

Rotavirus

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Objectives After completing this article, readers should be able to:

1. Recognize the signs and symptoms of rotavirus infection.
2. Describe how rotavirus is transmitted and how infection can be prevented.
3. Explain how to manage dehydration.
4. Describe other potential complications of rotavirus infection.
5. Discuss the risks and benefits of treating vomiting and diarrhea symptomatically.

Introduction

In 1959, Brenner and Horne described a novel technique for electron microscopy, ushering in a new era in experimental and diagnostic virology. (1) Among the panoply of newly discovered agents, rotavirus was first described as the agent of infantile murine diarrhea in 1963. Its importance as a pathogen in human gastrointestinal (GI) disease was not appreciated until 10 years later when Bishop and associates (2) identified it by electron microscopy in the inflamed mucosa of six children who had gastroenteritis and were cared for at the Royal Children's Hospital in Melbourne, Australia. In 1974, Flewett and colleagues (3) advanced the name "rotavirus" based on its "wheel-like" appearance (Figure). Since then, more readily available diagnostic techniques have resulted in a substantial growth of knowledge about the virus, which now is known to be the single most common cause of childhood diarrhea.

Disease Burden

Rotavirus is ubiquitous, but strikes particularly hard at children in developing nations. Worldwide, rotavirus accounts for 25% of all deaths due to diarrheal disease. In children, the incidence is about 600,000 to 900,000 deaths annually or 6% of all deaths of children younger than 5 years of age. (4) In the United States, mortality attributable to rotavirus is rare, accounting for fewer than 40 pediatric deaths annually. (4) However, even in the United States, rotavirus causes serious morbidity and is responsible for an estimated 500,000 outpatient visits and 50,000 hospitalizations. (4) The resulting financial burden on the United States health-care system has been estimated to be \$200 to \$500 million.

Classification

Rotavirus is a double-stranded RNA virus belonging to the Reoviridae family. The genomic material is encased in a triple-layer capsid, each layer of which contains various proteins that are important in antigenicity and infectivity. Antigenic specificities related to proteins within the capsid allow classification of rotavirus into groups, subgroups, and serotypes. Seven rotavirus groups, designated A through G, have been identified. Of these, Group A causes most endemic human disease. Subgroup and serotype classifications generally are performed only for research purposes. Serotypes tend to vary geographically as well as between humans and other species. Group B rotavirus, sometimes referred to as "adult diarrhea rotavirus," has been reported primarily in China and eastern Asia, but serologic global samplings suggest that it may occur outside this region. Group C rotavirus has been isolated globally but tends to be found only in small sporadic outbreaks.

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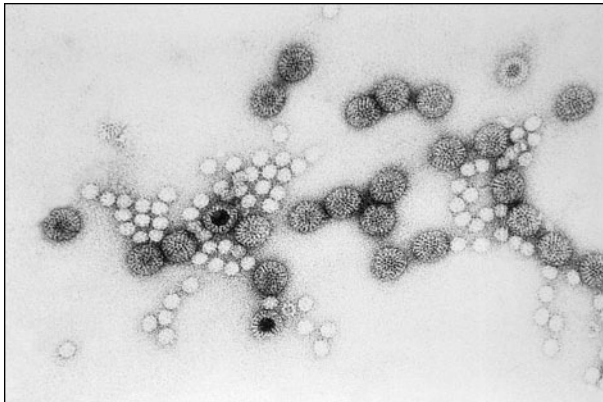


Figure. Human rotavirus seen through electron microscopy.

Epidemiology

In the United States, nearly all children have been infected with rotavirus by 2 to 3 years of age. (4) Most symptomatic disease occurs between 4 and 24 months of age. Reinfection occurs in all age ranges, but symptom severity varies considerably by age. Nosocomial spread is common in hospitalized children, but most children are infected through contact with shedding household members and at child care centers. Zoonotic spread is believed to be an uncommon source of infection. When it does occur, a variety of animal sources have been implicated, including livestock and family pets.

Rotavirus infection has a marked seasonal variation in temperate climates, as found in the United States. (5) The seasonal variability seems to correlate best with temperature rather than humidity, although humidity is known to affect the survival of the virus on fomite surfaces. In southern California, Nevada, and New Mexico, the peak incidence of rotavirus disease begins in November and December. The peak months of illness occur later in the winter and spring, moving north and east in the contiguous United States. This pattern can be interpreted as supporting the concept of annual contagious spread of the illness in the United States.

Transmission

Rotavirus classically has been believed to spread by fecal-oral transmission. Large numbers of infectious particles, as many as 10^{10} to 10^{12} /mL, are shed in the stool of infected persons. (6) Additionally, the mechanisms of intestinal cell entry have been elucidated.

Despite this understanding, an alternate means of transmission has been considered. The seasonal predilection for cooler months suggests the possibility of aerosolized transmission. (5) Rotavirus has been isolated from the respiratory tract, and respiratory symptoms may

accompany infection. It is not known if aerosol formation occurs from the respiratory involvement (coughing or sneezing) or if aerosols are elaborated during the act of vomiting. In animal experiments, rotavirus was shown to be transmissible by aerosols. (7)

No matter the source from which the virus is shed, fomites almost certainly play an important role in transmission. Rotavirus remains infectious for a prolonged period on a number of surfaces, especially nonporous surfaces such as metal and plastic. Not surprisingly, toilet handles and sinks are among surfaces believed to serve as fomites in rotavirus transmission.

Pathophysiology and Clinical Manifestations

Following oral exposure, most infectious rotavirus particles are inactivated by low gastric pH. However, it is estimated that as few as 1 to 10 organisms need to survive in the stomach to infect the small bowel. Once within the small bowel, the increased pH and the presence of trypsin induce conformational changes in the VP4 capsid protein that are important in binding to the mature enterocyte in the middle to upper portions of a villus.

Infection may be asymptomatic. The severity of GI disease may be related, in part, to subtype and serotype, but individual host and age-related differences probably are more important and reflect differences in acquired immunity. (8) Neonates may be asymptomatic or only mildly symptomatic. Nevertheless, a wide range of illness may occur in this age group. Watery stools predominate, as in older children, but bloody mucoid stools, abdominal distention, dilated bowel loops, and even frank necrotizing enterocolitis may be seen in preterm neonates. In fact, it is estimated that 30% to 40% of cases of necrotizing enterocolitis may be related to rotavirus infection. Adults are more likely to be asymptomatic. In a study of adult volunteers challenged with an oral rotavirus inoculum, 67% developed serologic evidence of infection, but only 33% of these developed symptoms. (8)

In patients who develop symptoms, manifestations of infection usually begin following a 2- to 4-day incubation period after inoculation. Delayed gastric emptying plays a role in promoting vomiting, which occurs in more than 75% of symptomatic cases. In the small bowel, both gross changes (ileal wall thickening) and microscopic changes (villus blunting, microvillus denudation, mononuclear infiltration, and morphologic intestinal cell alteration from columnar to cuboidal) mark the progression of healthy to diseased state. (2)(6) Such histologic changes, along with biochemical alterations, contribute to theories of the pathophysiology of the diarrhea that ensues.

On a histologic level, the relative sparing of the fluid- and electrolyte-secreting crypts and severe derangement of the absorptive villi contribute to a net fluid loss. (2)(6) On the biochemical level, inhibition of sodium cotransport mechanisms, putatively by one of the rotavirus nonstructural proteins, “NSP4,” and decreased brush border disaccharidase activity are two mechanisms that could explain an osmotic diarrhea. The NSP4 protein additionally may stimulate the enteric nervous system, speeding bowel transit beyond its absorptive capacity. (2)(6). Other theories exist, including a state of hypersecretion and reduced absorption due to a postischemic, hyperemia-induced alteration of a local osmotic counter-current mechanism. (9)

Vomiting tends to last 1 to 3 days. Diarrhea is usually watery, and the presence of gross blood is rare. Diarrhea typically lasts 5 or 6 days, but the range is wide. Most affected children are febrile, but the fever generally lasts no more than 1 to 2 days.

Extraintestinal manifestations, especially respiratory disorders, occur in 20% to 50% of infected children. Otitis media may complicate as many as 20% of rotavirus cases. Other classifiable extraintestinal disease entities, such as encephalitis, aseptic meningitis, and pneumonia, have been associated with rotavirus infection. Their frequency is not established, but such conditions probably are rare. The presence of viremia, which might allow extraintestinal spread, however, is not rare, occurring in 43% to 66% of serum samples taken from children who have rotavirus gastroenteritis.

Common complicating features of acute gastroenteritis (AGE) caused by rotavirus include dehydration, electrolyte disturbances, metabolic acidosis, nutritional deficiencies, and diaper rash. Rare complications include gastric rupture and central pontine myelinolysis. In children who are immunodeficient, extraintestinal spread is more common, a state of chronic diarrhea may occur, and infection is more likely to result in more severe illness and death.

Diagnosis

AGE, the most common illness caused by rotavirus, is a clinical diagnosis. Distinguishing among rotavirus and other specific enteric pathogens on clinical grounds is not possible. Studies have demonstrated significant differences among the clinical patterns manifested by different enteric organisms, but cutoff criteria have not been derived, and there has been no prospective evaluation of a diagnostic algorithm. However, it should be noted that the presence of gross blood is unusual in rotavirus-

induced diarrhea and often indicates the presence of an enteroinvasive organism.

Fever, acidic-reducing substance-positive stool, and low serum bicarbonate all are more likely to occur in rotavirus AGE than in AGE caused by other organisms. Additionally, appropriate patient age and occurrence during the colder months in temperate climates suggest rotavirus as the likely pathogen.

Enzyme-linked immunosorbent assay and latex agglutination are the stool tests used most frequently for rotavirus because they are easy to perform, provide rapid results, and are more sensitive than many of the other tests. Such tests, which detect the abundant VP6 protein present in the middle layer of the triple layer capsid, have sensitivities of 70% to 98% and specificities of 71% to 100%. Uncommonly used stool tests include radioimmunoassay, counter immunoelectro-osmophoresis, tissue culture, polyacrylamide gel electrophoresis, and polymerase chain reaction. Although not recommended for diagnosis, serum can be evaluated for acute and convalescent-phase antibody titers, immunofluorescence, neutralization, and complement fixation. Stool electron microscopy is not practical clinically.

It is important to note that during months of rotavirus endemicity, children continue to present with other illnesses whose complaints or physical findings could mimic those of rotavirus AGE with dehydration. Bacillary dysentery, hemolytic-uremic syndrome, myocarditis, congestive heart failure, intussusception, midgut volvulus, elevated intracranial pressure, sepsis, encephalitis, and meningitis are among a group of serious illnesses that could present similarly but require very different care. Additionally, the presence of rotavirus does not preclude the presence of another potentially more serious enteropathogen.

Treatment

Treatment of rotavirus AGE should address, in descending order of importance, hydration, nutrition, and symptomatic relief. Treatment of other manifestations of rotavirus infection is less understood. In neonates, necrotizing enterocolitis related to rotavirus tends to be milder and more distal than other forms. However, until evidence is obtained to the contrary, rotavirus-associated necrotizing enterocolitis should be managed similarly to necrotizing enterocolitis of nonrotaviral origin. When treating otitis media and pneumonia, it seems appropriate to focus on the treatment of potential bacterial superinfection. Central nervous system disease and abdominal solid organ involvement are rare enough that no guidance can be drawn from the literature at present.

Treatment of complications from rotavirus AGE are beyond the scope of this article except for a brief discussion. Routine laboratory assessment may not be necessary, but assessment and correction of hypoglycemia and electrolyte disturbances, especially hypernatremia, hyponatremia, and hypocalcemia, may be indicated. Related or unrelated to the degree of dehydration, metabolic acidosis may occur in the setting of rotavirus AGE. Presence or absence of an elevated anion gap may help determine if the acidosis is due to dehydration-related perfusion disturbances or diarrheal bicarbonate loss. In the latter case, bicarbonate or citrate-supplemented oral rehydration solution (ORS), if tolerated and clinically appropriate, should correct the acidosis better than standard nonbicarbonate-containing intravenous crystalloid hydration. Finally, barrier creams and pastes are appropriate for the diaper rashes that commonly accompany diarrheal illness.

Hydration

The appropriate setting and mode of hydration therapy for children suffering rotaviral AGE depends on the age, severity of illness, and individual symptoms. Children who are not dehydrated and who are not vomiting may continue their usual age-appropriate diets. Children who are not dehydrated but still are vomiting may benefit from recommended home fluids or ORSs. Recommended home fluids include human milk, formula, solutions (water, salt, and sugar) made according to a physician's instructions, soups, diluted fruit juices, and sports drinks. Much controversy surrounds which fluids are acceptable, and recommendations tend to be clinician-dependent. It is important that recommended home fluids not be used as a therapy for dehydration or a substitute for oral rehydration therapy. An additional approach to prevention of dehydration in those at risk is to supplement usual fluid intake with ORS as replacement for GI losses: 2 mL/kg for each emesis and 10 mL/kg for each watery stool. (10)

Children who are mildly or moderately dehydrated should be rehydrated with ORS. In the United States, a number of commercially produced solutions are available

Table 1. Constituents of Common Oral Rehydration Solutions and Other Beverages for Comparison

	Sodium (mEq/L) (mmol/L)	Potassium (mEq/L) (mmol/L)	Base (mEq/L) (mmol/L)	Osmolality (mOsm/L)
WHO ORS*	75	20	10	245
Rehydralyte ^{®+}	75	20	30	305
Pedialyte ^{®+}	45	20	30	250 to 270
Enfalyte ^{®S}	50	25	34	170
Ceralyte 50 ^{®**}	50	20	30	<250 to 260
Ceralyte 70 ^{®**}	70	20	30	<260
Ceralyte 90 ^{®**}	90	20	30	<275
Gatorade ^{®*}	20	3	N.A.	280 to 360
Apple Juice ^{††}	0.8	28	N.A.	697

*World Health Organization. Information available at http://www.who.int/child-adolescent-health/New_Publications/NEWS/Expert_consultation.htm. Accessed December 2005.
†Ross Products, Division of Abbott Laboratories, Columbus, Ohio. Information available at: http://rpdcon40.ross.com/pn/PediatricProducts.NSF/web_Ross.com_XML_PediatricNutrition/CCF3870065DFF53585256A80007546E8?OpenDocument. Accessed December 2005.
§Mead Johnson Nutritionals, Evansville, Ind. Information available at: <http://www.meadjohnson.com/professional/products/enfalyte.html>. Accessed December 2005.
**Cera Products, Inc, Columbia, Md. Information available at: http://www.ceraproductsinc.com/productline/nutrition_cl.html. Accessed December 2005.
†Personal communication with Gatorade representative or adapted from Gatorade Beverage Comparison Chart available at: http://www.gssiweb.com/Article_Detail.aspx?articleid=126. Accessed April 2006.
††Te Loo DM, van der Graaf F, Ten WT. The effect of flavoring oral rehydration solution on its composition and palatability. *J Pediatr Gastroenterol Nutr.* 2004;39:545–548.

that contain varying amounts of water, sodium, glucose or rice syrup solids, potassium, chloride, and either bicarbonate or citrate (Table 1). These or similar solutions should be administered frequently in small amounts, aiming at an intake of 50 to 100 mL/kg over a 4-hour period, depending on the degree of dehydration. (10)(11) For a 10-kg child, this regimen entails 1 to 2 oz in a 15-minute period. Additional supplementation, as described previously, is necessary to compensate for ongoing GI losses. If vomiting ceases after 4 hours, age-appropriate feeding should be reinstated. (11)

Children who are severely dehydrated should be referred for intravenous (IV) hydration. Some children may need IV rehydration even when not severely dehydrated if they cannot take ORS because of abdominal distention, ileus, excessive vomiting, or lethargy. Generally, 10- to 20-mL/kg boluses of normal saline or lactated ringer solution are delivered until hemodynamic stability is assured. (11) Additional crystalloid is administered over the ensuing 2 to 4 hours to create a combined total of all administered fluids of 40 to 100 mL/kg. Clinical assessment should supercede predetermined volumes; many children may begin to tolerate ORS after an initial 30 mL/kg of IV fluid.

Children who are severely dehydrated should be admitted for continued IV hydration until it can be estab-

lished that they can maintain oral hydration. Other indications for admission include failure to achieve adequate rehydration during a short emergency department visit, inability to resume oral therapy, serious underlying chronic illness, known or suspected serious complications of their illness, or social considerations that could affect the ability to care for the child as an outpatient. (10) Although admission should be decided on a case-by-case basis, recent Centers for Disease Control and Prevention (CDC) recommendations (10) suggest factoring into the decision information regarding prematurity, young maternal age, black race, and rural residence because some of these factors have been associated with a higher risk of mortality.

Nutrition

Although oral rehydration therapy has been successful in reducing deaths associated with severe diarrheal disease, nutritional disease continues to be a problem for some children. Because oral rehydration therapy is low in calories, refeeding is recommended as soon as possible after rehydration has occurred. (10)(11) When copious vom-

diarrheal fluid loss. The elements of the BRAT diet, therefore, are worth including in the refeeding regimen, but the range of foods should extend beyond those four. Current recommendations continue to focus on an early return to a child's usual age-appropriate unrestricted diet, including complex carbohydrates, meats, yogurt, and fruits. (10)(11)

Human milk as a food source deserves special consideration. Although there is no question that human milk is the optimal source of nutrition for the healthy young infant, it has less sodium and a higher osmolarity than do ORSs. Additionally, the carbohydrate source of human milk, lactose, may not be amenable to digestion in cases where severe disaccharidase deficiency accompanies AGE. Nevertheless, passive immunization in the form of antirotaviral immunoglobulin A and antirotaviral properties of human milk constituents, such as lactoferrin and lactadherin, are potential benefits conferred to the breastfeeding infant who develops rotavirus AGE. Thus, continued breastfeeding during AGE is recommended. If an infant presents with dehydration, it may be assumed that these inherent benefits have been inadequate and ORS or IV hydration is necessary. (11)

Symptomatic Care

Therapies to decrease diarrhea or vomiting have been criticized as having the capability of creating a "false sense of security,

potentially resulting in a delay in seeking care." (11) Symptomatic measures may distract the clinician and family from more important hydration, electrolyte, and nutritional concerns; (10) add to the cost of providing care; (10) and result in adverse reactions. (10)(11) Although most of these concerns are valid, the practitioner should be aware of emerging symptomatic therapies that may be useful in responding to the discomfort associated with AGE and the individual needs of a variety of patients. Additionally, because serious complications of rotaviral gastroenteritis stem from the severity of some of its symptoms, symptomatic therapies can have an important effect on health.

Antiemetics

Antiemetics of the dopamine receptor antagonist class have adverse effects that may be disruptive to oral rehydration (eg, sedation, akathisia, and dystonia), (10) but the newer class of antiemetics based on serotonin subtype

iting continues despite rehydration, it seems reasonable to delay resumption of normal feeding, substituting ORS or recommended home fluids until vomiting slows. This aspect of care has not been addressed in evidence-based investigations.

Limited empiric information exists regarding the benefits of one food choice over another in refeeding children who have AGE. The classic BRAT diet (bananas, rice, applesauce, and toast) has been criticized by expert sources as being "low energy, low protein and low fat" (11) and "unnecessarily restrictive." (10) In theory and in limited study, fruit pectins (such as those found in bananas and applesauce) and resistant starches (such as those found in rice) are degraded by colonic flora to short-chain fatty acids (SCFAs). SCFAs have a trophic effect on colonic mucosa, serve as a colonocyte energy source, and stimulate sodium absorption. Green bananas and pectin as part of dietary therapy and rice in the form of rice-based ORS have been demonstrated to reduce

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3 receptor antagonism are better tolerated. Randomized, controlled clinical trials of ondansetron have demonstrated a reduction of vomiting, a decreased need for IV rehydration, and a decreased rate of hospital admission. (12) Still, routine use of these agents cannot be recommended in acute gastroenteritis because experience still is accumulating for this off-label indication. Additionally, cost and the possibility of increasing diarrhea must affect the decision to use ondansetron. (12)

Conventional Antidiarrheal Agents

The symptomatic treatment of diarrhea is even more controversial than the treatment of vomiting. Some of the concern stems from the possibility that slowing bowel transit increases the exposure to potential infection-derived intraluminal toxins. In the case of *Escherichia coli* O157:H7, this concern is not just theoretical. Consequently, antimotility, antisecretory, and adsorbent pharmacologic agents have not been recommended for use against diarrhea. (10) Opiate- and anticholinergic-based agents have demonstrated toxicity and adverse effects in children, including reports of lethargy, ileus, coma, and even death. (11) One adsorbent, attapulgitte, was shown to reduce diarrhea and dehydration in a double-blind, randomized, controlled trial, but there are few pediatric data on efficacy or adverse effects. (13)

Probiotics

Probiotic species of *Lactobacillus* and *Bifidobacterium* may function literally as microbial barriers against more pathologic enteric species and may modulate humoral immunity against rotavirus. Many, but not all, therapeutic trials have shown antidiarrheal benefits in humans. A recent meta-analysis of *Lactobacillus* demonstrated a pooled effect of 0.7 fewer days of diarrhea and 1.6 fewer stools by day 2 of illness. (14)

Passive Immunization

Passive immunization against rotavirus infection in the form of breastfeeding appears to be beneficial. Outside of infancy, medical system-mediated passive immunization also is of potential benefit. A trial of nonspecific pooled human serum immune globulin administered orally to children who had severe rotavirus AGE demonstrated decreased diarrhea and reduced length of hospital stay. (15) Some have recommended the routine use of orally administered human immune globulin for children whose expected outcome from known rotavirus AGE is poor, such as those who have immunodeficiency.

Zinc

Zinc-based enzymes are important in cell function and growth. Injured bowel, if similar to other tissues that have high cellular turnover, may demand more zinc to fulfill demands of regrowth. Zinc has other functions, including downregulation of inflammatory cytokines. Many studies of nonspecific acute childhood diarrhea have shown that zinc supplementation results in decreased duration of diarrhea. The World Health Organization recommends 14 days of zinc supplementation for all children who have acute diarrhea: 10 mg daily for infants younger than 6 months of age and 20 mg daily for all older infants and children. Problems with this policy in the United States include the potential for increasing nausea and vomiting and the lack of certainty as to whether zinc supplementation would be helpful to United States children who are less likely than children in developing countries to be zinc-deficient. (10)

Homeopathic Antidiarrheal Agents

Homeopathic antidiarrheal medications (eg, *Arsenicum album*, *A sulfur*, *Podophyllum*, *Chamomilla*, and *Calcarea carbonicum*) have been studied in acute childhood diarrheal illness, but not specifically in rotavirus AGE. Three randomized, controlled clinical trials were examined recently by meta-analysis. The pooled effect was a reduction of 0.8 days of diarrhea. (16) Although the trials appear well-designed, the application of homeopathy to diarrheal disease has been met with some resistance. Homeopathy was not addressed in the 1996 American Academy of Pediatrics (AAP) practice parameters (11) or in the more recent CDC guidelines. (10) Because the choice of a particular homeopathic medication is individualized, based on particular features of the diarrheal illness, it is not known if homeopathic medications are effective when prescribed by caregivers who are not trained in homeopathic methods.

Prevention

Anticipatory Guidance

Nearly all children have been infected with rotavirus by 2 to 3 years of age, (4) many from household spread, others through child care-related contacts, and some through nosocomial exposure. Pediatricians should empower parents to break the chain of transmission by providing accurate information about modes of transmission. Rotavirus particles can survive on human hands for several hours, and tap water alone is a poor disinfectant. Therefore, thorough handwashing with soap and water must be advised. One of the most effective disinfectants for use on fomites is a commercially available

Table 2. Two Live Oral Attenuated (Weakened) Rotavirus Vaccines Licensed Within the Americas

Trade Name	Manufacturer	Genetic "Backbone"	Serotypes Represented in the Vaccine	Number of Doses in Series	Countries in Which It is Licensed
Rotarix™	GlaxoSmithKline	Human rotavirus	G1[P8]	2	Mexico and other countries in Latin America
RotaTeq™	Merck Vaccine Division	Bovine-human reassortant	G serotypes (G1, G2, G3, and G4) and one P serotype (P1)	3	United States

0.1% o-phenylphenol and 79% ethanol spray (eg, Lysol® disinfectant spray).

Some caregivers cannot identify signs of dehydration, and many believe that fruit juices should be offered to children who have diarrhea. Thus, in addition to treating dehydrated children who have AGE, clinicians must educate families. "Fast Facts for Families: What You Need to Know about Rotavirus," a brochure for parents published by the National Healthy Mothers, Healthy Babies Coalition, is available at http://www.hmhb.org/rotavirus/pdf/HMHB_rotavirus_final.pdf.

Active Immunization

Because natural infection with rotavirus confers clinical immunity and because elevated serum rotavirus antibody titers correlate with decreased risk of subsequent infection, the potential for a vaccine against rotavirus has been realized for some time.

The first efforts to develop a rotavirus vaccine began in the early 1970s. In 1998, a tetravalent rhesus-based vaccine was licensed by the United States Food and Drug Administration (FDA) and recommended by both the AAP and the Advisory Committee on Immunization Practices (ACIP) to the CDC. The CDC estimated that approximately 1 million doses of the vaccine were administered to more than 500,000 children over the course of the next year. Fifteen cases of intussusception following rotavirus vaccination were reported to the Vaccine Adverse Event Reporting System (VAERS). In-depth studies supported an association between the vaccine and intussusception as well as a spectrum of other GI illnesses. (17) Infants 90 days of age or older at the time of the first dose accounted for a disproportionately large number of cases of intussusception. In July 1999, the CDC recommended that clinicians suspend use of the vaccine, and in October 1999, the vaccine was withdrawn from the market.

Since that time, two rotavirus vaccines have been

licensed for use in North America (Table 2), both of which have been shown to be efficacious against severe rotavirus gastroenteritis and well tolerated in clinical trials. (18) On February 21, 2006, the ACIP again voted to recommend routine rotavirus vaccination for United States infants. RotaTeq™ (Merck Vaccine Division, Whitehouse Station, NJ), the only rotavirus vaccine currently licensed for use in the United States, is a live virus vaccine administered in three doses, typically at 2, 4, and 6 months of age. Children should receive the first dose between 6 and 12 weeks of age and the third dose no later than 32 weeks of age. In the prelicensure clinical trial, efficacy against G1 through G4 rotavirus AGE through the first full rotavirus season after vaccination was 74% for AGE of any severity and 98% against severe AGE. Vaccination was associated with an 86% reduction in clinic visits for G1 through G4 rotavirus AGE, and the risk of intussusception was similar for vaccine and placebo recipients.

Postlicensure surveillance to detect any rapid association between RotaTeq™ and intussusception as well as other potential adverse events will be performed by several organizations: 1) The CDC will use its Vaccine Safety Datalink Program, which evaluates vaccine safety in approximately 90,000 infants annually; 2) The CDC, working with the FDA, will monitor through the VAERS; and 3) Merck will study approximately 44,000 children and report cases of intussusception to the FDA within 15 days of receiving reports.

The future of rotavirus vaccination in the United States and abroad will be interesting and important. More candidate vaccines are in development. Surveillance will be needed to follow how well the vaccines in use cover the emerging strains. Efficacy of the vaccine in Africa and Asia will have to be assessed; the global diversity of rotavirus strains and blunted host responses due to malnourishment, other enteric infections, parasitic infection, or immune suppression may make efficacy

different in the developing world, where the vaccine is sorely needed. Affordability could be another potential major barrier to the vaccine's access.

Summary

In the United States, rotavirus is a seasonal enteric pathogen that most frequently causes AGE and is the most common cause of AGE. Necrotizing enterocolitis, respiratory illness, and other rare manifestations may be caused by this virus. Serious dehydration may occur, but appropriate therapy that focuses on hydration and attention to possible complications should make poor outcomes uncommon. Symptomatic relief, considered case by case, is indicated occasionally. Anticipatory guidance on this topic is essential. Safe and effective active immunization for rotavirus diarrhea is now a part of well child preventive care, with the aim of preventing a disease that has been an inevitable part of early childhood worldwide.

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Suggested Reading

- Block SL, Vesikari T, Goveia MG, et al. Efficacy, immunogenicity, and safety of a pentavalent human-bovine (WC3) reassortant rotavirus vaccine at the end of shelf life. *Pediatrics*. 2007;119:11–18
- Kempe A, Daley MF, Parashar UD, et al. Will pediatricians adopt the new rotavirus vaccine? *Pediatrics*. 2007;119:1–10

PIR Quiz

Quiz also available online at www.pedsinreview.org.

9. Among the following, the *most* important vehicle for transmission of rotavirus is:
 - A. Contaminated food.
 - B. Cough.
 - C. Family pet.
 - D. Fomite.
 - E. Kissing.

10. Among the following clinical findings, the one *most* typical of rotavirus infection is:
 - A. Grossly bloody stools.
 - B. Nonbilious vomiting.
 - C. Otitis media.
 - D. Pneumonia.
 - E. Prolonged fever.

11. Among the following clinical findings, the one most suggestive of a diagnosis other than rotavirus infection is:
 - A. Fever.
 - B. Grossly bloody stools.
 - C. Low serum bicarbonate concentrations.
 - D. Nonbilious vomiting.
 - E. Reducing substance-positive stool.

12. A previously well 9-month-old boy presents in January with a 1-day history of recurrent nonbilious vomiting and watery diarrhea. He attends child care. Given your knowledge of epidemic illness circulating in your community, you diagnose rotavirus infection presumptively. Based on your clinical examination, you estimate 3% dehydration and believe a trial of outpatient management is warranted. According to current consensus, your *first* choice should be:
 - A. Continuation of regular diet.
 - B. Oral antimotility agent.
 - C. Oral ondansetron.
 - D. Oral rehydration solution.
 - E. Oral zinc supplementation.

13. The *most* appropriate statement about the rotavirus vaccine licensed currently is that:
 - A. It does not contain live virus.
 - B. It is associated with an increased risk of intussusception.
 - C. It is highly effective against severe rotaviral disease.
 - D. The first dose must be administered before 1 month of age.
 - E. The third dose should not be administered to any infant older than 6 months of age.