The 7th Pandemic of Cholera (Mutreja, 2011)

Estimated cases in endemic countries

<table>
<thead>
<tr>
<th>WHO region</th>
<th>&lt;1y</th>
<th>1-4y</th>
<th>5-14y</th>
<th>15y+</th>
<th>Total</th>
<th>Total deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>160,436</td>
<td>569,855</td>
<td>359,418</td>
<td>321,744</td>
<td>1,411,453</td>
<td>53,632</td>
</tr>
<tr>
<td>EMR</td>
<td>19,192</td>
<td>71,041</td>
<td>47,243</td>
<td>51,317</td>
<td>188,793</td>
<td>6,020</td>
</tr>
<tr>
<td>SEAR</td>
<td>102,214</td>
<td>386,447</td>
<td>310,918</td>
<td>424,789</td>
<td>1,224,368</td>
<td>31,718</td>
</tr>
<tr>
<td>WPR</td>
<td>846</td>
<td>3,287</td>
<td>2,785</td>
<td>5,137</td>
<td>12,055</td>
<td>120</td>
</tr>
<tr>
<td>TOTAL</td>
<td>282,688</td>
<td>1,030,630</td>
<td>720,364</td>
<td>802,987</td>
<td>2,836,669</td>
<td>91,490</td>
</tr>
</tbody>
</table>

Bangladesh  | 28,000  | 102,000 | 86,000  | 136,000 | 352,000 | 5,300 |

In non-endemic countries, estimated burden is 87,000 cases and 2,500 deaths
Estimated number of patients with cholera treated at the icddr,b hospital in Dhaka from 1999 to 2012, based on laboratory testing of 2% of diarrheal patients.
Factors that Portend Continually Rising Cholera Caseloads: Urbanization

Figure 2-9. Projected urbanization of Bangladesh’s population

Factors that Portend Continually Rising Cholera Caseloads: Climate Change

- Rising sea surface temperatures
- Rising sea levels and progressive seawater incursion inland
- Increasing frequency of extreme weather events
- Bangladesh ranked #1 as the country most affected by climate change between 1990-2008
Increasing Frequency of Flood-Related Cholera Epidemics

Figure 2-7. Increasing frequency of flood-related cholera epidemics in Dhaka
Genetic characteristics of Matlab variants of *Vibrio cholerae* O1 that are hybrids between classical and El Tor biotypes

Ashrafus Safa,¹ N. A. Bhuyian,¹ Suraia Nusrin,¹ M. Ansaruzzaman,¹ Munirul Alam,¹ T. Hamabata,² Yoshifumi Takeda,³ David A. Sack¹ and G. Balakrish Nair¹

¹Laboratory Sciences Division, Enteric Microbiology Laboratory, International Centre for Diarrhoal Disease Research, Bangladesh (ICDDR, B), Centre for Health and Population Research, GPO Box 128, Dhaka 1000, Bangladesh

²International Medical Research Center of Japan, Toyama, Tokyo, Japan

³Cine-Science Laboratory, Tokiwadai, Tokyo, Japan
Increasing Clinical Severity of Cholera in Bangladesh (Siddique, 2006)

Figure 2-6. Dehydration status of patients infected with *V. cholerae* 01 (El Tor) in Bakerganj, 1998-2001 and 2004-2006.

- No dehydration
- Some dehydration
- Severe dehydration [2006 vs. 1998-2001 (*P < 0.01*), 2006 vs. 2004 (*P < 0.05*)].
## Comparative Features of Internationally Available Oral Cholera Vaccines

<table>
<thead>
<tr>
<th>Feature</th>
<th>rBS-WC (Dukoral™)</th>
<th>WC-only (Shanchol™)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constituents</td>
<td>Recombinant CTB&lt;br&gt;Killed 01 El Tor and classical WC</td>
<td>Killed 01 (El Tor and classical) and 0139 WC</td>
</tr>
<tr>
<td>Age group</td>
<td>≥2 years</td>
<td>≥1 year</td>
</tr>
<tr>
<td>Regimen</td>
<td>2 doses (3 doses for children 2-5 yrs)</td>
<td>2 doses</td>
</tr>
<tr>
<td>Oral buffer needed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Side-Effects</td>
<td>Negligible</td>
<td>Negligible</td>
</tr>
<tr>
<td>Duration of protection</td>
<td>2 yrs (6 mos for children 2-5 yrs)</td>
<td>5 yrs (2 yrs for children 2-5 yrs)</td>
</tr>
<tr>
<td>Herd protection?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>WHO prequalified?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Price per dose</td>
<td>$5.25</td>
<td>$1.85</td>
</tr>
</tbody>
</table>
Endemic Cholera in Bangladesh

Figure 3. Cholera patients treated at the Matlab field hospital, Bangladesh, by month, 1966–1980.
## Epidemic versus Endemic Cholera

<table>
<thead>
<tr>
<th>Feature</th>
<th>Epidemic</th>
<th>Endemic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occurrence</strong></td>
<td>Less predictable</td>
<td>More predictable</td>
</tr>
<tr>
<td><strong>Modes of transmission</strong></td>
<td>Few</td>
<td>Many</td>
</tr>
<tr>
<td><strong>Non-human reservoirs</strong></td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Pre-existing natural immunity</strong></td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Clinical severity</strong></td>
<td>Greater</td>
<td>Lesser</td>
</tr>
<tr>
<td><strong>Risk</strong></td>
<td>Children = Adults</td>
<td>Children &gt; Adults</td>
</tr>
</tbody>
</table>
## Deployment of OCVs: Preemptive or Reactive?

<table>
<thead>
<tr>
<th>Feature</th>
<th>Preemptive</th>
<th>Reactive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing</strong></td>
<td>Before outbreak begins</td>
<td>After outbreak begins</td>
</tr>
<tr>
<td><strong>Setting for Vaccination</strong></td>
<td>Routine</td>
<td>Emergency</td>
</tr>
<tr>
<td><strong>Impact</strong></td>
<td>Less dependent on timing</td>
<td>More dependent on timing</td>
</tr>
<tr>
<td><strong>Best suited for</strong></td>
<td>Predictable outbreak (endemic or epidemic)</td>
<td>Unpredictable outbreak</td>
</tr>
</tbody>
</table>
### Examples of Preemptive Delivery of Killed Oral Cholera Vaccines against Endemic Cholera

<table>
<thead>
<tr>
<th>Setting</th>
<th>Vaccine</th>
<th>Strategy</th>
<th>Feasible?</th>
<th>Acceptable?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hue, Vietnam</td>
<td>WC (ORCVAX\textsuperscript{TM})</td>
<td>Mass immunization, 2 doses; general population</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Beira, Mozambique</td>
<td>rBS-WC (Dukoral\textsuperscript{TM})</td>
<td>Mass immunization, 2 doses; general population</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Southern Myanmar</td>
<td>rBS-WC (Dukoral\textsuperscript{TM})</td>
<td>Mass immunization, 2 doses; general population</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>WC (Shanchol\textsuperscript{TM})</td>
<td>Mass immunization, 2 doses; general population</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Orissa, India</td>
<td>WC (Shanchol\textsuperscript{TM})</td>
<td>Mass immunization, 2 doses; general population</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Should vaccination against endemic cholera in Bangladesh be geographically targeted?
Risk of Cholera by Districts of Bangladesh (N=64)

Annual cases/1,000:
High (3); Medium (2); Low (1)
Breakdown of Case Load by Risk Status of Districts

- High-risk districts: 72%
- Medium risk districts: 17%
- Low-risk/no data districts: 11%
Should vaccination against endemic cholera in Bangladesh be targeted by age?
Age- and Sex-Specific Hospitalization Rates in Matlab, 1966-80 (Glass, 1981)

![Graph showing age and sex-specific hospitalization rates in Matlab, 1966-80.](image)
Age Breakdown of Cholera Cases (from 4 sentinel sites)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Percent of cholera cases</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>8.0%</td>
<td>8.0%</td>
</tr>
<tr>
<td>1-4</td>
<td>29.0%</td>
<td>37.0%</td>
</tr>
<tr>
<td>5-14</td>
<td>24.4%</td>
<td>61.4%</td>
</tr>
<tr>
<td>15 and older</td>
<td>38.6%</td>
<td>100%</td>
</tr>
<tr>
<td>Total</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>

*Sites are Bakerganj, Mathbaria, Chhatak and Chaugachha (see Section 2.1 above and Sack et al. 2003.*
Geographic Targeting Strategies

• “Large Target”
  - 28 high risk districts, accounting for about half of the population of Bangladesh, but 72% of the country’s cholera cases

• “Small Target”
  - Urban slums and rural areas without improved water supplies in the Large Target districts, accounting for 35% of the Large Target population and 25% of the country’s cholera cases
Targeting Strategies and Anticipated Impact on Cholera, 2014-30

Figure 7-3. Annual number of persons to be vaccinated and estimated reduction in the national incidence from cholera

- Small Target
  - 1-14: 2.1 million, 15%
  - 1+: 5.5 million, 19%
- Large Target
  - 1-14: 6.1 million, 43%
  - 1+: 15.8 million, 54%

Annual no. people vaccinated (millions)
Cases prevented as % of total cases without vaccination

Reduction in national cholera incidence
Vaccine Cost-Effectiveness, 2014-30

The chart shows the cost per DALY (Disability-Adjusted Life Year) for different age groups and target populations. The cost per DALY is measured in 2010 USD.

For the large target population:
- 1-14 years: $350
- 1+ years: $760

For the small target population:
- 1-14 years: $350
- 1+ years: $760

The chart also indicates the thresholds for very cost-effective and cost-effective interventions, with the very cost-effective line at $641 and the cost-effective line at $1,923.
Cholera Outbreaks are Precipitated by Floods

Figure 2-8. Cases per month of cholera and other enteric pathogens among all patients (adults and children) seen at the ICDDR,B Dhaka Hospital in 2007

Note: all values are estimated based on surveillance data in 2% of total cases. Source: Harris et al., 2008.
Age Breakdown of Cholera Cases during “Normal” Periods vs. Major Epidemics

Figure 2-5. Age breakdown of laboratory-confirmed cases of cholera during epidemic and non-epidemic periods

During 2007 outbreak in Dhaka

- <2: 8%
- 2-4: 9%
- 5-14: 16%
- ≥15: 67%

From hospital-based surveillance in 4 rural areas*

- <2: 16%
- ≥20: 31%
- 10-20: 15%
- 5-10: 17%
- 2-4: 21%
- 5-14: 16%

Source: Harris et al., 2008

*The 4 sites are Mathbaria (Matlab), Chaugachha, Bakerganj and Chhatak. Source: Sack et al., 2003.

Limiting reactive vaccination to young children and adolescents may be less rational for atypical outbreaks.
Decision-making Tree for Preemptive Vaccination

Decision-making tree for OCV use in complex emergencies

Step 1
Risk of cholera outbreak
- Limited risk
  - OCV use not relevant
- Risk exists
  - Good coping/response capacities
    - OCV use not relevant

Step 2
Capacity to contain potential outbreak
- Limited capacity
  - Not feasible
    - OCV use not relevant
- Feasible
  - Feasibility of OCV mass vaccination campaign
    - Feasible
      - Immunization can be considered
## Examples of Preemptive Delivery of Killed Oral Cholera Vaccines in Complex Emergencies

<table>
<thead>
<tr>
<th>Setting</th>
<th>Vaccine</th>
<th>Strategy</th>
<th>Feasible?</th>
<th>Acceptable?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refugee (N. Uganda)</td>
<td>rBS-WC (Dukoral™)</td>
<td>Preemptive mass immunization 2 doses; general population</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Refugee (Darfur)</td>
<td>rBS-WC (Dukoral™)</td>
<td>Preemptive mass immunization 2 doses; general population</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Post - Tsunami (Aceh)</td>
<td>rBS-WC (Dukoral™)</td>
<td>Preemptive mass immunization 2 doses; general population</td>
<td>Yes</td>
<td>+/-</td>
</tr>
</tbody>
</table>
## Examples of Reactive Delivery of Killed Oral Cholera Vaccines

<table>
<thead>
<tr>
<th>Setting</th>
<th>Vaccine</th>
<th>Strategy</th>
<th>Feasible?</th>
<th>Acceptable?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vietnam</td>
<td>WC (ORCVAX™)</td>
<td>Mass immunization</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>(multiple epidemics)</td>
<td></td>
<td>2 doses; general population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guinea</td>
<td>WC (Shanchol™)</td>
<td>Mass immunization</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>(large Epidemic)</td>
<td></td>
<td>2 doses; general population</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A→B : Improved water-sanitation
A→C : Vaccination
A→D : Improved water-sanitation + Vaccination
Views of Policymakers

- Policymaker survey conducted by IVI and ICDDR,B rated cholera as third most important infectious disease, after Tbc and pneumonia
- GOB spearheaded World Health Assembly resolution on cholera control
- GOB is collaborating with ICDDR,B on OCV introduction project in urban Bangladesh
How Would OCV Use be Implemented?

Policymaker survey underscored:

- Importance of an integrated approach
- 2 pronged approach: endemic disease and outbreak control
- Target vaccination to high risk geographic areas, but include broad age groups
- Phased approach: begin with urban slums in Dhaka
- Campaign approach, leveraging NIDs, nationwide measles vaccination catch up, vitamin A, deworming, and existing school based immunization
Summary

• Cholera is a major problem in Bangladesh, where it is endemic and where many signs point to an increase in the future.

• Despite this endemicity, major cholera outbreaks following major disasters in Bangladesh more closely resemble epidemic cholera.

• Modern OCVs offer the potential to improve the control in typical endemic form and in large outbreaks, in concert with other control measures.

• The public health infrastructure of Bangladesh, with its track record of mass delivery of vaccines and other health interventions, is well poised to deliver OCVs.
Summary

- Remaining challenges include:
  - Obtaining an adequate vaccine supply
  - Financing purchase of vaccine
  - Development of optimal vaccine delivery strategies for control of predictable endemic cholera
  - Development of approaches to control of outbreaks occurring in the setting of natural disasters, either preemptively, with validated predictive instruments to anticipate post-disaster outbreaks, or reactively
  - Institution of countrywide surveillance for cholera to identify populations at risk and to monitor vaccine impact