infection and in protection.

Recovery from a first rotavirus infection usually does not lead to permanent immunity. After a single natural infection, 40% of children are protected against any subsequent rotavirus infection, 75% are protected against rotavirus diarrhea, and 88% are protected against severe diarrhea. Reinfection can occur at any age. Subsequent infections confer progressively greater protection and are generally less severe than the first. Recurrent rotavirus infections affect persons of all ages. Recurrent infections are usually asymptomatic or result in mild diarrhea that may be preceded or accompanied by vomiting and low-grade fever.

Clinical Features

Rotavirus Clinical Features

- Incubation period 1-3 days
- Variable clinical presentation– asymptomatic to severe diarrhea
- First infection after age 3 months generally most severe
- Illness not specific for rotavirus
- Confirmation requires laboratory testing

The incubation period for rotavirus diarrhea is 1–3 days. The clinical manifestations of infection vary and depend on whether it is the first infection or reinfection. Infection may be asymptomatic, may cause self-limited watery diarrhea, or may result in severe dehydrating diarrhea with fever and vomiting. The first infection after 3 months of age is generally the most severe. Up to one-third of infected children may have a temperature greater than 102°F (39°C). The gastrointestinal symptoms generally resolve in 3–7 days.

The clinical features and stool characteristics of rotavirus diarrhea are nonspecific, and similar illness may be caused by other pathogens. As a result, confirmation of a diarrheal illness as rotavirus requires laboratory testing.

Complications

Rotavirus Complications

- Severe diarrhea
- Dehydration
- Electrolyte imbalance
- Metabolic acidosis
- Immunodeficient children may have more severe or persistent disease

Rotavirus infection in infants and young children can lead to severe diarrhea, dehydration, electrolyte imbalance, and metabolic acidosis. Immunodeficient children may have more severe or persistent disease and may have evidence of abnormalities in multiple organ systems, particularly the kidney and liver.

Laboratory Diagnosis

The most widely available method for confirmation of rotavirus infection is detection of rotavirus antigen in stool by enzyme immunoassay (EIA). Several commercial test kits are available that detect an antigen common to human rotaviruses. These kits are simple to use, inexpensive, and very sensitive. Other techniques (such as electron microscopy, reverse transcription polymerase chain reaction, nucleic acid hybridization,

sequence analysis, and culture) are used primarily in research settings. Rotavirus antigen has also been identified in the serum of patients 3–7 days after disease onset, but at present, routine diagnostic testing is based primarily on testing of fecal specimens.

Epidemiology

Occurrence

Rotavirus occurs throughout the world. The prevalence of rotavirus strains varies by geographic area, and strains not included in the vaccine are present in some parts of the world.

Rotavirus Epidemiology

• Reservoir	Human
• Transmission	Fecal-oral, fomites
• Temporal pattern	Fall and winter (temperate areas)
• Communicability	2 days before to 10 days after onset

Reservoir

The reservoir of rotavirus is the gastrointestinal tract and stool of infected humans. Although rotavirus infection occurs in many nonhuman mammals, transmission of animal rotaviruses to humans is believed to be rare and probably does not lead to clinical illness. Although immunodeficient persons may shed rotavirus for a prolonged period, a true carrier state has not been described.

Transmission

Rotaviruses are shed in high concentration in the stool of infected persons. Transmission is by fecal-oral spread, both through close person-to-person contact and by fomites (such as toys and other environmental surfaces contaminated by stool). Rotaviruses are also probably transmitted by other modes such as fecally contaminated food and water and respiratory droplets.

Temporal Pattern

In temperate climates, disease is more prevalent during cooler months. In the United States, annual epidemic peaks usually progress from the Southwest during November and December and spread to the Northeast by April and May. The reason for this seasonal pattern is unknown. In tropical climates, the disease is less seasonal than in temperate areas.

Communicability

Rotavirus is highly communicable, as evidenced by the nearly universal infection of children by age 5 years. Infected persons shed large quantities of virus in their stool beginning 2 days before the onset of diarrhea and for up to 10 days after onset of symptoms. Rotavirus may be detected in the stool of immunodeficient persons for more than 30 days after infection. Spread within families, institutions, hospitals, and child care settings is common.

Rotavirus Disease Burden in the United States

- Estimated 2.7 million cases per year
- 95% of children infected by 5 years of age
- Highest incidence among children 3 to 35 months of age
- Responsible for 5%-10% of all gastroenteritis episodes among children younger than 5 years of age

Secular Trends in the United States

Rotavirus infection is not nationally notifiable in the United States. Estimates of incidence and disease burden are based on special surveys, cohort studies, and hospital discharge data.

Rotavirus infection is nearly universal. An estimated 2.7 million cases occur each year in the United States alone, and 95% of children experience at least one rotavirus infection by age 5 years. The incidence of rotavirus is similar in developed and developing countries, suggesting that improved sanitation alone is not sufficient to prevent the infection.

Infants younger than 3 months of age have relatively low rates of rotavirus infection, probably because of passive maternal antibody, and possibly breastfeeding. The incidence of clinical illness is highest among children 3 to 35 months of age. Rotavirus infection of adults is usually asymptomatic but may cause diarrheal illness.

Rotavirus Disease in the United States

- Annually responsible for:
  - —More than 400,000 physician visits
  - —More than 200,000 emergency dept visits
  - —55,000-70,000 hospitalizations
  - —20-60 deaths
- Annual direct and indirect costs are estimated at approximately $1 billion

In the United States, rotaviruses are responsible for 5%–10% of all gastroenteritis episodes among children younger than 5 years of age. However, they are the most common cause of severe diarrheal disease and account for a higher proportion of severe episodes leading to clinic or hospital visits. Rotavirus accounts for 30%–50% of all hospitalizations for gastroenteritis among U.S. children younger than 5 years of age, and more than 70% of hospitalizations for gastroenteritis during the seasonal peaks.

Rotavirus infection is responsible for more than 400,000 physician visits, more than 200,000 emergency department (ED) visits, 55,000–70,000 hospitalizations each year, and 20–60 deaths. Annual direct and indirect costs are estimated at approximately $1 billion, primarily due to the cost of time lost from work to care for an ill child.

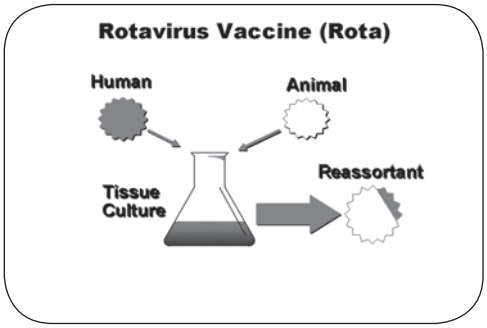
Risk Groups for Rotavirus Diarrhea

- Groups with increased exposure to virus
  - —Children in child care centers
  - —Children in hospital wards (nosocomial rotavirus)
  - —Caretakers, parents of these children
  - —Children, adults with immunodeficiency-related diseases (e.g. SCID, HIV, bone marrow transplant)

Groups at increased risk for rotavirus infection are those with increased exposure to virus. This includes children who attend child care centers, children in hospital wards (nosocomial rotavirus), caretakers and parents of children in child care or hospitals, and children and adults with immunodeficiency-related diseases (e.g., Severe Combined Immunodeficiency Disease (SCID), HIV, bone marrow transplant).

Rotavirus Vaccine

The first rotavirus vaccines were derived from either bovine (cow) or rhesus (monkey) origin. Studies demonstrated that these live oral vaccines could prevent rotavirus diarrhea in young children, but efficacy varied widely. Because immunity to G (VP7) and P (VP4) proteins was associated with disease protection and recovery, new live virus vaccines were developed that incorporated G proteins or both G and P proteins for each of the predominant serotypes.



The process by which these vaccine viruses were created is called genetic reassortment. Tissue culture cells were infected with two different rotavirus strains—a nonhuman "parent" strain and a human strain that contained the VP7 gene of a predominant serotype. When the viruses replicated, the offspring viruses had various combinations of gene segments from the two strains. Offspring were selected that contained the gene segment coding for a human G (VP7) serotype. The remainder of the gene was identical to the parent nonhuman strain. By this process, viruses—known as reassortants—were developed that expressed human G1, G2, G3, and G4 serotypes of the VP7 antigen.

In 1998, a rhesus-based tetravalent rotavirus vaccine (RRV-TV, Rotashield) was licensed and recommended for routine immunization of U.S. infants. However, RRV-TV was withdrawn from the U.S. market within one year of its introduction because of its association with intussusception. The risk of intussusception was most elevated (more than a 20-fold increase) within 3–14 days after receipt of the first dose of RRV-TV, with a smaller (approximately 5-fold) increase in risk within 3–14 days after the second dose. Overall, the risk associated with the first dose of RRV-TV was estimated to be about one case per 10,000 vaccine recipients. Some researchers have suggested that the risk of intussusception associated with RRV-TV was age-dependent and that the absolute number of intussusception events, and possibly the relative risk of intussusception associated with the first dose of RRV-TV, increased with increasing age at vaccination.

Characteristics

In February 2006, the Food and Drug Administration approved a new rotavirus vaccine (Rota), RotaTeq, produced by the Merck Vaccine Division. RotaTeq is a live, oral vaccine that contains five reassortant rotaviruses developed from human and bovine parent rotavirus strains. Four reassortant rotaviruses express one of the outer proteins (G1, G2, G3, or G4) from the human rotavirus strain and the attachment protein (P7[5]) from the bovine rotavirus parent strain. The fifth reassortant virus expresses the attachment protein from the human rotavirus strain and the outer protein (G6) from the bovine rotavirus parent strain. The parent

bovine rotavirus strain Wistar Calf 3 (WC3) was isolated in 1981 from a calf with diarrhea in Chester County, Pennsylvania. The virus was passaged 12 times in African green monkey kidney cells. The reassortants are propagated in Vero cells using standard tissue culture techniques.

Rotavirus Vaccine (RotaTeq)

- Approved by FDA in February 2006
- Contains five reassortant rotaviruses developed from human and bovine parent rotavirus strains
- Vaccine viruses suspended in a solution of buffer (sodium citrate and phosphate) and stabilizer
- Contains no preservatives or thimerosal

RotaTeq consists of the five human–bovine reassortants suspended in a solution of buffer (sodium citrate and phosphate) and stabilizer (sucrose). Each 2-mL vial of vaccine contains approximately 2 x 10^6 infectious units of each of the five reassortant strains. The vaccine formulation contains sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, and tissue culture media. Trace amounts of fetal bovine serum might be present. The vaccine contains no preservatives or thimerosal.

Fecal shedding of vaccine virus was evaluated in a subset of persons enrolled in the phase III trials. Vaccine virus was shed by 32 (8.9%) of 360 infants after dose 1, but none of 249 and 385 infants after doses 2 and 3, respectively. Shedding was observed as early as 1 day and as late as 15 days after a dose. The potential for horizontal transmission of vaccine virus was not assessed through epidemiologic studies.

Rotavirus Vaccine Efficacy

- Phase III trials included more than 70,000 infants in 11 countries
- Efficacy
  - –All rotavirus disease – 74%
  - –Severe rotavirus disease – 98%
  - –Significantly reduced office and ED visits and hospitalization for rotavirus gastroenteritis
- Efficacy of fewer than 3 doses is not known

N Eng J Med 2006;354:23-33

Immunogenicity and Vaccine Efficacy

Phase III clinical trials of Rotateq immunogenicity and efficacy have involved more than 70,000 infants 6–12 weeks of age in 11 countries.

The immune correlates of protection from rotavirus infection and disease are not fully understood. In clinical trials, a rise in titer of rotavirus group-specific serum IgA antibodies was used as one of the measures of immunogenicity. Sera were collected before vaccination and approximately 2 weeks after the third dose. Seroconversion was defined as a threefold or greater rise in antibody titer from baseline. Seroconversion rates for IgA antibody to rotavirus were 93%–100% among 439 vaccine recipients versus 12%–20% among 397 placebo recipients.

After completion of a three-dose regimen, the efficacy of rotavirus vaccine against rotavirus gastroenteritis of any severity was 74%, and against severe rotavirus gastroenteritis (defined by severity of fever, vomiting, diarrhea and changes in behavior) was 98%. Vaccine efficacy varied by rotavirus serotype.

In a large study, the efficacy of rotavirus vaccine against rotavirus gastroenteritis requiring office visits was evaluated among 5,673 persons, and efficacy against rotavirus gastroenteritis requiring ED visits and hospitalizations was evaluated among 68,038 persons during the first 2 years of life. Rotavirus vaccine reduced the incidence of office visits

by 86%, ED visits by 94%, and hospitalizations for rotavirus gastroenteritis by 96%.

The efficacy of fewer than three doses is not known.

Duration of Immunity

The duration of immunity from rotavirus vaccine is not known. At least one clinical trial has demonstrated that protection lasts through at least 2 rotavirus seasons, although efficacy was somewhat lower in the second season than in the first.

Vaccination Schedule and Use

The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination of all infants without contraindications with three doses of rotavirus vaccine administered orally at ages 2, 4, and 6 months. The minimum age for the first dose is 6 weeks. The first dose should be administered between 6 and 12 weeks of age (that is, until age 13 weeks). Vaccination should not be initiated for infants older than 12 weeks because of insufficient data on safety of the first dose of rotavirus vaccine in older infants.

Rotavirus Vaccine Recommendations

- Routine immunization of all infants without contraindications
- Administered at 2, 4, and 6 months of age
- Minimum age of first doses is 6 weeks
- First dose should be administered between 6 and 12 weeks of age (until age 13 weeks)
- Do not initiate series after 12 weeks of age

All three doses should routinely be separated by 2 months. However, the minimum interval between doses may be a short as 4 weeks if an accelerated schedule is required. Special effort should be made to immunize infants before the winter rotavirus season, and the use of an accelerated schedule may facilitate this effort.

Rotavirus Vaccine Recommendations

- Minimum interval between doses is 4 weeks
- Maximum age for ANY dose is 32 weeks
- Do not administer on or after age 32 weeks, even if fewer than three doses have been administered

The maximum age for any dose of rotavirus vaccine is 32 weeks because of insufficient data on the safety and efficacy of rotavirus vaccine in infants after this age. Rotavirus vaccine should not be administered on or after age 32 weeks, even if fewer than three doses have been administered.

Rotavirus vaccine may be administered simultaneously with all other vaccines that are routinely given at the same ages (hepatitis B, DTaP, IPV, Hib, PCV).

Rotavirus Vaccine Recommendations

- Administer simultaneously with all other indicated vaccines
- Breastfeeding infants should be vaccinated on usual schedule
- Vaccinate infants who have recovered from documented rotavirus infection
- Do not repeat dose if infant spits out or regurgitates vaccine- administer remaining doses on schedule

Breastfeeding does not appear to diminish immune response to three doses of vaccine. Children who are being breastfed should be vaccinated on schedule.

Infants who have recovered from documented rotavirus infections may not be immune to all five serotypes present in the vaccine. These infants should complete the three-dose vaccination series by 32 weeks of age.

Data on the safety of administering a dose higher than the recommended dose, or on the efficacy of a partial dose are

very limited. As a result, a second dose of rotavirus vaccine should not be administered to an infant who regurgitates, spits out some or all of the dose, or vomits during or after administration of vaccine. The infant should receive the remaining recommended doses, if needed, on the usual schedule.

Adverse Reactions Following Vaccination

Intussusception

The risk for intussusception was evaluated in more than 70,000 infants enrolled in phase III efficacy trials. During the 42 days after vaccination six cases of intussusception were observed in the vaccine group and five cases in the placebo group. There was no evidence, regardless of dose, of clustering of cases of intussusception within 7–14 days postvaccination, the period of greatest risk for intussusception associated with the RRV-TV vaccine. For the 1-year follow-up period after administration of the first dose, 13 cases of intussusception were observed in the vaccine group and 15 cases of intussusception in the placebo group (relative risk: 0.9).

Rotavirus Vaccine and Intussusception

	Vaccine Recipients	Placebo Recipients
Within 42 days of vaccination	6 cases	5 cases
Within 1 year of vaccination	13 cases	15 cases

New Eng J Med 2006;354:23-33

Reports of intussusception among rotavirus vaccine have been received by the Vaccine Event Reporting System (VAERS). However, the number of reports is not greater than are expected by chance.

Other Adverse Events

In the 42-day period after vaccination, vaccine recipients had a small increased risk of certain symptoms compared with placebo recipients, including vomiting (15% versus 14%), diarrhea (24% versus 21%), nasopharyngitis (7% versus 6%), otitis media (15% versus 13%), bronchospasm (1.1% versus 0.7%).

Rotavirus Vaccine Adverse Reactions

- Vomiting 15%
- Diarrhea 24%
- Nasopharyngitis 7%
- Fever 43%
- No serious adverse reactions reported

MMWR 2006;55(RR-12):1-13

Contraindications and Precautions to Vaccination

Rotavirus vaccine is contraindicated for infants who are known to have had a severe allergic (anaphylactic) reaction to a vaccine component or following a prior dose of vaccine.

Rotavirus Vaccine Contraindications

- Severe allergic reaction to a vaccine component or following a prior dose of vaccine

Precaution conditions are those that may increase the chance of a vaccine adverse reaction or reduce the efficacy of the vaccine. In general, infants with precautions to vaccination, described below, should not receive the vaccine until the condition improves unless the benefit of vaccination outweighs the risk of an adverse reaction. The decision to withhold rotavirus vaccine if a precaution is present means that the infant will be infected with wild-type rotavirus,

which is more likely to cause severe illness than the attenuated vaccine virus.

Clinicians should consider the potential risks and benefits of administering rotavirus vaccine to infants with known or suspected altered immunocompetence. Children and adults who are immunocompromised because of congenital immunodeficiency, hematopoietic transplantation, or solid organ transplantation sometimes experience severe, prolonged, and even fatal rotavirus gastroenteritis. However, no safety or efficacy data are available regarding administration of rotavirus vaccine to infants who are or are potentially immunocompromised due to either disease or drugs (including HIV infection or high-dose systemic corticosteroids for more than 2 weeks). Data from the clinical trials are insufficient to support administration of rotavirus vaccine to infants with indeterminant HIV status who are born to mothers with HIV/AIDS.

The effect of recent receipt of an antibody-containing blood product on the efficacy of rotavirus vaccine is unknown. However, ACIP recommends deferral of vaccination for infants who have received an antibody-containing product, including blood and immunoglobulin, for 6 weeks after receipt of the blood product. However, if the 6-week deferral would cause the first dose of rotavirus vaccine to be scheduled at an age older than 12 weeks, a shorter deferral interval should be used to ensure the first dose is administered before age 13 weeks.

Usually, rotavirus vaccine should not be administered to infants with acute, moderate to severe gastroenteritis or other acute illness until the condition improves. However, infants with mild acute gastroenteritis can be vaccinated, particularly if the delay in vaccination will delay the first dose of vaccine until 13 weeks of age or older.

The safety and efficacy of rotavirus vaccine in children with pre-existing chronic gastrointestinal (GI) conditions, such as congenital malabsorption syndromes, Hirschsprung disease, or short-gut syndrome, has not been determined. The decision to vaccinate children with these conditions must be made on a case-by-case basis.

Additional postlicensure surveillance data are required to confirm that rotavirus vaccine is not associated with intussusception at a lower rate than would have been detected in prelicensure trials. In addition, data suggest that infants with a history of intussusception might be at higher risk for a repeat episode than other infants. Therefore, until postlicensure data on the safety of rotavirus vaccine are available, the risks for and the benefits of vaccination should be

Rotavirus Vaccine Precautions*

- Altered immunocompetence
- Recent receipt of blood product
- Acute, moderate to severe gastroenteritis or other acute illness
- Pre-existing chronic GI disease
- Infants with history of intussusception

*the decision to vaccinate if a precaution is present should be made on a case-by-case risk and benefit basis

considered when vaccinating infants with a previous episode of intussusception.

Rotavirus Vaccine and Preterm Infants

- Few data available
- Safety and efficacy of rotavirus vaccine appear to be similar for preterm and term infants
- ACIP considers that the benefits of rotavirus vaccine vaccination of preterm infants outweigh the theoretical risks

Practitioners should consider the potential risks for and benefits of vaccinating preterm infants against rotavirus. Limited data suggest that preterm infants are at increased risk for hospitalization from viral gastroenteritis during their first year of life. In clinical trials, the safety and efficacy of rotavirus vaccine appear to be similar for preterm and term infants, although a relatively small number of preterm infants have been evaluated. The lower level of maternal antibody to rotaviruses in very low birthweight, preterm infants theoretically could increase the risk for adverse reactions from rotavirus vaccine. ACIP supports vaccination of preterm born infants if they are at least 6 weeks of age, are being or have been discharged from the hospital nursery, and are clinically stable. Until further data are available, ACIP considers that the benefits of vaccination of preterm infants with rotavirus vaccine outweigh the theoretical risks.

Immunosuppressed Household Contacts of Rotavirus Vaccine Recipients

- Protection of the immunocompromised household member afforded by vaccination of young children in the household outweighs the small risk for transmitting vaccine virus to the immunocompromised household member
- Household should employ measures such as good handwashing after contact with the feces of the vaccinated infant

Infants living in households with persons who have or are suspected of having an immunodeficiency disorder or impaired immune status can be vaccinated. The majority of experts believe the protection of the immunocompromised household member afforded by vaccination of young children in the household outweighs the small risk for transmitting vaccine virus to the immunocompromised household member and any subsequent theoretical risk for vaccine virus–associated disease. To minimize potential virus transmission, all members of the household should employ measures such as good handwashing after contact with the feces of the vaccinated infant (e.g., after changing a diaper). Infants living in households with a pregnant woman can be vaccinated.

Vaccine Storage and Handling

Rotavirus Vaccine Storage and Handling

- Provided as a single 2-mL oral dose in a buffered stabilizer solution
- Store at 35°-46°F (2°-8°C)
- Shelf life of properly stored vaccine is 24 months
- Do not freeze
- Administer as soon as possible after being removed from refrigeration

RotaTeq is provided in a squeezable plastic dosing tube with a twist-off cap designed to allow for the vaccine to be administered directly to infants by mouth. Each tube contains a single 2-mL dose of the vaccine as a liquid buffered stabilizer solution that is pale yellow in color but might have a pink tint. This formulation protects the vaccine virus from gastric acid and stabilizes the vaccine. The vaccine must be stored at refrigerator temperatures (35°–46°F [2°–8°C]). The shelf life of properly stored vaccine is 24 months. The vaccine must not be frozen. RotaTeq should be administered as soon as possible after being removed from refrigeration. Additional information on stability under conditions other than those recommended is available from the manufacturer at 800-637-2590.

Rotavirus Surveillance

Rotavirus gastroenteritis is not a reportable disease in the United States, and testing for rotavirus infection is not always performed when a child seeks medical care for acute gastroenteritis. Establishing rotavirus disease surveillance systems that are adequately sensitive and specific to document the effectiveness of vaccination programs will be necessary. National surveillance systems for rotavirus infections include review of national hospital discharge databases for rotavirus-specific or rotavirus-compatible diagnoses and reports of rotavirus isolation from a sentinel system of laboratories and surveillance in three sites that participate in the New Vaccine Surveillance Network. At state and local levels, additional surveillance efforts at sentinel hospitals or by review of hospital discharge databases will be necessary to monitor the impact of the vaccination program. Special studies (e.g., case-control studies and retrospective cohort studies) will be needed to confirm the effectiveness of rotavirus vaccine in routine programmatic use.

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