

COMMON VIRUS AND SENSELESS KILLER: A Briefing Paper on Rotavirus



DIARRHEA KILLS. MOTHERS IN THE WORLD'S POOREST COUNTRIES KNOW THIS ALL TOO WELL. It's a fact few people in wealthier nations realize. Rotavirus—the most common and lethal form of diarrhea—is one of the most deadly diseases children in the developing world face. Each year rotavirus kills more than 500,000 children and hospitalizes millions.

Preventing rotavirus through vaccination is the best way to protect children. In June, the World Health Organization's (WHO) Strategic Advisory Group of Experts (SAGE) on Immunization recommended rotavirus vaccines for global use, stating that rotavirus vaccination should be included in every country's national immunization program. The WHO recommendation was based on clinical trial data demonstrating vaccine efficacy in impoverished, high-mortality settings. It builds on a 2006 recommendation incorporating rotavirus vaccines into the national immunization programs of countries in North America, Latin America, and Europe.¹

Informed by the WHO's recent global recommendation, the GAVI Alliance has expanded financial support for rotavirus vaccine introduction to developing countries in Africa and Asia, and is now accepting applications from eligible countries.

Rotavirus vaccines stand to make the greatest impact in high-burden regions in Africa and Asia, where more than 85 percent of rotavirus deaths occur.² Limited access to urgent medical care in developing world settings means that prevention through rotavirus vaccination provides the best hope for survival.

| WHAT IS ROTAVIRUS? |

Whether you have heard of rotavirus before or not, it may surprise you to know that you've probably had it.

Nearly every child in the world will have at least one rotavirus infection before age 3.

Rotavirus is resilient. It is found everywhere. Incidence rates are nearly the same worldwide, regardless of water quality, hygiene, and socioeconomic conditions. Rotavirus is transmitted through the fecal-oral route and often spreads through contact with contaminated water, food, or objects such as a child's toy or bottle. It is highly contagious.

THE MOST COMMON CAUSE OF DIARRHEA



40% Hospitalizations from rotavirus

60% Hospitalizations from other causes of diarrheal disease

SOURCE: WHO. *Weekly Epidemiological Record*. 2008; 83(47):423.

Children under the age of two are most at risk of severe rotavirus infection. Symptoms include profuse diarrhea, vomiting, and fever that can lead to severe dehydration. Urgent medical care can help rehydrate children with serious infections. However, in places where access to urgent care is limited, the acute dehydration, left untreated, can lead to shock, cardiac arrhythmia, and death.

In the United States and other industrialized nations, where medical care is easily accessible and over-the-counter rehydration products are readily available, a child infected with rotavirus will almost certainly recover, even in a severe case. But in developing nations, where access to urgent care is often limited, diarrhea caused by rotavirus can be a death sentence.

Each year rotavirus is responsible for:

- 114 million illnesses
- 24 million clinic visits
- 2.4 million hospitalizations

SOURCE: Vaccine, 2008; 26:3192-3196.

In fact, while around 70 deaths each year are attributed to rotavirus in industrialized nations, nearly 1,400 children die from rotavirus each day in the developing world. While many factors contribute to this disproportionate burden, from malnutrition to limited access to medical care, one fact is certain: rotavirus is one of the most deadly diseases children in the developing world face. It is also one of the most preventable.

| THE PROMISE OF NEW ROTAVIRUS VACCINES |

If rotavirus vaccines were used in the world's poorest countries, they would have the potential to prevent the deaths of approximately 225,000 children each year and more than 2.5 million children between 2007 and 2025.³ Vaccines are particularly critical in areas where appropriate medical care for severe diarrhea and dehydration is limited and access to safe water is inadequate.

In 2006, two orally administered rotavirus vaccines—Rotarix™, manufactured by GlaxoSmithKline (GSK), and RotaTeq®, manufactured by Merck and Co., Inc—were demonstrated to be safe and effective in large-scale clinical trials in Europe, Latin America, and North America. With a 90 to 100 percent efficacy

rate against severe rotavirus, the vaccines were licensed for use in those regions.⁴ They are currently part of the routine immunization programs in several countries throughout the world. Manufacturers in Brazil, China, and India are also working to develop promising new rotavirus vaccine candidates.

In the United States, rotavirus vaccination has led to dramatic drops in severe rotavirus-related hospitalizations and has reduced emergency room visits by as much as 80 percent. The vaccines also may have prevented illness in unvaccinated children by limiting the number of circulating infections.⁵

“Vaccines against rotavirus remain the most effective way to prevent this deadly disease,” said Dr. John Wecker, director of PATH’s Rotavirus Vaccine Program. “Making rotavirus vaccines available to the children in poor countries who face the greatest risk of dying must be a priority.”

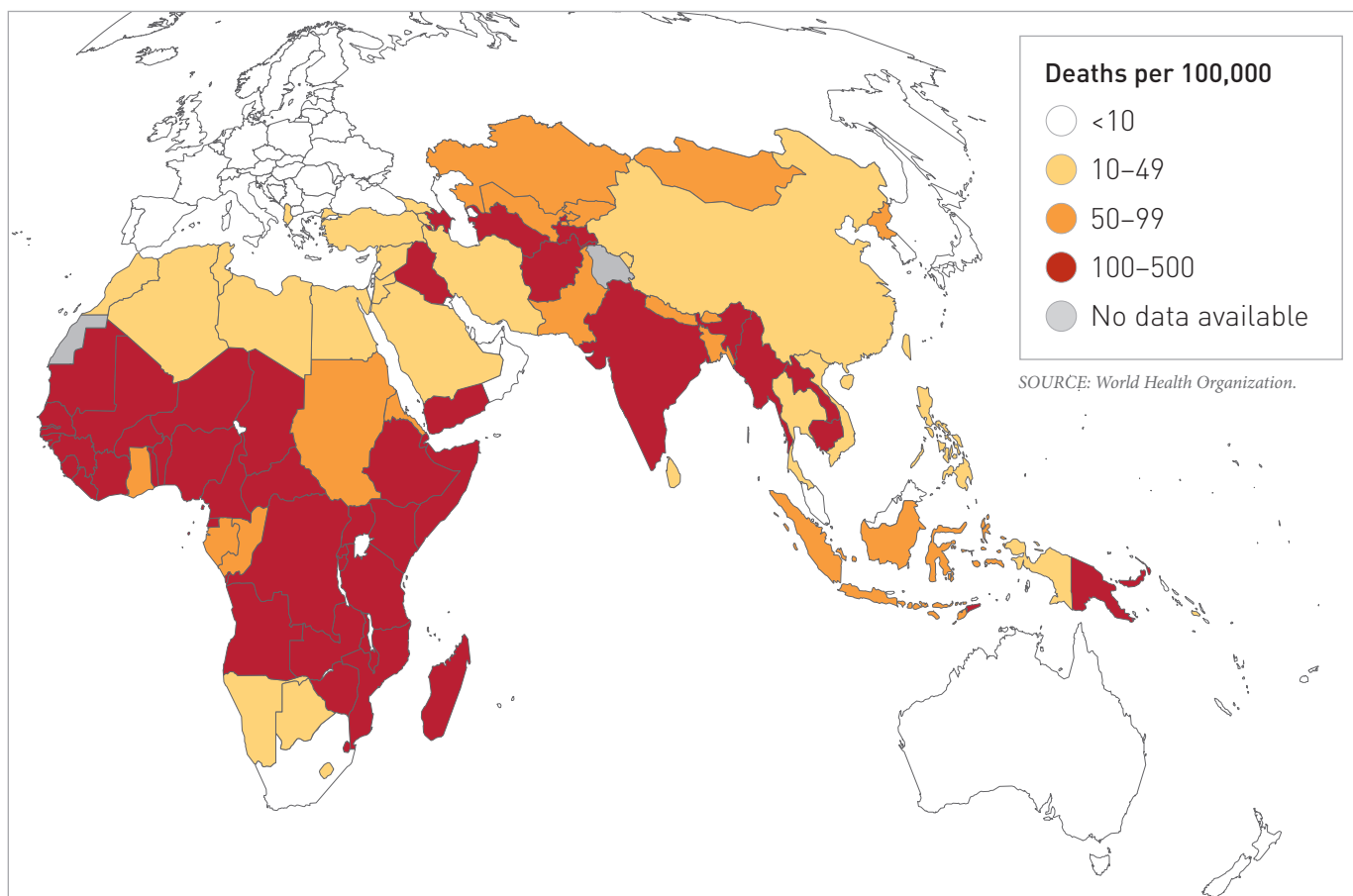
| REGIONS IN NEED |

Rotavirus burden is highest in Africa and Asia where vaccines preventing rotavirus are not yet widely available.

New data from recent clinical trials evaluating safety and efficacy in real-world, high-mortality settings in Africa demonstrated that rotavirus vaccines significantly reduced severe diarrhea episodes due to rotavirus. These results led to the WHO recommendation for global use of rotavirus vaccines. Data from further testing in high-mortality populations in Asia will be available later this year.

The African and Asian clinical trials were funded by the GAVI Alliance, and conducted through a

ROTAVIRUS BURDEN IN AFRICA AND ASIA



AFRICA:⁶

- 25 to 40 percent of African children hospitalized with acute diarrheal illness are infected with rotavirus.
- By the time children in Africa have reached 18 months of age, 83 percent will have contracted rotavirus.
- In South Africa, more than 75 percent of children will contract rotavirus before their first birthday.

ASIA:⁷

- During its first years of monitoring the impact of rotavirus, the Asian Rotavirus Surveillance Network found significantly higher incidence of rotavirus than anticipated.
- Nearly half of all children hospitalized in Asia for diarrhea had rotavirus.
- Researchers project that if every child in Asia were vaccinated against rotavirus, it would prevent an estimated 109,000 to 171,000 deaths, 1.4 million to 1.9 million hospitalizations, and 7.7 million to 13.5 million outpatient visits over five years. Further, universal immunization against rotavirus in Asia could save US\$191 million in direct medical costs (depending on the vaccine price and country's income level).

partnership between PATH, WHO, and vaccine manufacturers. The studies were unprecedented in their commitment to test the vaccines in low-resource settings. The clinical trials were also significant because the effectiveness of oral vaccines can vary in different populations, and it was critical to demonstrate vaccine safety and efficacy in conditions like those found in developing African and Asian countries.¹

| PARTNERING TO ACCELERATE ACCESS |

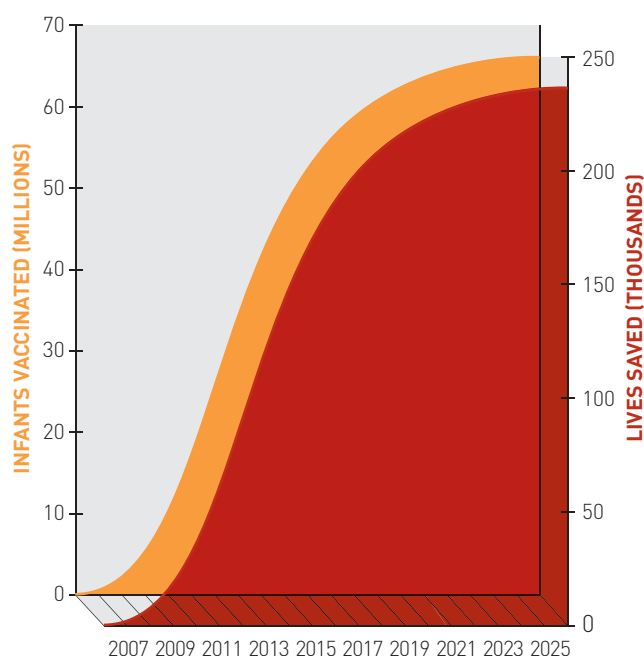
Historically, it can be as long as 10 to 15 years from the time a vaccine is licensed for use in industrialized nations to the time it reaches developing nations.⁸ To address this access gap, PATH, the US Centers for Disease Control and Prevention, and the WHO joined forces to establish the Rotavirus Vaccine Program in 2003 with support from the GAVI Alliance. The partnership set out to accelerate the availability of rotavirus vaccines in the developing world by conducting clinical trials, gathering disease burden data through routine surveillance, forecasting demand, conducting advocacy, and disseminating a solid evidence base to inform policymakers considering rotavirus vaccine introduction.

In 2004, the Rotavirus Vaccine Program took the unprecedented step to partner with manufacturers GSK and Merck to conduct rigorous clinical trials in the developing world. Efforts to evaluate and disseminate results from these trials, along with continuing vaccine effectiveness studies in Bangladesh, El Salvador, and Nicaragua, continue under the auspices of the Rotavirus Vaccine Trials Partnership. The partnership will play a key role in evaluating the safety and impact of new rotavirus vaccines for children in the developing world.

| LOOKING AHEAD |

Because cost can be a major challenge that developing countries face when introducing new vaccines, many of the countries that stand to benefit from rotavirus vaccines will likely rely on support from the GAVI Alliance. The WHO global recommendation on

POTENTIAL LIVES SAVED BY ROTAVIRUS VACCINATION



SOURCE: PATH/D. Atherly.

rotavirus vaccination provides the basis for low-income countries to apply to the GAVI Alliance for vaccine introduction financial support. The GAVI Alliance is committed to making rotavirus vaccines available as quickly as possible by reducing the traditional 10 to 15 year lag time between when vaccines are first introduced in industrialized nations and when they are finally introduced in low-income nations. GAVI Alliance support for rotavirus vaccine introduction was first made available to eligible countries in Latin America and Eastern Europe in 2006 and, today, the global health community stands ready to accelerate access to these lifesaving vaccines in low-income, high-burden countries in Africa and Asia.¹

| COORDINATING INTERVENTIONS |

While vaccines hold great potential in the fight against rotavirus, a coordinated approach to combat all diarrheal diseases will be necessary to halt this global killer. In areas where appropriate medical care for severe diarrhea and dehydration is limited and access to safe water is inadequate, prevention through vaccination is a critical

CASE STUDY: MAKING A DIFFERENCE IN NICARAGUA

When an outbreak of rotavirus nearly crippled Nicaragua's health system six years ago, several Ministry of Health departments formed a dedicated alliance to reduce the burden of diarrheal disease, including a unique team of experts on hygiene, epidemiology, nutrition, and child health. In less than two years, a team of representatives from the ministry—along with NicaSalud (a local coalition of nongovernmental organizations), PATH, UNICEF, and others—brought public-sector clinics on board and trained health care workers to provide zinc and oral rehydration therapy throughout the country. A parallel demonstration project by the Ministry of Health and Merck, which donated more than one million doses of rotavirus vaccine, offered the opportunity to integrate rotavirus vaccination. The introduction of the rotavirus vaccine in 2006 marked the first time in history that a developing country took up a vaccine in the same year as its adoption in the United States. More than 85 percent of vaccine-eligible children were reached in the project's first year. Citing cross-disciplinary cooperation as fundamental to the program's achievements, the ministry credited the alliance with building awareness of zinc treatment, oral rehydration therapy, and rotavirus vaccines. The approach is well under way and informing similar strategies throughout the region and the world.

component in the strategy to reduce the incidence and severity of diarrhea. While rotavirus vaccines do not protect against all causes of diarrheal disease, they do help prevent and reduce the severity of one of its harshest causes. Enhancing diarrheal disease control through a combined prevention and treatment strategy that includes new tools such as rotavirus vaccines, improved oral rehydration solution, and zinc treatment, as well as existing interventions like exclusive breastfeeding and improved hygiene, sanitation, and nutrition, can rapidly and significantly reduce child mortality in areas where diarrheal disease is a critical health issue.

I THIS IS THE TIME TO STOP ROTAVIRUS I

The broader introduction of rotavirus vaccines provides an opportunity to educate policymakers, health workers, and the global community about new and proven mechanisms to control diarrheal disease. With increased awareness about the virus and the use of available vaccines, we can significantly reduce one of the biggest threats to children in the developing world.

CONTROLLING DIARRHEAL DISEASE

Dramatic gains have been made in diarrheal disease control:

- **Existing interventions we know work** include exclusive breastfeeding; oral rehydration therapy; and improved hygiene, sanitation, and nutrition.
- **New tools that are available now** include rotavirus vaccines, low-osmolarity oral rehydration solution, and zinc treatment.
- **More tools that are in the pipeline** include new vaccine candidates, safe water technologies, and rapid diagnostics.

But the momentum has slowed in the poorest parts of the world because of limited access to and awareness of simple life-saving interventions.

What's needed?

- **A coordinated strategy that combines prevention and treatment** can significantly reduce diarrheal disease and mortality.
- **Political will and dedicated resources** to implement this approach can save children's lives.

FOR MORE INFORMATION ABOUT ROTAVIRUS PLEASE VISIT WWW.ROTAVIRUSVACCINE.ORG.

(END NOTES)

- 1 Global use of rotavirus vaccines recommended: vaccines can protect millions of children from diarrhoeal disease [press release]. Geneva/Seattle: WHO/PATH; June 5, 2009. Available at: http://www.who.int/mediacentre/news/releases/2009/rotavirus_vaccines_20090605/en/index.html. Accessed July 9, 2009.
- 2 WHO. Global networks for surveillance of rotavirus gastroenteritis, 2001–2008. *Weekly Epidemiological Record*. 2008;83(47):421–428.
- 3 Atherly D, Dreifelbis R, Parashar U, et al. Rotavirus vaccination: cost and impact on child mortality in the developing world. *Journal of Infectious Diseases*. In press.
- 4 WHO. Rotavirus vaccines. *Weekly Epidemiological Record*. 2007;82(32):285–295.
- 5 US CDC. Delayed onset and diminished magnitude of rotavirus activity—United States, November 2007–May 2008. *Morbidity and Mortality Weekly Report*. 2008;57(25):697–700.
- 6 Cunliffe N, Kilgore PE, Bresee JE, et al. Epidemiology of rotavirus diarrhea in Africa: a review to assess the need for rotavirus immunization. *Bulletin of the World Health Organization*. 1998;76(5):525–537.
- 7 Nelson EAS, Bresee JS, Parashar UD, Widdowson M-A, Glass RI. Rotavirus Epidemiology: The Asian Rotavirus Surveillance Network. *Vaccine*. 2008;26:3192–3196.
- 8 McKinsey & Company. *Accelerated Development and Introduction of Priority New Vaccines: The Case of Pneumococcal and Rotavirus Vaccines*. Geneva: GAVI Alliance; 2002.

(SOURCES AND RESOURCES)

WEBSITES

Controlling Diarrheal Disease: <http://www.path.org/diarrheal-disease.php>

PATH's Vaccine Resource Library: <http://www.path.org/vaccineresources>

Resources for Diarrheal Disease Control: <http://www.eddcontrol.org>

Rotavirus Vaccine Program: <http://www.rotavirusvaccine.org>

Rotavirus Update and RotaFlash: <http://www.path.org/publications/details.php?i=1498>

FACT SHEETS

Advancing New Rotavirus Vaccines: http://www.path.org/files/VAC_rotavirus_fs.pdf

An Integrated Approach to Confronting Diarrheal Disease: http://www.path.org/files/VAC_dd_approach_fs.pdf

Rotavirus Questions and Answers: http://www.path.org/vaccineresources/files/RotaQA_Aug08.pdf

Rotavirus Vaccines: http://www.path.org/files/IMM_EDD-rotavaccines_fs.pdf

KEY RESOURCES

Atherly D, Dreifelbis R, Parashar U, et al. Rotavirus vaccination: cost and impact on child mortality in the developing world. *Journal of Infectious Diseases*. In press.

Cunliffe N, Kilgore PE, Bresee JE, et al. Epidemiology of rotavirus diarrhea in Africa: a review to assess the need for rotavirus immunization. *Bulletin of the World Health Organization*. 1998;76(5):525–537.

McKinsey & Company. *Accelerated Development and Introduction of Priority New Vaccines: The Case of Pneumococcal and Rotavirus Vaccines*. Geneva: GAVI Alliance; 2002.

Nelson EAS, Bresee JS, Parashar UD, Widdowson M-A, Glass RI. Rotavirus Epidemiology: The Asian Rotavirus Surveillance Network. *Vaccine*. 2008;26:3192–3196.

US CDC. Delayed onset and diminished magnitude of rotavirus activity—United States, November 2007–May 2008. *Morbidity and Mortality Weekly Report*. 2008;57(25):697–700.

WHO. Evaluating clinical trial data and guiding future research for rotavirus vaccines. *Weekly Epidemiological Record*. 2008;83(43):385–388.

WHO. Global networks for surveillance of rotavirus gastroenteritis, 2001–2008. *Weekly Epidemiological Record*. 2008; 83(47):421–428.

WHO. Meeting of the immunization Strategic Advisory Group of Experts, April 2009 – conclusions and recommendations. *Weekly Epidemiological Record*. 2009;84(23):213–236.

WHO. Rotavirus vaccines. *Weekly Epidemiological Record*. 2007;82(32):285–295.



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