REVIEW ARTICLE

Rotavirus infection and the current status of rotavirus vaccines

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Among children, rotaviruses are the most common cause of severe gastroenteritis worldwide and of diarrheal deaths in developing countries. Current vaccines (e.g., Rotarix, GlaxoSmithKline Biologicals; RotaTeq, Merck and Company) effectively reduce rotaviral gastroenteritis, emergency department visits, and hospitalizations. The tremendous burden of rotavirus-related diarrhea in children across the world continues to drive the remarkable pace of vaccine development. This review assesses the global epidemiological and economic burden of rotavirus diseases, summarizes the relevant principles of the development of rotavirus vaccines, and presents data on the efficacy and effectiveness of currently licensed vaccines in both developed and developing countries.

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Introduction

Rotavirus is the leading cause of severe gastroenteritis in infants and young children worldwide. Globally, infection results in more than 600,000 deaths each year in children less than 5 years old who die from severe dehydration and electrolyte and acid-base disturbances.1 It is estimated that more than 80% of all rotavirus-related deaths occur in resource-limited countries in south Asia and sub-Saharan Africa.2 Nearly every child is infected with rotavirus by 5 years of age, irrespective of location (e.g., urban or rural area) or socioeconomic status.2 Because improvements in housing, water supply, sanitation, personal hygiene, food quality, nutrition, and maternal education do not appear to reduce the overall incidence of rotavirus infections, non-fecal routes of infection may play a role in transmission.4 Consequently, vaccines are the most effective public health intervention for the control of rotavirus disease.5

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This review assesses the global epidemiological and economic burden of rotavirus disease, summarizes the relevant principles of the development of rotavirus vaccines, and presents data on the efficacy and effectiveness of currently licensed vaccines in both developed and developing countries. We searched MEDLINE, PubMed, and The Cochrane Collaboration using ‘rotavirus’ and ‘rotavirus vaccines’ as both the medical subject headings and keywords. Articles not published in English were excluded from this review.

**Virology**

Rotaviruses were discovered in animals in the 1960s. The virus was first described in humans by electron microscopic examination of duodenal biopsies from children with acute gastroenteritis. The rotavirus, a 70-nm icosahedral virus that belongs to the family Reoviridae and the genus Rotavirus, is a nonenveloped, double-stranded RNA virus that contains 11 segments of genomic RNA surrounded by a triple-layered capsid. The viral genome encodes six structural (VP1, VP2, VP3, VP4, VP6, and VP7) and six nonstructural (NSP1–NSP6) proteins. The most abundant viral protein is VP6, which bears the group-specific antigenic determinants and forms the middle capsid layer; the outer-layer proteins, VP7 and VP4, act as independent neutralizing antigens. NSP4 is antigenic, allowing categorization into different genotypes, and acts as an enterotoxin capable of causing diarrhea.

Within the Rotavirus genus, there are seven antigenically distinct serogroups (A through G), that are distinguished by different VP6 proteins. Group A rotaviruses are the predominant cause of illness in humans and animals. There are two major outer capsid-surface proteins: VP7 and VP4. These two proteins define the serotype of the virus and are considered critical to vaccine development because they are targeted by neutralizing antibodies that may provide both serotype-specific and, in some instances, cross-reactive protection. The VP7 protein is glycosylated, and the serotypes determined by this protein are termed “G serotypes.” VP4 is a protease-cleaved protein, and the serotypes determined by this protein are termed “P serotypes.” P serotypes are difficult to characterize using traditional methods of virus neutralization; therefore, molecular methods were used to determine its genotype using sequence analysis. These genotypes correlate well with the known serotypes, so the genotypes are tentatively designated in brackets (e.g., P1B[8]).

Human rotaviruses exhibit enormous diversity. The gene segments that encode the G and P proteins can independently segregate, giving rise to strains with at least 42 different P-G serotype combinations; however, a small number of rotavirus strains—those bearing VP7 G serotypes G1–G4 and G9 and VP4 P genotypes P1B[8], P2A[6], and P1A[8]—are predominant worldwide.

**Clinical illness**

The severity of rotavirus infection is age-dependent. Although the disease can occur at any age, clinically significant incidents most commonly occur in young infants and children. Rotavirus infections can range from asymptomatic infection to mild diarrhea to severe gastroenteritis with dehydration. After an incubation period of 2–4 days, the symptoms typically abruptly begin with fever and vomiting, followed by watery diarrhea lasting for 3–8 days. Compared with other viral enteropathogens, rotaviruses are more likely to result in symptomatic illness and lead to dehydration, electrolyte imbalance, and even convulsions in severely ill patients. Fever was found more commonly in patients with rotavirus gastroenteritis than those with norovirus gastroenteritis.

Following a severe episode of rotavirus-induced diarrhea, most children will shed the rotavirus within 1–3 weeks; however, approximately one in five will continue to shed the virus for 4–8 weeks, especially if the child experiences mild or intermittent gastrointestinal symptoms.

Rotavirus disease is most common and severe in children between 3–36 months of age. Multiple infections can occur throughout life, although cumulative immunity usually makes subsequent episodes mild or asymptomatic in older children and adults. Rotaviruses are traditionally believed to infect only the mature epithelial cells that line the intestinal tract; in contrast, clinical illness is uncommon in neonates. The immaturity of the neonatal gut, the presence of maternal antibodies, and the reduced virulence of the rotavirus strains capable of replicating in the neonatal gut may play a role in the asymptomatic nature of neonatal infections. Meanwhile, rotaviruses are associated with prolonged illness and stool shedding in infants with severely compromised T-cell immunity and in children and adults immediately following bone marrow transplantation. Notably, children with asymptomatic or symptomatic HIV infection and impaired immunity do not appear to be at increased risk of developing severe rotavirus disease, although they, too, may shed rotavirus particles for longer than other children.

The reported incidence of concomitant rotavirus and Salmonella infection varies between 1.3–7.4%. Concomitant infection is associated with a more prolonged clinical course, higher fever, higher incidence of green-colored stool with blood and mucus, higher levels of C-reactive protein (CRP), and a higher incidence of hypokalemia than rotavirus infection alone. Rotavirus infection also increases the risk of bacteremia in children with non-typhoid Salmonella gastroenteritis.

**Immunity**

The immune correlates of protection from rotavirus infection and disease are still incompletely understood. Mouse models have been extensively used to investigate the contributions of different components of the immune system to protect against rotavirus. These studies have suggested that both humoral and cell-mediated immunity are important in the resolution of ongoing rotavirus infection and in protection against subsequent infections.

The highest levels of serum rotavirus antigen are typically detected on day 2 of illness, with a gradual decrease in antigen levels to nearly undetectable levels by day 6. The quantity of rotavirus antigen is significantly higher in sera collected from patients with fever than in sera...
collected from those without fever. Nonetheless, the clinical significance of extraintestinal rotavirus infection other than for fever associated with viremia or antigenemia is unknown. The impact of antigenemia on the development of natural and vaccine-induced immunity has not yet been determined. A study by Desselberger and Huppertz examined the immune responses to natural rotavirus infection and rotavirus vaccination in both experimental animals and humans as potential correlates of protection.

**Transmission**

Rotaviruses are highly contagious. The infectious dose is low (as few as 10 particles), and the virus is shed in large quantities (as many as $10^{11}$ particles per gram of stool) both before the onset of symptoms and for several weeks afterward. Furthermore, the virus can survive on dry surfaces for more than 10 days and on human hands for up to 4 hours. Transmission to susceptible individuals occurs mainly by the fecal-oral route through direct contact with the rotavirus, including children and adults with asymptomatic illness and contact with contaminated fomites, food, water, and environmental surfaces. It has been reported that improvements in hand hygiene in hospitals can decrease the incidence in healthcare-associated rotavirus infections. It has also been suggested that aerosol transmission might be important. Evidence of the airborne spread of rotavirus gastroenteritis is primarily circumstantial, including the short incubation period (1–3 days) and the fact that the virus often presents in explosive outbreaks. Rotavirus has also been detected in the respiratory secretions from a small number of patients, and cases of pneumonia have been described. In addition, some studies have noted the presence of respiratory symptoms and otitis media in up to 50% of patients with rotavirus. The preliminary findings from RNA obtained from air samples taken from the rooms of hospitalized children with rotavirus infections suggest that airborne spread may be a major route of transmission in hospital and day-care settings.

Rotavirus epidemics exhibit a seasonal pattern. In temperate climates, rotavirus infections peak in the winter months. Seasonality is less marked closer to the equator, but the disease is more common during drier and cooler months. Recent data suggest that the seasonality of rotavirus could have been changed by the introduction of rotavirus vaccines.

**Disease burden**

Acute gastroenteritis is second only to pneumonia as the leading global cause of childhood mortality and morbidity, accounting for 15% of all deaths in children less than 5 years of age. The disease is estimated to be associated with the deaths of more than 600,000 children per year worldwide, with the majority of these deaths occurring in Africa and Asia; more than half of these deaths occur in only six countries: India, Nigeria, Congo, Ethiopia, China, and Pakistan. Most deaths occur in malnourished infants living in socioeconomically disadvantaged rural regions in these low-income countries, where access to healthcare is poor. While deaths from rotavirus are rare in developed countries in North America, Europe, East Asia, and Australia, the incidence of disease in young children is similar to that of developing countries. In the pre-rotavirus vaccine era, rotavirus gastroenteritis resulted in 220,000 annual hospital admissions, 1.8 million healthcare visits, and 7.1 million episodes of diarrhea among children living in developed countries. By 5 years of age, approximately 1 in 50 children from these countries will have been hospitalized following rotavirus infection. In the United States, for example, rotaviruses were responsible for 20–60 deaths, 410,000 physician visits, 205,000–272,000 emergency department visits, and 55,000–70,000 hospitalizations each year during the 1990s and early 2000s. Thus, between 1 in 67 and 1 in 85 children in the United States will be hospitalized with rotavirus infection by the age of 5 years. Meanwhile, prior to the introduction of the rotavirus vaccine in Taiwan, rotavirus was estimated to have caused more than 150,000 cases of gastroenteritis, 106,000 clinic visits, 12,800 emergency department attendances, as many as 15,000 hospitalizations, and almost 7 deaths each year between 2000–2003. Most (90%) of case of rotavirus diarrhea occurred in children less than 5 years of age (Fig. 1).

The annual societal costs due to rotavirus infection were almost $US 900 million in the United States in 2004, $US 21.5 million in Taiwan in 2005, and €350 million in the European Union in 2002. In comparison, a total societal cost of only $US 423 million was reported for all developing countries in 2007.

**Global surveillance of rotavirus**

As rotavirus vaccination continues to increase in prevalence worldwide, global surveillance of rotavirus has become an important tool. Surveillance is used to describe serotype distributions in different countries and their regions, identify and predict the development of emerging strains, monitor the impact of vaccines by identifying successes and gaps, and identify the causes of diarrhea other than rotavirus. In 2002, the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC) developed a generic protocol for the standardized surveillance of rotavirus, with a focus on severe diarrhea requiring hospitalization among children less than 5 years of age. This protocol was first implemented in Asia. With the support of the Rotavirus Vaccine Program (RVP), the implementation of this protocol was expanded to include the Americas, the eastern Mediterranean region, eastern Europe, and sub-Saharan Africa. In recent years, these systems have generated data from 196 sites in 59 countries throughout the world (Fig. 2). This regional surveillance model has led to improved data standardization, increased visibility and perceived validity of data, and, potentially, improved sustainability of the surveillance platforms. The results of the global surveillance program using the common generic protocol demonstrate that, among children hospitalized for severe diarrhea in different regions of the world, 39% (regional median) test positive for rotavirus. Although the percentage of diarrhea cases that are positive for rotavirus ranges from 20–73% in individual...
countries, the predominant role of rotavirus as a cause of severe diarrhea is consistent across all regions.

Rotavirus surveillance also generates valuable data on the circulating rotavirus strains (Table 1). These data are vital to improving vaccine development, tracking emergent types, and helping to assess vaccine effectiveness and changes in strain diversity after vaccines are introduced. Globally, G1, G2, G3, G4, and G9 are the most prevalent VP7 serotypes; P[4], P[6], and P[8] are the most common VP4 genotypes, and G1P[8], G2P[4], G3P[8], G4P[8], and G9P[8] comprise 70–90% of circulating rotavirus strains.64–68 In Taiwan, G1 (40%), G3(27%), G9 (18%), and G2 (8%) are the most common VP7 serotypes.69–75

Strain diversity is the greatest in Africa and Asia, where mixed infections with multiple rotavirus strains and proximity to domestic animals that also shed the rotavirus are common.66 In addition to regional differences, major changes in one or more dominant circulating genotypes can occur from one season to the next.76 Both G9 and G12 have emerged and spread globally over the past decade.77 Multiple rotavirus serotypes can circulate within the same region at the same time. Therefore, continued surveillance of rotavirus strains remains important to monitoring the molecular epidemiology of rotavirus infection and the efficacy of vaccination.

Rotavirus vaccines

Immunity to rotavirus infection in infants was first demonstrated by Bishop et al.,78 who observed that newborns infected with rotavirus were protected against severe diarrhea following reinfection. The development of rotavirus vaccines has mainly focused on the delivery of live-attenuated rotavirus strains by oral administration. The most extensively evaluated approach is the “Jennerian” concept, which involves immunization of infants with an animal rotavirus considered to be naturally attenuated in
showed that LLR induced neutralizing antibodies (range: children aged 6 to 27% against all G-type rotaviruses.87 Evidence of the efficacy of LLR is derived from a case-control study that was performed in Guangzhou province that enrolled 838 children aged 2 months to 5 years who were hospitalized with rotavirus infections and 838 community-matched controls.86 The study demonstrated a 73% (95% CI: 61–82%) efficacy for one dose of LLR against hospitalized rotavirus diarrhea. Immunological studies on children aged 6–24 months before and after vaccination showed that LLR induced neutralizing antibodies (range: 40–70%) against all G-type rotaviruses.87 LLR has never been tested in a randomized, placebo-controlled phase III clinical trial;86 so the true efficacy of the vaccine is unknown. In all of the reported trials, the majority of children were vaccinated during or after the peak age for rotavirus disease. It is unknown whether the vaccinated children had prior infection with a natural rotavirus, in which case LLR could simply have boosted a pre-existing immune response.87 It is currently licensed in China to be given to children aged 2–36 months, with yearly boosters.87 Between 2001–2008, approximately 10 million doses were administered in China.87 The vaccine is not routinely being used in national immunization programs in China or elsewhere.

Human-animal reassortant vaccines

In view of the inconsistent protection conferred by monovalent animal rotavirus-based vaccines, vaccine development efforts began to focus on either naturally attenuated human rotavirus strains or reassortant rotavirus strains with the human rotavirus gene for the VP7 protein together with the other 10 genes from an animal rotavirus strain.88 The next generation of vaccines was formulated to include more than one rotavirus G serotype in order to provide heterotypic as well as homotypic immunity. The ability of rotavirus to reassociate during mixed infections in vitro allowed the production of reassortant vaccines, in what was termed the “modified Jennerian” approach.79 The goal was to evoke an immune response to a G-type antigen from a human virus. Reassortants were initially created by co-infecting a monkey with bovine and human rotaviruses and allowing the reassortment to occur by chance. Subsequent reassortants were created in laboratories and propagated in Vero cells.89

Human-animal rotavirus reassortants contain the gene(s) that encode VP7, with or without VP4, derived from their human rotavirus parent; however, the remaining genes are derived from the animal rotavirus parent. These reassortant viruses were developed as vaccine candidates. They could induce immune responses in human capsid proteins while still maintaining the attenuated properties of the parent strain.88 Several reassortant vaccines based on either simian or bovine strains have been produced and tested.88,89

Quadrivalent human-rhesus reassortant vaccine

The first multivalent, live, orally administered, reassortant vaccine developed was RotaShield (a rhesus rotavirus tetravalent [RRV-TV] vaccine). This tetravalent vaccine contains a mixture of four virus strains representing the most commonly seen G types (G1–G4): three rhesus-human reassortant strains containing the VP7 genes of human rotavirus serotypes G1, G2, and G4 strains were substituted for the VP7 gene of the parent RRV, and the fourth strain contained the serotype G3 of rhesus RRV.88 Efficacy trials were conducted, and the vaccine elicited 57–76% protection against all forms of rotavirus-induced diarrhea and 82–96% protection against severe rotavirus disease.89 RotaShield was associated with a short duration of fever after the first vaccination; however, no other adverse events were commonly associated with the vaccine at the time of licensing.90

This vaccine was licensed in the United States in 1998; however, use of the vaccine was suspended and ultimately withdrawn in 1999 after investigations demonstrated a significant association between the vaccine and an elevated risk of intussusception.91 The risk of intussusception was 1 per 100,000 vaccinated persons, and cases were clustered mostly within 3–14 days of the first dose. The risk of intussusception appeared to be highest in those receiving

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Sources: references 67–78.
their first dose after 3 months of age.92 The exact association between RotaShield and intussusception remains unclear; however, the error has made it necessary for subsequent candidate rotavirus vaccines to undergo large field trials, not only to prove efficacy in the absence of a reliable correlate to protection, but also to demonstrate safety (less than a 1 per 100,000 risk of intussusception).76 As an added precaution, strict vaccination schedules have been implemented, requiring the first dose to be administered between 6–14 weeks of age, and no “catch-up” schedules are allowed. Moreover, several countries have introduced post-licensing monitoring of intussusception.93

Human-bovine rotavirus reassortant vaccine

Like RRV, the WC3 vaccine strain was developed in a series of human-bovine reassortant vaccine strains, which were then combined into a polyvalent vaccine.94 Compared with the rhesus reassortants, the bovine-human reassortants appear to cause less fever while still maintaining immunogenicity.95 RotaTeq is a pentavalent, live-attenuated, human-bovine reassortant oral vaccine developed by Merck & Co., Inc., Whitehouse station, NJ, USA. This vaccine contains five live reassortant rotavirus strains representing the most common human VP7 types (G1–G4) and the attachment protein (P7[5]) from the WC3 bovine rotavirus parent strain.78,79 The fifth reassortant virus expresses the attachment protein (P1A[8]) from the human rotavirus parent strain and the G6 outer capsid protein from the bovine rotavirus parent strain.72,96 RotaTeq is administered in three oral doses at 1- to 2-month intervals, beginning at 6–12 weeks of age.96

Table 2 outlines the major phase III trials on human rotavirus efficacy in various settings.89,97–104 A large efficacy trial on RotaTeq has been completed: the study found 74% and 98% efficacy against all and severe forms of disease, respectively.105 RotaTeq also has efficacy against each of the common circulating serotypes. A large safety trial with more than 70,000 infants and various subgroup analyses, including a large European cohort,96,106 shows that RotaTeq has high efficacy for covering the main period of risk for rotavirus gastroenteritis, reduces rotavirus gastroenteritis-associated hospitalization and emergency department and physician visits, and shows no evidence of increased risk of intussusception following vaccination compared with placebo recipients. An efficacy and safety trial conducted in developing countries also shows that the vaccine reduces healthcare-resource utilization attributed to rotavirus gastroenteritis in infants without increased risk of intussusception or other serious adverse events.107

Khoury et al projected the effectiveness of the RotaTeq vaccine against rotavirus gastroenteritis-related (RGE) hospitalizations and deaths in six Asian countries (China, Hong Kong, India, South Korea, Taiwan, and Thailand) using a simple mathematical model. The model projected an overall effectiveness in the range of 82–89% against RGE-related hospitalizations and a substantial reduction in RGE-related deaths.104

Merck has received approval for RotaTeq in the United States, and the vaccine was recommended by the Advisory Committee on Immunization Practices (ACIP) for the routine immunization of infants in 2006.108 Post-marketing surveillance data from the United States have not identified any concern, such as association with intussusceptions or Kawasaki disease, related to the safety of RotaTeq.109

UK-based bovine-human reassortant vaccine

Another multivalent bovine-human reassortant vaccine has been independently developed by the National Institute of Allergy and Infectious Diseases (NIAID). This bovine rotavirus tetravalent (BRVT) vaccine incorporates four reassorted viruses with a single gene for VP7 (G1, G2, G3, or G4 human serotype) and 10 genes from the UK bovine rotavirus strain (P7[7]G6). In a trial in the United States, the vaccine demonstrated satisfactory levels of attenuation, safety, infectivity, and immunogenicity for each monovalent reassortant in infants.110 Its development has been taken over by manufacturers in Brazil, India, and China.

Human rotavirus-strain vaccines

The human rotavirus strains that have been developed as vaccines or vaccine candidates are either attenuated common strains or uncommon strains that have been isolated from asymptomatic neonates.

Monovalent human G1-rotavirus vaccine

A live-attenuated human rotavirus vaccine strain (strain 89-12) was originally obtained from an infant with rotavirus infection in Cincinnati, OH, by tissue culture passage of a wild-type human rotavirus isolate.51 This vaccine is a P1A [8]G1 strain and, thus, represents the most common human rotavirus VP7 and VP4 antigens. The vaccine was further developed by Avant Immunotherapeutics and licensed to GlaxoSmithKlone Biologicals, who further modified it by cloning and tissue culture passaging of the parent 89-12 vaccine strain112: the result was the RIX4414 vaccine (Rotarix) (Table 2). Rotarix showed high efficacy in early trials in the United States and Finland.112 The vaccine has been tested in Latin America, and the first results from these multicountry trials were reported in Mexico, Brazil, and Venezuela, where efficacy against severe rotavirus disease was 86%.113 Efficacy has been confirmed in a series of trials that enrolled more than 63,000 children. In these studies, efficacy against hospitalization was 85% and efficacy against non-G1 serotypes was 75%.113 A large efficacy and safety trial that enrolled more than 15,000 healthy infants aged 6–13 weeks from 10 Latin American countries has reported a vaccine efficacy of 81–82% against wild-type G1, 78% against pooled non-G1 strains, 81% against pooled non-G1P[8] strains, 83% against hospital admission for rotavirus gastroenteritis, and 39% against admission for diarrhea of any cause.114 No significant adverse events or increased risk of intussusception were observed among the vaccine recipients.114 The vaccine was first licensed in Mexico and the Dominican Republic in 2004, and it was also licensed in the United States in 2008 when the vaccine was recommended by the ACIP for inclusion in the routine childhood vaccination schedule.
immunization of infants. As of May 2007, Rotarix had been approved in 90 countries worldwide.

**RV3 neonatal-strain vaccine**

RV3, a P2A[6]G3 strain, was first isolated in newborns at the Children’s Hospital in Melbourne, Australia. The development of this vaccine was based on an observation that neonates in hospital nurseries who were infected with this rotavirus strain were usually asymptomatic and later protected against severe disease in early childhood. Initial safety trials, in which a single dose of the vaccine was used, demonstrated no significant adverse events; however, serum immune responses were poor. A trial using three doses of vaccine did induce immune responses in 54% of infants, and the vaccinated children who developed immune responses were protected from rotavirus disease. Because of these promising results, the developers are working with BioPharma (Bandung, Indonesia) to increase the titer of this vaccine and then return to clinical trials.

**Indian neonatal-strain vaccines**

Two strains isolated from newborns in India are currently being prepared as potential vaccines. Strain 116E, isolated in 1985 from an outbreak of asymptomatic rotavirus infections in New Delhi, is a P8[121] G9 natural reassortant between a human parent strain and a VP4 gene of bovine origin. The sequence of the VP4 gene is homologous to P[11], a genotype commonly found in cattle. A nosocomial outbreak of infection at a maternity center in Bangalore led to the identification of another "outbreak" of strain I321, also a bovine-human reassortant strain. Unlike strain 116E, strain I321 has a base of nine bovine gene segments; only gene segments 5 and 7, which encoded nonstructural proteins 1 and 3, respectively, were of human origin. A strain with the same G and P segments as strain I321 has since emerged as a cause of diarrhea in children in Vellore, India.

**Other approaches to rotavirus vaccination**

Nonspecific (innate) and acquired virus-specific humoral and cellular immune responses are elicited by rotavirus infection or rotavirus vaccination. The immunological mechanism by which protection against rotavirus disease occurs after natural infection or after immunization is unknown. Rotavirus infection results in the production of both serum and intestinal antibodies and protects against severe diarrheal illness on subsequent infection. The difficulty in understanding the mechanism of protection has complicated the interpretation of various clinical trials, in which variable efficacy results were obtained. In brief, most studies on immune responses have indicated that the presence of fecal IgA or serum antibodies serves as a good surrogate marker for protection, although other effector mechanisms of the immune response are believed to be important. These mechanisms are undefined in humans at the present, although animal studies point to the importance of CD4 and CD8 T cells.

Although orally administered live virus vaccines represent the primary approach to rotavirus vaccine development, other approaches and routes of administration are being evaluated and tested in animal models. Work on virus-like particles, cold-adapted strains, inactivated strains, and DNA vaccines is ongoing. These approaches could have some advantages in the future if they could improve the variable immune response to oral vaccines, be
combined with other parenterally administered vaccines, or avoid the risk of intussusception.

Conclusion

Rotavirus is responsible for a substantial disease burden in infants, parents, and communities worldwide. Rotavirus vaccination provides a high degree of protection against severe rotavirus gastroenteritis and is the best available choice for the prevention of disease. The challenges of the rotavirus vaccination program in the developing world are many and ongoing: these challenges include the limited availability of vaccine, the necessity of “cold chain” delivery to the population, and the need for comprehensive diarrheal control by improving water quality, hygiene, and sanitation.

The evolving story of rotavirus vaccines is unique in that these new lifesaving vaccines have been initiated simultaneously in developed and developing countries. Continued surveillance is necessary if these vaccines are to contribute to reducing childhood mortality by one-third from 1990–2015, in accordance with the United Nations Millennium Development Goals. Ongoing epidemiologic surveillance will be used to determine whether observed regional differences in serotype data will help in the development of new vaccines; in the future, new vaccines will be needed if rotavirus becomes able to evade current vaccine immunity. Surveillance data should also be used to assess rotavirus immunization programs in developing and developed countries from the perspective of public health and policy and to elicit support from governments for preventive medicine programs.

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Rotavirus infection


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