Global Surveillance for rotavirus disease

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Centers for Disease Control and Prevention

8th International Rotavirus Symposium
Sheraton
Istanbul

June 3-4, 2008
VACCINE INTRODUCTION

SUSTAINABLE VACCINE PROGRAM WITH MEASURABLE IMPACT ON SEVERE DISEASE/DEATH

IMPACT ASSESSMENT (Vaccine effectiveness and case reduction)

Continued Safety

Strain monitoring

VACCINE INTRODUCTION

WHO recommendation

POLITICAL WILL

COST-EFFECTIVENESS / AFFORDABILITY

DISEASE BURDEN % positive number cases

ADVOCACY

STRAIN DATA

OTHER FACTORS eg cultural

SAFE, EFFECTIVE VACCINES
Objectives - preintroduction

n Develop disease and economic burden evidence base for vaccine using standardized methods
  - Global evidence base
  - Locally - countries take ‘ownership’ of problem leads to local “Champions”

n Understand rotavirus epidemiology in different settings

n Better understand strain diversity

n Advocacy - data dissemination

n Provide longitudinal pre-introduction data for impact evaluation
Networks

- **Network of sites**
  - Standardization of data collection / case definition
  - Compare, contrast and combine data
  - Stronger advocacy globally and regionally - data more visible

- **Network of partners involved in coordination / funding**
  - Widespread data ownership - stakeholders
  - Sustainability
Partners and funders

- Rotavirus Vaccine Program - PATH
- WHO HQ
- WHO Regional Offices
- WHO Country Offices
- Centers for Disease Control and Prevention
- International Vaccine Institute
- Ministeries of Health
- Academic institutions / Public Health Institutes
- Industry
Surveillance in different settings
WHO’s Generic Protocol

- Hospital-based surveillance
- Simple data collection
- Outcomes:
  - % Rv positive
  - Rates of rotavirus hospitalizations
- Guidelines for strain typing
- Platform for measuring other outcomes
  - Outpatient visits
  - Costs
  - intussusception
ARSN Phase II 2004 -- 2007

Melbourne, Australia
(reference lab)

19 countries
>60 Sites

ARSN member, 2001-4
9 countries, 36 sites
ARSN member, 2004 - -
14 countries, 38 sites
<table>
<thead>
<tr>
<th>Country</th>
<th># sites</th>
<th># tested</th>
<th># positive</th>
<th>% pos 2005-2007</th>
<th>% pos 2001-2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>8-11</td>
<td>2243</td>
<td>957</td>
<td>43%</td>
<td>44%</td>
</tr>
<tr>
<td>Philippines</td>
<td>7</td>
<td>1653</td>
<td>453</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>Nepal</td>
<td>1</td>
<td>1273</td>
<td>421</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>Indonesia</td>
<td>6</td>
<td>2240</td>
<td>1345</td>
<td>60%</td>
<td>53%</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>2</td>
<td>457</td>
<td>114</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Pakistan (+clinic)</td>
<td>2</td>
<td>575</td>
<td>97</td>
<td>17%</td>
<td></td>
</tr>
<tr>
<td>Myanmar</td>
<td>1</td>
<td>4184</td>
<td>2128</td>
<td>50%</td>
<td>57%</td>
</tr>
<tr>
<td>Cambodia</td>
<td>1</td>
<td>2296</td>
<td>1278</td>
<td>56%</td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>6</td>
<td>4346</td>
<td>1779</td>
<td>41%</td>
<td>44%</td>
</tr>
<tr>
<td>Sri Lanka (+clinic)</td>
<td>1</td>
<td>1806</td>
<td>428</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Mongolia</td>
<td>1</td>
<td>1151</td>
<td>458</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>Laos</td>
<td>1</td>
<td>1158</td>
<td>624</td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>37-40</td>
<td>23382</td>
<td>10082</td>
<td>43%</td>
<td>46%</td>
</tr>
</tbody>
</table>
Age distribution of rotavirus hospitalizations, ARSN sites
Strain diversity and trends

Kang et al JID, 2005
6th Asian Rotavirus Surveillance Network meeting
Asian Rotavirus Surveillance

- China
- Myanmar
- Indonesia
- Thailand
- Philippines
- Uzbekistan
- Kyrgyzstan
- Bangladesh
- Nepal
- Sri Lanka
- Mongolia
- Cambodia
- Pakistan
- Laos

2006 2007 2008 2009 2010

POST - ROTAVIRUS ADIP

• WPRO
• INDUSTRY
• PATH
• SELF-SUSTAINING

Recommendation

ADD FUJI, PAPUA NEW GUINEA AND VIETNAM

End of Phase 2 of ARSN
African Rotavirus Surveillance Network, Status in Jan 2008

Started June 06

- Rotavirus surveillance supported by AFRO
- Enhanced surveillance
- No Rotavirus surveillance
- EMRO countries
- Countries conducting clinical trials
- Rotavirus Regional Reference lab

Courtesy: Jason Mwenda, AFRO: from newsletter
AFRO network June 06-07 - 7 countries

<table>
<thead>
<tr>
<th>Sentinel Site/Country</th>
<th># &lt; 5 yr children hospitalized</th>
<th># (%) stool samples collected</th>
<th># (%) EIA Rota +ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korle Bu Teaching Hospital, Ghana</td>
<td>653</td>
<td>158 (24)</td>
<td>93 (59)</td>
</tr>
<tr>
<td>Kenyatta National Hospital, Kenya</td>
<td>895</td>
<td>895 (100)</td>
<td>423 (47)</td>
</tr>
<tr>
<td>Mulago National Referral Hospital, Uganda</td>
<td>1269</td>
<td>673 (53)</td>
<td>314 (47)</td>
</tr>
<tr>
<td>University Teaching Hospital, Zambia</td>
<td>233</td>
<td>233 (100)</td>
<td>66 (28)</td>
</tr>
<tr>
<td>Institut Pasteur de Dakar, Senegal</td>
<td>N/A²</td>
<td>47</td>
<td>15 (32)</td>
</tr>
<tr>
<td>Parirenyatwa Hospital, Zimbabwe</td>
<td>51³</td>
<td>51 (100)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Oluranti Oyeneye, MRC Laboratory,</td>
<td>N/A²</td>
<td>57</td>
<td>57 (100)</td>
</tr>
</tbody>
</table>

African Rotavirus Surveillance newsletter: Jason Mwenda: AFRO 46%
### AFRO network (March 08) - 10 countries

<table>
<thead>
<tr>
<th>Country/site</th>
<th>Duration of Surveillance</th>
<th># &lt;5 acute diarrhea hospitalizations</th>
<th># (%) with stool specimen collected</th>
<th># (%) EIA Rotavirus confirmed cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghana Site 1: KBTH</td>
<td>Aug 06 – Jan 08</td>
<td>991</td>
<td>404 (41)</td>
<td>254 (63)</td>
</tr>
<tr>
<td>Site 2 : NHRC</td>
<td>Apr 07 - Mar 08</td>
<td>411</td>
<td>399 (97)</td>
<td>186 (47)</td>
</tr>
<tr>
<td>Kenya (KNH)</td>
<td>Aug 06 – Jan 08</td>
<td>1198</td>
<td>1198 (100)</td>
<td>576 (49)</td>
</tr>
<tr>
<td>South Africa (Dr George Mukhari Hospital)</td>
<td>Jan 06-Dec 07</td>
<td>2321</td>
<td>1361 (59%)</td>
<td>374 (27)</td>
</tr>
<tr>
<td>Uganda/MNH-ACU</td>
<td>June 06 – Jan 08</td>
<td>1277</td>
<td>990 (78)</td>
<td>428 (43)</td>
</tr>
<tr>
<td>Zambia/UTH</td>
<td>Aug 06 – Feb 08</td>
<td>529</td>
<td>505 (95)</td>
<td>172 (34)</td>
</tr>
<tr>
<td>Zimbabwe/ Parirenyatwa Hosp</td>
<td>Jan 07 – Feb 08</td>
<td>225</td>
<td>225 (100)</td>
<td>44 (20)</td>
</tr>
<tr>
<td>Cameroon/Chantal BIYA Hospital, Centre Mère et Enfant.</td>
<td>Sept 07 – Jan 08</td>
<td>484</td>
<td>108 (22)</td>
<td>33 (31)</td>
</tr>
<tr>
<td>Ethiopia/ AAU-MF</td>
<td>Sept 07 – Feb 08</td>
<td>102</td>
<td>102 (100)</td>
<td>46 (45)</td>
</tr>
<tr>
<td>Senegal (CHNEAR)</td>
<td>July 07 – Jan 08</td>
<td>369</td>
<td>369 (100)</td>
<td>76 (21)</td>
</tr>
<tr>
<td>Tanzania/MNH</td>
<td>Sept 07 – Feb 08</td>
<td>143</td>
<td>143 (100)</td>
<td>ND</td>
</tr>
</tbody>
</table>

African Rotavirus Surveillance newsletter: Jason Mwenda: AFRO
The Journal of Infectious Diseases
Rotavirus in Asia
Epidemiology, Burden of Disease, and Current Status of Vaccines

First Report from the Asian Rotavirus Surveillance Network

PERSPECTIVES

Rotavirus remains the most common cause of severe, dehydrating diarrhea among children worldwide. Several rotavirus vaccines are under development. Decisions about new vaccine introduction will require reliable data on disease impact. The Asian Rotavirus Surveillance Network, begun in 2000 to facilitate collection of these data, is a regional collaboration of 36 hospitals in nine countries to conduct surveillance for rotavirus hospitalizations using a uniform World Health Organization protocol. Via surveillance, the network has documented 25,120 infections and 5,029 hospitalizations from August 2001 through July 2002. During this period, 45% of acute diarrheal hospitalizations among children 0–6 years were attributable to rotavirus, higher than previous estimates. Rotavirus was isolated in all age groups, and the proportion attributable to rotavirus increased with age. This network is an important tool for vaccine-preventable diseases. Such a network should provide increased visibility and advocacy, enable more efficient data collection, facilitate training, and serve as the paradigm for rotavirus surveillance activities in other regions.

In recent years, several international agencies, including the World Health Organization (WHO), the Global Alliance for Vaccines and Immunization (GAVI), and the Children’s Vaccine Program at the Program for Appropriate Technology in Health (PATH), have identified the accelerated development and introduction of a rotavirus vaccine as among their top priorities. This decision was made based on the high incidence of rotavirus, the most common cause of severe diarrhea in children worldwide. An estimated 440,000 children die of rotavirus each year (1), and in developing countries, 3% of all deaths in children 4 years of age are due to rotavirus. Furthermore, rotavirus is responsible for 75% to 90% of all hospitalizations of children for diarrhea in both industrialized and developing countries (2). After 3 decades of vaccine development and testing, the principles for making safe and effective live oral vaccines have been firmly established, and several new candidate vaccines are currently in the late stage of development (3). Given the importance of rotavirus, GAVI has initiated the Accelerated Development and Introduction Program to expedite the development, evaluation, and introduction of rotavirus vaccines into the poorest countries with the goal of preventing most rotavirus deaths and hospitalizations within the next decade.
Global Rotavirus Surveillance

Rotavirus

Global Rotavirus Surveillance

Globally, rotavirus is the cause of about 600,000 diarrheal deaths every year, 80% of which occur in poorer countries. In addition, many more children will get dehydrated and require medical intervention and hospitalization. Several vaccines against rotavirus have been or are being developed to reduce this burden.

The Rotavirus Vaccine Program (RVP), a collaboration between the World Health Organization (WHO), the Program for Appropriate Technology in Health (PATH), and the U.S. Centers for Disease Control and Prevention (CDC), is funded by the Global Alliance for Vaccines and Immunizations (GAVI).

The RVP aims to expedite the development and introduction of rotavirus vaccines. One component of this agenda is the derivation of regional and local disease burden estimates to help make the case for vaccination and to support countries in deciding to introduce rotavirus vaccines or not. The CDC and WHO have developed a generic protocol for standardized surveillance of rotavirus disease, and in collaboration with other RVP partners, CDC supports rotavirus surveillance in the national networks under AG.
Rotavirus Surveillance News

September 2005, Volume 1 Issue 1

Welcome

Welcome to the publication of Rotavirus Surveillance News, a quarterly newsletter edited by the Rotavirus Surveillance Team at the CDC.

Update - November

In this edition of Rotavirus Surveillance News, we continue to highlight the latest rotavirus surveillance activities and developments around the world. This edition features updates from the following regions:

- Asia
- Africa
- Europe
- Americas
- Australia

We encourage you to visit our website (www.cdc.gov) for more detailed information and to stay updated with the latest rotavirus surveillance activities.

Questions or comments?

If you have any questions or comments, please feel free to contact us at surveillance@cdc.gov.

What's New?

- New surveillance methods and tools
- Updates on rotavirus outbreaks and surveillance activities
- Collaboration with international partners

Figure 1

Rotavirus Surveillance News - September 2005, Volume 1 Issue 1

The surveillance data presented in this newsletter represents the most current information available on rotavirus surveillance activities worldwide. The data are compiled and analyzed by the Rotavirus Surveillance Team at the CDC and are presented in a user-friendly format to aid in the planning and implementation of rotavirus control programs.

CDC and PATH

CDC and PATH are collaborating to improve rotavirus surveillance activities and support national surveillance systems.

References

- World Health Organization (WHO)
- Centers for Disease Control and Prevention (CDC)
- PATH

Contact Information

Surveillance@cdc.gov

Additional Resources

- CDC website (www.cdc.gov)
- PATH website (www.path.org)
Global distribution of rotavirus strains 2004-8

N=18735

P[8],G1 43.5%
P[8],G9 21.5%
P[8],G3 7.5%
P[4],G2
P[8],G4 6.6%
Unusual 7.5%
Rare 0.5%

P[8],G12 or P[6],G12 or P[4],G12 or P[9],G12 1.2%

Courtesy K Banyai & Jon Gentsch
Countries where G12 has been detected since 2004

Courtesy K Banyai & Jon Gentsch
Limitations of hospital-based surveillance

- Illnesses that do not get to hospital
  - Mortality
  - Milder disease

- Health care seeking behaviour difficult to assess

- Representativeness of sentinel sites

- Limited data collected for other hypotheses
  - e.g. long term or unusual outcomes

- Other pathogens: relative disease burden / mixed infection
Non-fatal and fatal diarrhea among hospitalized children <5 years, Western Kenya, 2005-2006

Hospitalizations (N=547)
- Unknown: 55%
- Shigella: 5%
- Nontyphoid Salmonella: 12%
- Campylobacter: 8%
- Rotavirus: 22%

Deaths (N=48)
- Unknown: 40%
- Shigella: 21%
- Nontyphoid Salmonella: 13%
- Campylobacter: 8%
- Rotavirus: 2%
% and rates of rotavirus hospitalisation

<table>
<thead>
<tr>
<th></th>
<th>% RV children</th>
<th>Estimated risk by age 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States**</td>
<td>35%</td>
<td>1:60</td>
</tr>
<tr>
<td>Global (lowincome)*</td>
<td>20%</td>
<td>1:63</td>
</tr>
<tr>
<td>New Delhi+</td>
<td>24%</td>
<td>1:59</td>
</tr>
<tr>
<td>Western Kenya++</td>
<td>19%</td>
<td>1:181</td>
</tr>
</tbody>
</table>

Outpatient morbidity and rotavirus mortality, Western Kenya*

Outpatient

15% RV positive: Risk by age five years for RV clinic visit: 1:1

Mortality

Estimate using verbal autopsy data from demographic surveillance system

- 9393 annual rotavirus deaths (unadjusted)

WHO rotavirus mortality estimate for Kenya:

- 7541 annual rotavirus deaths

* Tate et al; unpublished data
Representativeness
Where to?
Future of new vaccine surveillance

**ADIP’s phasing out schedule**
- Pneumo and Rota ADIPs - by December 2008
- Hib Initiative - by June 2009

**Post ADIP surveillance**
- Moving from time-limited surveillance projects to sustainable networks
- Country-owned
- Sentinel surveillance, "layer approach"
- Integrated with existing networks
- WHO regional offices coordination
- Technical support from WHO and partners
The future

- Global Framework for Immunization Monitoring and Surveillance (GFIMS)
  - revamping of VPD surveillance
  - integration of surveillance of different diseases

- Global new vaccine surveillance meeting, November, Geneva
  - 1-2 sites per country more for larger countries?
Special challenges & studies

- Measurement of impact - trend:
  - Need high coverage
  - Year to year variation in incidence
  - Good baseline
  - Good secondary data sources

- Measurement of impact - Vaccine effectiveness
Special challenges & studies

- **Mortality**
  - Vaccine probe studies: in DSS areas?
  - Case-control studies for effectiveness versus all cause AGE death

- **Understanding strain diversity**
  - More formal assessment?

Need for enhanced population-based sites


We identified 21 rotaviruses in 129 patients with diarrhea in a Brazilian city with high rotavirus vaccine coverage. All rotaviruses were genotype P[4]G2, with 1 mixed infection with P[NT]G9. Although virus predominance could have occurred randomly, the vaccine may be less protective against P[4]G2. Prospective surveillance is urgently needed.
Sunrise over Mount Ararat