

Rotavirus

Questions and Answers

What is rotavirus?

Rotavirus is the most common cause of severe diarrhea in young children worldwide. It can result in acute dehydration, vomiting, and fever and is responsible for more than 500,000 deaths each year, mostly in developing countries.¹

How is rotavirus spread?

Rotavirus is highly contagious and is typically transmitted by the fecal-oral route. Contaminated water, hands, or objects pass the virus. The virus can survive well on toys or other surfaces. It may also be spread through droplets in the air.

What are the symptoms of rotavirus infection?

After an incubation period of 18 to 36 hours, a child may develop diarrhea that lasts for 3 to 7 days. The illness often begins with explosive vomiting and may be accompanied by fever. With severe diarrhea and vomiting, a child can become dehydrated from acute loss of fluid and electrolytes, which can lead to shock, cardiac arrhythmia, and death.

Where does rotavirus infection occur?

Rotavirus is found in every country. Regardless of where they live, virtually all children become infected in the first 3 of life. Because of greater access to medical care, children in industrialized countries are at lower risk of death. However, in the United States alone, rotavirus causes an estimated 50,000 hospitalizations each year.²

Why haven't we heard of rotavirus before?

Rotavirus is a relatively "new" disease, only clinically discovered in 1973. Since then it has taken many years to get a sound estimate of the disease burden, and complete, accurate data from Asia and Africa are still needed.

What can be done to prevent rotavirus and diarrheal disease in general?

In the past 20 years, diarrhea mortality has decreased significantly due to improvements in sanitation and nutrition and the availability of oral rehydration solution (ORS).

Mortality due to rotavirus remains a stubborn exception. Improvements in water, sanitation, and hygiene do not significantly reduce its spread. Vaccination is the only way to prevent severe episodes of rotavirus infection, and rotavirus vaccines will be an important new addition to a portfolio of interventions to prevent and manage diarrheal disease. This portfolio should include rotavirus vaccines, as well as ORS, zinc, breastfeeding, and improvements in nutrition, hygiene, and water quality.

Why does cleaning the water reduce diarrhea but not rotavirus?

Rotavirus is so contagious and resilient that providing safe water and promoting good hygiene do not significantly impact incidence. Incidence is nearly the same around the world, regardless of water quality and hygiene practices.

What is the treatment for rotavirus?

ORS is a common intervention for managing diarrhea, and it can be effective in treating mild rotavirus infections. In severe cases when rapid dehydration occurs, however, ORS is not sufficient, and urgent medical care is required. Tragically, such care is out of reach for many children in developing countries. Due to the persistent vomiting sometimes associated with rotavirus infection, parents or caregivers will often stop administering ORS because the child can't keep it down, further limiting its effect.³

New research indicates that zinc treatment can significantly reduce the burden of dehydration caused by diarrheal disease,⁴ but no studies have specifically evaluated its effect on rotavirus infections. Additionally, as with ORS, the profuse vomiting associated with rotavirus may discourage caregivers from administering zinc.

Is there a vaccine against rotavirus?

Two live, oral, attenuated vaccines against rotavirus infection (Rotarix®, manufactured by GSK; and RotaTeq®, manufactured by Merck) were licensed by WHO-recognized regulatory authorities in 2006. Clinical trials in Europe, Latin America, and the US demonstrated that they are safe and highly efficacious at preventing rotavirus-associated severe gastroenteritis.⁵

A number of countries, including some developing countries, have licensed these vaccines. Rotarix® attained WHO prequalification status in early 2007, making it acceptable for procurement by United Nations agencies in countries where safety and efficacy data are available. RotaTeq® is currently under review.

Both vaccines are orally administered. The Rotarix® series is given in 2 doses. The series should be initiated at 6 to 14 weeks of age. The second dose should be given at least 4 weeks later but before the infant reaches 24 weeks of age. RotaTeq® is given in 3 doses, and the first dose should be given at 6 to 12 weeks of age, with 2 subsequent doses administered at 4- to 10-week intervals. The complete series of RotaTeq® should be administered by 32 weeks of age.

So far, these vaccines have been primarily studied in middle- and high-income countries and, historically, oral vaccines have been shown to perform differently in different regions of the world. The global health community recognizes the need to carry out additional studies of the safety and efficacy of these vaccines in developing countries of Africa and Asia, where disease burden is very high.⁶ PATH is collaborating with vaccine manufacturers to design and execute such trials.

Sufficient evidence of a vaccine's safety, efficacy, and affordability is necessary for national governments to make informed decisions on the introduction of rotavirus vaccines in the public sector. Through its support of clinical trials and dissemination of key materials, PATH is generating and distributing this critical information.

How much will a vaccine cost?

To ensure broad use of a rotavirus vaccine in developing countries, cost is an important issue. Presently, rotavirus vaccines are offered in the private sectors of several middle-income countries for as much as \$50 per dose. Public sector pricing is often lower, but still well out of acceptable range for the poorest countries.

To ensure rotavirus vaccines are accessible in the developing world, the GAVI Alliance agreed to subsidize funding for countries with a gross national income (GNI) less than US\$1,000. Based on clinical trial data, countries in Latin America and Europe are currently eligible for this support. GAVI will review eligibility of countries in Africa and Asia upon the completion of the clinical trials currently underway.

Efforts are underway to develop sustainable financing options for greater access in the poorest countries. As more manufacturers develop rotavirus vaccines and introduce them to the market, the price will be further reduced. To ensure a sufficient supply and competitive pricing, PATH is working

with manufacturers in China and India to develop new rotavirus vaccines.

Wasn't there a vaccine in the past?

In August 1998, a rotavirus vaccine, Rotashield®, was licensed in the United States, and approximately 1 million children were vaccinated within 9 months. About 100 (0.01%) of these children developed a type of bowel obstruction called intussusception.

Intussusception occurs for unknown reasons in about 1 child per 10,000, most often in infants 4 to 10 months of age, regardless of whether or not they have received a vaccine. Because of the uncertainty about the relationship between Rotashield® and intussusception, the manufacturer voluntarily pulled the product off the market.

The current rotavirus vaccines were tested extensively to determine any risk for adverse events, including intussusception. Researchers found that the risk of intussusception was similar among children who received the vaccine and those who received a placebo, indicating that the vaccines are safe for use.⁵

What does the PATH Rotavirus Vaccine Program do?

The PATH Rotavirus Vaccine Program aims to dramatically reduce the typical 10- to 15-year timeline between introduction of new vaccines in wealthy countries and their availability in the developing world. Activities include measuring disease burden; determining vaccine efficacy and safety in developing countries; communicating the value of rotavirus vaccines; and generating information on the health economics of rotavirus vaccination.

The program is a partnership with WHO and the US Centers for Disease Control and Prevention, established in 2003 with funding from the GAVI Alliance.

**For more information about rotavirus visit
www.rotavirusvaccine.org or email rvinfos@path.org**

¹ Parashar U, Gibson C, Bresee J, Glass R. Rotavirus and severe childhood diarrhea. *Emerging Infectious Diseases*. 2006;12(2). Available online: <http://www.cdc.gov/ncidod/EID/vol12no02/05-0006.htm>.

² Parashar U, Holman R, Clarke M, Bresee J, Glass R. Hospitalizations associated with rotavirus diarrhea in the United States, 1993 through 1995: Surveillance based on the new ICD-9-CM rotavirus-specific diagnostic code. *Journal of Infectious Diseases*. 1998;177(1). Available online: http://www.journals.uchicago.edu/JID/journal/issues/v177n1/ja07_13/ja07_13.web.pdf.

³ Ahmed F. Children at risk of developing dehydration from diarrhea: A case-control study. *Journal of Tropical Pediatrics*. 2002;48: 259–263.

⁴ Zinc Investigators' Collaborative Group: Bhutta Z, Black R, Brown K, et al. Prevention of diarrhea and pneumonia by zinc supplementation in children in developing countries: Pooled analysis of randomized controlled trials. *Journal of Pediatrics*. 1999;135:689–697.

⁵ Ruiz-Palacios G, Pérez-Schael I, Velázquez F, et al. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *New England Journal of Medicine*. 2006;354(1):11–22. Available online: <http://content.nejm.org/cgi/content/full/354/1/11>.

Vesikari, T, Matson D, Dennehy P, et al. Safety and efficacy of a pentavalent human-bovine (wc3) reassortant rotavirus vaccine. *New England Journal of Medicine*. 2006;354(1):23–33. Available online: <http://content.nejm.org/cgi/content/full/354/1/23>.

⁶ World Health Organization. Rotavirus vaccines. *Weekly Epidemiological Record*. 2007;82(32). Available online: <http://www.who.int/wer/2007/wer8232/en/index.html>.