Epidemiology & Disease Burden: Asian Rotavirus Surveillance Network

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Department of Paediatrics
The Chinese University of Hong Kong
1st ARSN Meeting
Bangkok
Feb 1999
Messages

- Rotavirus vaccine now available in US
- Decision makers will need disease burden data
- What data do we have?
- What data do we need?
Are decision-makers aware of rotavirus disease burden?

• Diarrhoea recognised as leading cause of morbidity and mortality \textbf{BUT} most doctors & policy makers often don’t appreciate importance of rotavirus

• Aetiology does not usually alter management – thus diagnosis of rotavirus often not made

• Policy makers may think improving water and sanitation may prevent rotavirus - incorrect
WHO’s Generic Protocol

✓ Hospital-based surveillance
✓ Simple data collection
✓ Outcomes:
  □ rates of diarrhoea hospitalisations
  □ and/or % RV positive
✓ Strain characterisation
Back home ...

Planning surveillance & cost study
Intussusception Among Recipients of Rotavirus Vaccine — United States, 1998–1999

On August 31, 1998, a tetravalent rhesus-based rotavirus vaccine (RotaShield®, Wyeth Laboratories, Inc., Marietta, Pennsylvania) (RRV-TV) was licensed in the United States for vaccination of infants. The Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics, and the American Academy of Family Physicians have recommended routine use of RRV-TV for vaccination of healthy infants (1,2). During September 1, 1998–July 7, 1999, 15 cases of intussusception (a bowel obstruction in which one segment of bowel becomes enfolded within another segment) among infants who had received RRV-TV were reported to the Vaccine Adverse Event Reporting System (VAERS). This report summarizes the clinical and epidemiologic features of these cases and preliminary data from ongoing studies of intussusception and rotavirus vaccine.

VAERS
• Reinvigorating the competition
  - Big pharma (GSK, Merck)
  - Local producers (China/India)
• Parallel testing in both developed & developing countries
• Increasing awareness of the potential for rotavirus vaccines

Glass. Lancet 2004;363:1547
Will intussusception occur with other rotavirus vaccines?

The Asian Rotavirus Surveillance Network: Phase 1

- China
- Hong Kong
- Indonesia
- Malaysia
- Myanmar
- South Korea
- Taiwan
- Thailand
- Vietnam

GAVI eligible
2nd Workshop of ARSN
Bangkok, May 2002
Publication of 1st year results

- August 2001 to July 2002
- South Korea started in June 2002
- 33 hospitals in 8 countries
- Data of 16,000 hospitalisations for diarrhoea during 1st year
- Data collation by CDC

Stools Tested

• 11,498 stools from 16,1173 patients = 71%
• 45% of tested specimens positive for rotavirus
# Rates of Rotavirus Detection

**Aug 2001–Jul 2002**

<table>
<thead>
<tr>
<th>Sites</th>
<th>Tested</th>
<th>RV+ %</th>
<th>Range</th>
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<td>52</td>
<td>47-57</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td>11,498</td>
<td>45</td>
<td>18-67</td>
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</table>
Figure 1. Seasonality of rotavirus in member countries of the Asian Rotavirus Surveillance Network
Spring 2003 Meeting of the Asian Rotavirus Surveillance Network
Workshop of the Members of the Asian Rotavirus Surveillance Network
Manila, Philippines
21-22 October 2003
Launch of Phase 2 of ARSN

- Bangladesh (2)
- Cambodia (1)
- Kyrgyzstan (2)
- Lao PDR (1)
- Mongolia (2)
- Nepal (1)
- Pakistan (2)
- Philippines (7)
- Sri Lanka (1)
- Uzbekistan (2)

- China (8)
- Indonesia (5)
- Myanmar (1)
- Thailand (2)

GAVI eligible
- **Disease Burden**: Taiwan, Korea, Hong Kong, Malaysia, Thailand, China, Japan, Myanmar, India, Vietnam
- **Economic Burden**: HK & Japan, cost-effectiveness projections for Asia
- **Vaccine updates**: RIX4414, Pentavalent & Hexavalent human-bovine, Indian neonatal strains
Taiwan RV disease burden

- Enrolled 2600
- RV+ rate 43%
- Bacteria 11%
- Adenovirus 2.5%
- RV + other 3.9%

Chen et al. JID. 2005;192:S44-48
Korea RV disease burden

RV+ rate (4106 children)
- INPATIENTS = 73%
- OUTPATIENTS = 18%

Incidence of hospitalisation for RV:
11.6 per 1000 children < 5yrs

Overall incidence of RV:
57 per 1000 children < 5yrs
Hong Kong RV disease burden

RV+ rate = 30%

Incidences of hospitalisation for RV
• 8.8 per 1000 children < 5yrs
• 4x previous “passive” estimate

1 in 24
cumulative risk of hospitalisation
for RV by age 5 years

Nelson et al. JID. 2005;192:S71-79
Malaysia RV disease burden

- Ministry of Health Data
- ~14,000 GE admissions
- RV+ rate for hospitalised RV = 50%

1 in 61 cumulative risk of hospitalisation for RV by age 5 years

Hsu et al. JID. 2005;192:S80-86
Thailand RV disease burden

- Enrolled 4057
- RV+ rate 43%
- Community RV+ rate 12%

*Figure 3. Summary of disease burden associated with rotavirus infection in Thailand*

*Jiraphongsa et al. JID. 2005;192:S87-93*
China RV Disease Burden

• 6 sentinel hospitals
• n = 3149
• RV+ rate 50%

Figure 1. Locations of the 6 sentinel hospitals for rotavirus surveillance, People’s Republic of China, 1 August 2001–31 July 2003

Fang ZY et al. JID. 2005;192:S94-99
Japan RV disease burden

• 3 sentinel hospitals (n=443)
• RV+ rate = 58%

Incidence of hospitalisation for RV
• ~ 15 per 1000 children < 5yrs

1 in 15
cumulative risk of hospitalisation for RV by age 5 years

Nakagomi T et al. JID. 2005;192:S106-110
Myanmar RV disease burden

- Diarrhea 18% of hospitalisations
- n=1736
- RV+ rate = 53%

Moe K et al. JID. 2005;192:S111-113
Vietnam RV disease burden

- RV+ rate = 55%

Nguyen Van Man et al. JID. 2005;192:S127-132
India RV disease burden

- Passive surveillance study
- 6 hospitals (~65% admissions)
- RV+ rate = 24%

Incidence of hospitalisation for RV
- 3.4 per 1000 children < 5yrs

Bahl R et al. JID. 2005;192:S114-119
## Asian Rotavirus Disease Burden

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<thead>
<tr>
<th>Sites</th>
<th>% RV+</th>
<th>Cases/Population</th>
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<td>1590/3149</td>
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<td>Overall</td>
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*Data from JID. 2005;192:*
Asian RV Disease Burden

“Much higher than anticipated”
Variation in peak age of onset

GDP/capita
## Asian Rotavirus Serotypes (%)

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<th>Sites</th>
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<th>G3</th>
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Data from JID. 2005;192:
Economic Burden of Rotavirus and Potential Cost-effectiveness of Vaccination in Asia
Economic Burden in Hong Kong

- Sub-sample of 471 children admitted with diarrhoea
- Hospital costs & Outpatient costs
  - Government costs
  - Family costs
- Out of pocket expenses
- Indirect costs

Nelson et al. JID. 2005;192:S64-70
Cost estimations for Hong Kong

- Total social cost USD 4.3 M
- Total direct medical cost USD 4 M
- 4 x higher than previous estimate

- Government cost ~ USD 1800
- Family cost USD 120
Preliminary cost-effectiveness analysis for Hong Kong

- High disease burden (1 in 24)
- High cost of hospital admission (USD1800)
- Depending on vaccine price, a universal immunization programme for rotavirus could be cost saving for government
Japan Economic Burden of rotavirus-associated admissions

- Direct medical cost USD 1236
- Extrapolated total direct medical cost USD 96 M

Nakagomi T et al. JID. 2005;192:S106-110
Projected Cost-Effectiveness of Rotavirus Vaccination for Children in Asia

Laura Jean Podewils, Lynn Antil, Erik Hummelman, Joseph Bresee, Umesh D. Parashar, and Richard Rheingans

1Respiratory and Enteric Viruses Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, and 2Department of International Health, Rollins School of Public Health, Emory University, Atlanta, Georgia

Background. New rotavirus vaccines may soon be licensed, and decisions regarding implementation of their use will likely be based on the health and economic benefits of vaccination.

Methods. We estimated the benefits and cost-effectiveness of rotavirus vaccination in Asia by using published estimates of rotavirus disease incidence, health care expenditures, vaccine coverage rates, and vaccine efficacy.

Results. Without a rotavirus vaccination program, it is estimated that 171,000 Asian children will die of rotavirus diarrhea, 1.9 million will be hospitalized, and 13.5 million will require an outpatient visit by the time the Asian birth cohort reaches 5 years of age. The medical costs associated with these events are approximately $191 million; however, the total burden would be higher with the inclusion of such societal costs as lost productivity. A universal rotavirus vaccination program could avert approximately 109,000 deaths, 1.4 million hospitalizations, and 7.7 million outpatient visits among these children.

Conclusions. A rotavirus vaccine could be cost-effective, depending on the income level of the country, the price of the vaccine, and the cost-effectiveness standard that is used. Decisions regarding implementation of vaccine use should be based not only on whether the intervention provides a cost savings but, also, on the value of preventing rotavirus disease-associated morbidity and mortality, particularly in countries with a low income level (according to 2004 World Bank criteria for the classification of countries into income groups on the basis of per capita gross national income) where the disease burden is great.
Projected cost-effectiveness RV vaccines in Asia

• In Asia by 5 years of age
  - 171,000 will die (109,000)
  - 1.9 M hospitalisations (1.4M)
  - 13.5 M outpatient visits (7.7M)
• Medical cost $191 M
• Cost-effectiveness depends on income level, vaccine price & standard used

Podewils L et al. JID. 2005;192:S133-145
Prospects for the early introduction of rotavirus vaccines into universal programmes in Asia?
Declaration
by Representatives of Ministries of Health in the Americas‡

Sixth International Rotavirus Symposium
Mexico City, Mexico
July 7–9, 2004

‡ Argentina, Bolivia, Brazil, Ecuador, Guatemala, Honduras, Jamaica, Mexico, Nicaragua, Panama, Peru, Paraguay, Saint Vincent, Suriname, Trinidad and Tobago, and Venezuela.

• To call upon PAHO and its Revolving Fund for the acquisition of vaccines to work together with bilateral and multilateral agencies, the Global Alliance for Vaccines and Immunization and the manufacturers of vaccines to facilitate the introduction of the rotavirus vaccine, as soon as it becomes available at affordable price for the countries in the region.
What we have ...

- Good local disease burden data from a mix of developed & developing countries in the ARSN
- More data on its way
- Evidence of a safe & effective vaccines including data from regional trials
- Some information on economic burden and cost effectiveness
What Asia still needs ...

- More LOCAL data on cost-effectiveness
- More support of local opinion leaders
- More high-level regional support
### Human Development Reports

**Home > Statistics > Get Data > Advanced Search Results**

<table>
<thead>
<tr>
<th>HDI Rank</th>
<th>Human Development Index (HDI Value)</th>
<th>Health Expenditure per Capita (PPP US$)</th>
<th>Physicians (per 100,000 People)</th>
<th>Under-five Mortality Rate (per 1,000 Live Births)</th>
<th>GDP per Capita (PPP US$)</th>
<th>Inequality Measures - Gini Index</th>
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Because the underlying household surveys differ in method and in the type of data collected, the distribution data are not strictly comparable across countries.

**Notes:**

- Data refers to the most recent year available during the period specified.
- A value of 0 represents perfect equality, and a value of 100 perfect inequality.
Thank you
Acknowledgements

• 1st Phase Members of ARSN

• Funding support
  - World Health Organization
  - Children’s Vaccine Program at PATH
  - CDC Foundation
  - GlaxoSmithKline
  - Merck
India epidemiological profile

• Data from 9 studies
• RV+ rate = 23%
• Marked diversity of strains circulating

Kang G et al. JID. 2005;192:S120-126
### Human Development Reports

#### Indicators

<table>
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<tr>
<th>Indicator</th>
<th>Hong Kong, China (SAR)</th>
<th>Korea, Rep. of</th>
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<td><strong>GDP per capita</strong> (PPP US$) (HDI)</td>
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<td>Under-five mortality rate (per 1,000 live births)</td>
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**Notes:**
- Data refer to year other than that specified.

**Source:**
- *Column 1:* Calculated on the basis of data in column 8.9 of table 1 (HDR 2005); see technical note 1 for details.
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<td>129</td>
<td>Myanmar</td>
<td>0.578</td>
<td>.. d.e.</td>
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<tr>
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<td>Cambodia</td>
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<tr>
<td>133</td>
<td>Lao People's Dem. Rep.</td>
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</table>

Aggregate for Education Index are based on aggregates of gross enrolment data calculated by the UNESCO Institute for Statistics and literacy data as used to calculate the HDI.

Notes:
2. Data refer to year other than that specified.
3. Data refer to year other than that specified.
4. Data refer to year other than that specified.
5. Estimate based on regression.

Source: