Rotavirus and Rotavirus Vaccines

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Professor of Medicine and Pediatrics
Director, Center for Vaccine Development

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Rotavirus vaccines: Their value in different settings

- Review rotavirus and rotavirus vaccines
- How do we design optimal studies?
- How do we understand and improve real world impact?
Rotavirus: The Beginning

Table 1  Etiological gastroenteritis in children admitted to Royal Children’s Hospital, Melbourne

<table>
<thead>
<tr>
<th></th>
<th>1972</th>
<th>1974</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total admissions</td>
<td>539</td>
<td>378</td>
</tr>
<tr>
<td>Salmonella sp.</td>
<td>39 (7.2%)</td>
<td>40 (10%)</td>
</tr>
<tr>
<td>Shigella sp.</td>
<td>2 (0.4%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Pathogenic E. coli</td>
<td>23 (4.3%)</td>
<td>7 (2%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>475 (88%)</td>
<td>102 (29%)</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>not tested</td>
<td>197 (52%)</td>
</tr>
<tr>
<td>Enteric adenovirus</td>
<td>not tested</td>
<td>27 (7%)</td>
</tr>
</tbody>
</table>
Histopathology of piglet intestine infected with rotavirus shows extensive damage to gut

Normal piglet villi

Rotavirus infected showing denuded micro-villi

Villous atrophy = malabsorptive diarrhoea

Rotavirus in humans

- Ubiquitous virus infection globally
- Causes acute dehydrating diarrhea
- Peak incidence of clinical disease is among children 6 to 18 months
- All children will be infected by 2 to 3 years of age
- Improvements in water and sanitation are not sufficient to prevent infection
- First infections are generally symptomatic and re-infections are common
- Subsequent infections are typically less severe or asymptomatic
Rotavirus is the most common cause of severe, dehydrating diarrhea among children worldwide.

**Hospital-based gastroenteritis cases positive for rotavirus**

- Kenya (rural west): 20%
- Ethiopia: 21%
- Uganda (Kampala): 33%
- Sudan: 36%
- Mauritius: 42%
- Togo: 48%
- Zimbabwe: 49%
- Ghana (south): 49%
- Nigeria (southeast): 56%

African total: 40.7%

Global Enteric Multicenter Study (GEMS): Attributable incidence of pathogen-specific moderate to severe diarrhea

Rotavirus is 1 of 4 pathogens causing the majority of moderate-to-severe diarrhea in children under age 5

Rotavirus is the #1 cause of diarrhea in children under age 2

Classification scheme defining the rotavirus genome constellation

Defines P genotype (n=37)
Cell attachment/penetration
Neutralizing antigen

Defines G genotype (n=27)
Structural glycoprotein
Neutralizing antigen

Most human rotaviruses are of
VP4: P[4] or P[8] and
VP7: G1, G2, G3, G4, G9 or G12
Example: G1P1A[8] (most common)
Jennerian then “modified Jennerian” approach taken for developing rotavirus vaccines

• Animal strains are naturally attenuated for humans
• Belief that homotypic protection was essential
• First designed to include the VP7 (G) gene coding the outer capsid antigens of human rotaviruses
• First licensed vaccine was a rhesus-human strain, RotaShield (in 1999 it was withdrawn because of an adverse event following immunization)
• Later bovine-human reassortants were developed and licensed, as RotaTeq (Merck & Co., Inc.)

B Buckland, Nat Med: doi:10.1038/nm1218
Intussusception: an unexpected safety signal

- Intussusception is a telescoping of a portion of the intestine (usually the distal small intestine) into an adjoining segment
- It is most common in children less than 24 months of age
- Untreated, it can lead to rupture of the bowel, sepsis, shock and death
Previous Rotavirus Vaccine -- Rotashield

- Linked with intussusception
  - 1 case in 10,000 vaccinated infants

Withdrawal of Rotavirus Vaccine Recommendation

In July 1999, CDC recommended that health-care providers and parents postpone use of the rhesus rotavirus vaccine-tetravalent (RRV-TV) (Rotashield®, Wyeth Laboratories, Inc., Marietta, Pennsylvania), for infants, at least until November 1999. This action was based on reports to the Vaccine Adverse Event Reporting System of intussusception (a type of bowel obstruction that occurs when the bowel folds in on itself) among 15 infants who received rotavirus vaccine. Also at that time, the manufacturer, in consultation with the Food and Drug Administration, voluntarily ceased further distribution of the vaccine.
Safety and efficacy trial results published in 2006 for next generation live-attenuated vaccines (Merck and GSK)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of a Pentavalent Human–Bovine (WC3) Reassortant Rotavirus Vaccine


The NEW ENGLAND JOURNAL of MEDICINE

Safety and Efficacy of an Attenuated Vaccine against Severe Rotavirus Gastroenteritis

Guillermo M. Ruiz-Palacios, M.D., Irene Pérez-Schael, M.Sc., F. Raúl Velázquez, M.D., Hector Abate, M.D., Thomas Breuer, M.D., SueAnn Costa Clemens, M.D., Brigitte Cheuvart, Ph.D., Felix Espinoza, M.D., Paul Gillard, M.D., Bruce L. Innis, M.D., Yolanda Cervantes, M.D., Alexandre C. Linhares, M.D., Pio López, M.D., Mercedes Macías-Parra, M.D., Eduardo Ortega-Barría, M.D., Vestia Richardson, M.D., Doris Maribel Rivera-Medina, M.D., Luis Rivera, M.D., Belén Salinas, M.D., Noris Pavia-Ruz, M.D., Jorge Salmerón, M.D., Ricardo Röttgermann, M.D., Juan Carlos Tinoco, M.D., Pilar Rubio, M.D., Ernesto Núñez, M.D., M. Lourdes Guerrero, M.D., Juan Pablo Yarzábal, M.D., Silvia Damoso, M.Sc., Nadia Tornieporth, M.D., Xavier Sáez-Llorens, M.D., Rodrigo F. Vergara, M.D., Timo Vesikari, M.D., Alain Bouckenhooge, M.D., Ralf Clemens, M.D., Ph.D., Béatrice De Vo, M.D., and Miguel O’Ryan, M.D., for the Human Rotavirus Vaccine Study Group*
Two rotavirus vaccines subsequently licensed and recommended in the U.S., Europe, Latin America

<table>
<thead>
<tr>
<th></th>
<th>Rotarix® (GSK Bio)</th>
<th>RotaTeq® (Merck &amp; Co)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Origin</strong></td>
<td>Human monovalent</td>
<td>Bovine pentavalent</td>
</tr>
<tr>
<td><strong>Vaccine course</strong></td>
<td>2 doses - oral</td>
<td>3 doses - oral</td>
</tr>
<tr>
<td><strong>Pivotal Phase III trial</strong></td>
<td>n=63,225 (20,169 for efficacy) Latin America and Finland</td>
<td>n=70,301 (5,673 for efficacy) Latin America, US and Finland</td>
</tr>
<tr>
<td><strong>Efficacy vs rotavirus GE</strong></td>
<td>85% - 100% vs severe rota gastroenteritis</td>
<td>98% vs severe rota gastroenteritis</td>
</tr>
<tr>
<td><strong>Intussusception risk</strong></td>
<td>No association observed in clinical trials</td>
<td>No association observed in clinical trials</td>
</tr>
</tbody>
</table>

United States: Reduction in gastroenteritis hospitalizations among children who received vaccine, also in those too young or too old to be vaccinated

Curns AT et al. JID 2010; 201: 1617.
Reduction in diarrheal deaths among children < 5 years after introduction of rotavirus vaccines in Mexico

**Figure 1.** Number of Diarrhea-Related Deaths among Children 59 Months of Age or Younger from July 2002 through December 2010 in Mexico, According to Age Group.

Clinical studies required in low-resource countries of Africa and Asia

- WHO advisory group recommended “inclusion of rotavirus vaccination into the national immunization programmes of regions and countries where vaccine efficacy data suggest a significant public health impact…”
- Because of concerns that “live oral vaccines may not be fully effective in protecting the poorest children in developing countries,” SAGE noted “the need for urgently generating efficacy data in Asia and Africa, where the disease burden is very high.”

Situation in 2006: No recommendation for rotavirus vaccine in the countries in Asia and Africa with the greatest rotavirus disease burden.
Goal: Design and execute clinical trials that will inform policy (WHO) and financing (Gavi) decisions

• Which vaccine?
• Where?
• Who?
• Efficacy or effectiveness?
• Outcome measure?
• Logistical considerations.
3 large RCT’s, involving over 12,000 children in 7 countries

- Bangladesh
- Vietnam
- Kenya
- South Africa
- Malawi
- Ghana
- Mali

GSK-RVP partnership
Merck-RVP partnership
Categorize settings/sites that might be used as prototypes for countries where trials are not conducted.

**Figure 2.** Ranking of the site countries for rotavirus vaccine trials against various parameters. Data are derived from [15]. GDP, gross domestic product; HIV, human immunodeficiency virus.
Categorize settings/sites that might be used as prototypes for countries where trials are not conducted.

<table>
<thead>
<tr>
<th>WHO mortality strata</th>
<th>Mortality rate among children aged &lt;5 years</th>
<th>Mortality rate among men</th>
<th>Vaccine trial sites in Africa</th>
<th>Vaccine trial sites in Asia</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Very low</td>
<td>Very low</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>B</td>
<td>Low</td>
<td>Low</td>
<td>…</td>
<td>Vietnam</td>
</tr>
<tr>
<td>C</td>
<td>Low</td>
<td>High</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>D</td>
<td>High</td>
<td>High</td>
<td>Ghana, Mali</td>
<td>Bangladesh</td>
</tr>
<tr>
<td>E</td>
<td>High</td>
<td>Very high</td>
<td>South Africa, Malawi, Kenya</td>
<td>…</td>
</tr>
</tbody>
</table>

**NOTE.** Data are derived from [15].
Common elements of study design

- Routine EPI vaccines, including oral polio vaccine (OPV), co-administered
- HIV-positive infants not excluded
- Breastfeeding not restricted
- Focused on severe disease
Rotavirus Vaccines for Infants in Developing Countries in Africa and Asia: Considerations from a World Health Organization–Sponsored Consultation

A. Duncan Steele,¹² Manish Patel,³ Umesh D. Parashar,³ John C. Victor,² Teresa Aguado,¹ and Kathleen M. Neuzil²

¹Initiative for Vaccine Research, World Health Organization, Geneva, Switzerland; ²Rotavirus Vaccine Programme, PATH, Seattle, Washington; and ³Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia
Efficacy of pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in infants in developing countries in sub-Saharan Africa: a randomised, double-blind, placebo-controlled trial

George F Amah, Samba O Sew, Robert F Breiman, Michael J Dallas, Milagritos D Tapia, Daniel R Fekin, Fred N Binka, A Duncan Steele, Kayla F Laserson, Nano A Amah, Myron M Levine, Kristen Lewis, Michele L Cois, Margaret Atchoh-Poku, Joel Owendo, Stephen B Rivers, John C Victor, Geoffrey Nyombane, Abraham Hodges, Florian Schödel, Max Ciarlet, Kathleen M Neuzil

Efficacy of pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in infants in developing countries in Asia: a randomised, double-blind, placebo-controlled trial

### Efficacy against severe rotavirus gastroenteritis in the first year of life

<table>
<thead>
<tr>
<th>Region</th>
<th>Vaccine</th>
<th>Countries</th>
<th>VE</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>Rotarix™</td>
<td>Malawi, South Africa</td>
<td>61.7</td>
<td>44.0, 73.2</td>
</tr>
<tr>
<td>Africa</td>
<td>RotaTeq®</td>
<td>Ghana, Kenya, Mali</td>
<td>64.2</td>
<td>40.2, 79.4</td>
</tr>
<tr>
<td>Asia</td>
<td>RotaTeq®</td>
<td>Bangladesh, Vietnam</td>
<td>51.0</td>
<td>12.8, 73.3</td>
</tr>
</tbody>
</table>

Madhi SA, Cunliffe NA, Steele AD et al. NEJM 2010; 362: 346-357.
Efficacy against severe rotavirus gastroenteritis in the first year of life

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</tr>
<tr>
<td>Asia*</td>
<td>Rotarix™</td>
<td>Bangladesh</td>
<td>48.0</td>
<td>27.0, 63.0</td>
</tr>
</tbody>
</table>

Madhi SA, Cunliffe NA, Steele AD et al. NEJM 2010; 362: 346-357.
*Unpublished. Cluster-randomized design
Efficacy and severe rotavirus GE episodes prevented per 100 children

<table>
<thead>
<tr>
<th>Country</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>61.2%</td>
</tr>
<tr>
<td></td>
<td>(44.0 – 73.2)</td>
</tr>
<tr>
<td>South Africa</td>
<td>76.9%</td>
</tr>
<tr>
<td></td>
<td>(56.0 – 88.5)</td>
</tr>
<tr>
<td>Malawi</td>
<td>49.5%</td>
</tr>
<tr>
<td></td>
<td>(19.2 – 68.3)</td>
</tr>
</tbody>
</table>

3 episodes prevented

2.5 episodes prevented

3.9 episodes prevented
Efficacy of pentavalent rotavirus vaccine in a high HIV prevalence population in Kenya

Daniel R. Feikin\textsuperscript{a,*,} Kayla F. Laserson\textsuperscript{a}, Joel Ojwando\textsuperscript{a}, Geoffrey Nyambane\textsuperscript{a}, Victor Ssem pijja\textsuperscript{a}, Allan Audi\textsuperscript{a}, Daveline Nyakundi\textsuperscript{a}, Janet Oyieko\textsuperscript{a}, Michael J. Dallas\textsuperscript{b}, Max Ciarlet\textsuperscript{b,1}, Kathleen M. Neuzil\textsuperscript{c}, Robert F. Breiman\textsuperscript{a}

\textsuperscript{a} Kenya Medical Research Institute/Centers for Disease Control and Prevention, Research and Public Health Collaboration, Kenya
\textsuperscript{b} Merck Research Laboratories, North Wales, PA, USA
\textsuperscript{c} PATH Rotavirus Vaccine Program, Seattle, WA, USA

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Efficacy (95% CI)</th>
<th>Cases prevented per 100 person-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe rotavirus GE</td>
<td>83.4% (25.5, 98.2)</td>
<td>3.3</td>
</tr>
<tr>
<td>AGE with severe dehydration</td>
<td>34.4% (5.3, 54.6)</td>
<td>19.0</td>
</tr>
</tbody>
</table>

Adapted from Feikin et al. Vaccine 2012:30S; A52-60
Number of cases prevented per 100 vaccinated is greater in low income settings despite lower VE.

<table>
<thead>
<tr>
<th>Severe RVGE Incidence</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.4</td>
<td>0.8</td>
<td>1.6</td>
<td>3.2</td>
</tr>
<tr>
<td>50</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>60</td>
<td>0.6</td>
<td>1.2</td>
<td>2.4</td>
<td>4.8</td>
</tr>
<tr>
<td>70</td>
<td>0.7</td>
<td>1.4</td>
<td>2.8</td>
<td>5.6</td>
</tr>
<tr>
<td>80</td>
<td>0.8</td>
<td>1.6</td>
<td>3.2</td>
<td>6.4</td>
</tr>
<tr>
<td>90</td>
<td>0.9</td>
<td>1.8</td>
<td>3.6</td>
<td>7.2</td>
</tr>
<tr>
<td>100</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

Vaccine Efficacy

- High Income
- Low Income
WHO recommends the inclusion of rotavirus vaccination of infants into all national immunization programs

Rotavirus vaccination
Data from trials in Latin America, Europe and the United States of 2 oral, live, attenuated rotavirus vaccines, Rotarix (GlaxoSmithKline) and RotaTeq (Merck & Co., Inc.) were reviewed by SAGE in 2005. Noting the variable efficacy of live, oral vaccines in different populations, SAGE considered that the introduction of vaccines would be appropriate only in regions where successful phase III efficacy trials had been conducted. SAGE therefore recommended that rotavirus vaccines be included in national immunization programmes in countries where data on vaccine efficacy suggest a significant public health impact; SAGE also noted the need to urgently generate such data in Africa and Asia.

Vaccination antirotavirus
En 2005, le SAGE a examiné les données d’essais cliniques menés en Amérique latine, en Europe et aux États-Unis concernant 2 vaccins antirotavirus vivants atténués pour voie orale, le Rotarix (GlaxoSmithKline) et le RotaTeq (Merck & Co. Inc.). Notant que l’efficacité des vaccins vivants pour voie orale variait selon les populations, le SAGE a estimé judicieux de les adopter seulement dans les Régions où des essais d’efficacité de phase III avaient été effectués avec succès. Il a par conséquent recommandé que les vaccins antirotavirus soient inclus dans les programmes de vaccination nationaux des pays où les données sur l’efficacité des vaccins semblent indiquer qu’ils ont des répercussions importantes en santé publique; il a par ailleurs noté qu’il était urgent d’obtenir des données de ce type en Afrique et en Asie.
2016 National RV introductions: 80 countries*

*As of January 1, 2016
RV = rotavirus vaccine
What variables might affect vaccine performance with routine introduction?

<table>
<thead>
<tr>
<th>Adversely?</th>
<th>Favorably?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
What variables might affect vaccine performance with routine introduction?

**Adversely?**
- Entire rather than select population
  - Includes children with poorer immune responses
- Less controlled storage and transport conditions
  - Vaccine potency
- Missed vaccine doses

**Favorably?**
- Indirect effects
  - Demonstrated in higher resource settings
- Children administered vaccine at older ages
  - Overcome maternal antibody effects
- Rotavirus vaccine administered with IPV rather than OPV
# Immunogenicity of the pentavalent rotavirus vaccine in African infants

George E. Armah\textsuperscript{a}, Robert F. Breiman\textsuperscript{b}, Milagritos D. Tapia\textsuperscript{c,d}, Michael J. Dallas\textsuperscript{e}, Kathleen M. Neuzil\textsuperscript{f}, Fred N. Binka\textsuperscript{g}, Samba O. Sow\textsuperscript{c,d}, Joel Ojwando\textsuperscript{b,h}, Max Ciarlet\textsuperscript{e,1}, A. Duncan Steele\textsuperscript{f,*}

\textsuperscript{a} Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana, Legon, Ghana  
\textsuperscript{b} Centers for Disease Control and Prevention Kenya, Nairobi, Kenya  
\textsuperscript{c} Centre pour le Développement des Vaccins, Bamako, Mali  
\textsuperscript{d} University of Maryland, United States  
\textsuperscript{e} Merck Research Laboratories, North Wales, PA, United States  
\textsuperscript{f} PATH Rotavirus Vaccine Program, Seattle, WA 98121, United States  
\textsuperscript{g} School of Public Health, College of Health Sciences, University of Ghana, Legon, Ghana  
\textsuperscript{h} Kenyan Medical Research Institute, Nairobi, Kenya

## Table 3

Immunogenicity summary for SNA responses to G1, G2, G3, G4, and P1 in the per protocol population among subjects in Africa.

<table>
<thead>
<tr>
<th></th>
<th>PRV</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>G1</td>
<td>G2</td>
</tr>
<tr>
<td><strong>Predose 1 vaccination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjects tested with data available for analysis\textsuperscript{a}</td>
<td>220</td>
<td>220</td>
</tr>
<tr>
<td>GMT (dilution units and 95% confidence interval)</td>
<td>48.2 (41.9, 55.4)</td>
<td>47.7 (42.2, 53.7)</td>
</tr>
<tr>
<td><strong>Postdose 3 vaccination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjects tested with data available for analysis\textsuperscript{b}</td>
<td>192</td>
<td>192</td>
</tr>
<tr>
<td>GMT (dilution units and 95% confidence interval)</td>
<td>33.1 (28.2, 38.9)</td>
<td>29.1 (25.4, 33.4)</td>
</tr>
<tr>
<td><strong>Three-fold rise</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjects tested with Predose 1 and Postdose 3 data available for analysis\textsuperscript{b}</td>
<td>189</td>
<td>189</td>
</tr>
<tr>
<td>Number (% of subjects with ≥ 3-fold rise in antibody titer, and 95% confidence interval)</td>
<td>35 (18.5)</td>
<td>17 (9.0)</td>
</tr>
</tbody>
</table>

Note: Data that fall outside limits of detection and/or include < or > signs are eligible for GMT calculations and 3-fold rise in antibody titer calculations to different rules, which are outlined in the SAP [16.1.9.1]. SNA, neutralization assay; GMT, geometric mean titer; EIA, enzyme immunoassay.

Vaccine 30S (2012) A86–A93

*With invalid data based on laboratory determinations.

**With invalid data based on laboratory determinations, subjects with rotavirus-positive stool antigen EIA results, or subjects with samples taken out of a specified day range.
How might we improve the performance of rotavirus vaccines in low resource settings?
How might we improve the performance of rotavirus vaccines in low resource settings?

• Substitute IPV for OPV
• Different vaccine schedules
• Booster doses
• New vaccines
  – Higher potency oral vaccines
  – Inactivated vaccines
Rationale for booster dose studies

- Weak primary antibody responses in low resource settings
- Waning of protection in low resource settings
- Burden of disease remains high in second rotavirus season
- WHO allows administration of rotavirus vaccines up to 24 months of age
  - Although this was done in the context of the primary series; a booster dose has not been assessed or recommended
Two trials: Immunogenicity of additional RV dose at 9 months

<table>
<thead>
<tr>
<th></th>
<th>Matlab, Bangladesh</th>
<th>Bamako, Mali</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine</td>
<td>Rotarix</td>
<td>Rotateq</td>
</tr>
<tr>
<td>Previous RV?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Age</td>
<td>9 months</td>
<td>9 months</td>
</tr>
<tr>
<td>Comparator</td>
<td>Measles-rubella</td>
<td>MR and yellow fever</td>
</tr>
<tr>
<td>Post time point</td>
<td>11 months</td>
<td>10 months</td>
</tr>
<tr>
<td>Target enrollment</td>
<td>480</td>
<td>600</td>
</tr>
</tbody>
</table>

K Zaman et al, *Non-interference and safety of concomitant administration of measles-rubella and rotavirus vaccines at 9 months of age in Bangladesh*; Poster presentation, 11th International Rotavirus Symposium, New Delhi, India, September 2014.
Noninterference of Rotavirus Vaccine With Measles-Rubella Vaccine at 9 Months of Age and Improvements in Antirotavirus Immunity: A Randomized Trial

K. Zaman,1 Jessica A. Fleming,2 John C. Victor,2 Mohammad Yunus,1 Tejul Islam A. Bari,3 Tasnim Azim,3 Mustafizur Rahman,1 Syed Mohammad Niaz Mowla,1 William J. Bellini,4 Monica McNeal,5 Joseph P. Icenogle,6 Ben Lopman,4 Umesh Parashar,4 Margaret M. Cortese,4 A. Duncan Steele,2,8 and Kathleen M. Neuzil2,8

1International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh; 2PATH, Seattle, Washington; 3Office of the Directorate General of Health Services, Dhaka, Bangladesh; 4Centers for Disease Control and Prevention, Atlanta, Georgia; and 5Cincinnati Children’s Hospital Medical Center, Ohio

### Immunoglobulin G (IgG) Seroconversion

<table>
<thead>
<tr>
<th>Immune Measure</th>
<th>Subjects, Proportion</th>
<th>% (95% CI)</th>
<th>GMT9 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seropositivityb,c</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antirotavirus IgA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before vaccination</td>
<td>126/239</td>
<td>52.7 (46.4–59.0)</td>
<td>43.6 (34.8–54.5)</td>
</tr>
<tr>
<td>After vaccination</td>
<td>160/230</td>
<td>69.6 (63.3–75.2)</td>
<td>60.6 (49.4–74.2)</td>
</tr>
<tr>
<td>Antirotavirus IgG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before vaccination</td>
<td>159/240</td>
<td>66.3 (60.1–71.9)</td>
<td>79.2 (61.4–102.1)</td>
</tr>
<tr>
<td>After vaccination</td>
<td>204/231</td>
<td>88.3 (83.5–91.8)</td>
<td>168.6 (137.3–207.2)</td>
</tr>
</tbody>
</table>
Noninterference of Rotavirus Vaccine With Measles-Rubella Vaccine at 9 Months of Age and Improvements in Antirotavirus Immunity: A Randomized Trial

K. Zaman,1 Jessica A. Fleming,2 John C. Victor,2 Mohammad Yunus,1 Tajul Islam A. Bari,3 Tasnim Azim,1 Mustafizur Rahman,1 Syed Mohammad Niaz Mowla,1 William J. Bellini,6 Monica McNeal,5 Joseph P. Icenogle,6 Ben Lopman,5 Umesh Parashar,4 Margaret M. Cortese,4 A. Duncan Steele,2,3 and Kathleen M. Neuzeil2,3

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Country Specific Rota Coverage Rates 2014

Rota Coverage Rates 2014
Reaching every child with rotavirus vaccines
Rotavirus Vaccines

- Before vaccines, rotavirus was the most common cause of severe dehydrating diarrhea among young children worldwide
- Rotavirus vaccines have higher efficacy in high income settings
- Severe disease prevention is an important measure of vaccine value