Epidemiology of Diarrheal Diseases

Robert Black, MD, MPH
Johns Hopkins University
Robert Black, MD, MPH

- Chairman, Department of International Health
- Researches the interaction of infectious diseases and nutrition
- Engaged in randomized trials and effectiveness evaluations of vaccines for rotavirus, *Hemophilus influenzae* type B, pneumococcal, and shigella
- Assesses nutritional interventions to reduce infectious disease morbidity and mortality
Overview

- The pathophysiology of the major causes of childhood infectious diarrhea
- The importance of diarrhea in children globally and the associated pathogens
- Risk factors and transmission patterns for diarrhea and related preventive interventions
Section A

Definition of Diarrhea and Pathophysiology
What Is Diarrhea?

- Stools of decreased consistency and increased volume due to imbalance of secretion and absorption of water and salts in the intestine
Types of Diarrhea in Developing Countries

- Noninfectious (infrequent), e.g., congenital, inflammatory bowel disease
- Infectious (predominant), e.g., bacterial, viral, parasitic
Pathophysiology of Infectious Diarrhea

- Secretory (noninflammatory), i.e., toxin stimulates chloride secretion and reduces absorption of sodium and water (e.g., *V. cholerae* or organism reduces small bowel absorptive villus structure and function (e.g., rotavirus)
- Invasive (inflammatory), i.e., organism penetrates and damages cells of intestinal mucosa (e.g., shigella)
Virulence Factors of Enterotoxigenic Coli

Virulence Factors of Enterotoxigenic

*E. Coli*

- Flagellar “H” Antigen
- LPS “O” Antigen
- Capsular “K” Antigen
- Uncharacterized CFA pili
- Heat Stable (ST) Enterotoxin
- Heat Labile (LT) Enterotoxin
- Plasmids
- Colonization Factor Antigen (CFA) I
- Colonization Factor Antigen (CFA) II
Enterotoxigenic E. coli Infection
Rotavirus Infection

1. VP4 spikes attach to lining and outer shell is shed
2. Subparticle enters cytoplasm
3. Virus multiplies and produces toxin
4. New virus leaves infected cells to invade healthy ones
5. Epithelial cells die and fluids exit the body
Shigella Infection

1. Invasion
2. Phagosome lysis and macrophage apoptosis
3. Release of IL-1 and PMN transmigration
4. Shigella migration through disrupted tight junctions
5. Multiplication and intercellular spread
6. Epithelial cells die and fluids are lost
Section B

Importance Globally and Associated Pathogens
Annual mortality from diarrhea in children less than five years old in developing countries
- 1.8 million deaths
- Decreased from 4.5 million deaths in last 20 years
Annual Under-Five Episodes in Developing Countries

- Annual incidence of diarrheal disease episodes in children less than five years old in developing countries
  - Median incidence rate 3.2 episodes per child
  - Two billion diarrheal episodes globally
Effect of Gender on Diarrhea Incidence

- Male-to-female ratio
  - Community-based studies = 1.2
  - Hospital-based studies = 1.4
  - Demographic and health surveys = 1.0
- Some countries (e.g., in South Asia) have greater care seeking for boys
Age-Specific Incidence of Diarrhea in Bangladesh

Annual Age-Specific Incidence of Diarrhea per 1000 Persons Assessed by Village Surveillance December 1977 - November 1978
Identified Enteropathogens: 61 Community-Based Studies

- Percentage of identification of selected enteropathogens from children with diarrhea in 61 community-based studies

<table>
<thead>
<tr>
<th>Enteropathogen</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterotoxigenic <em>E. coli</em></td>
<td>14</td>
</tr>
<tr>
<td>Enteropathogenic <em>E. coli</em></td>
<td>9</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>8</td>
</tr>
<tr>
<td>Campylobacter</td>
<td>8</td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>6</td>
</tr>
<tr>
<td>Shigella</td>
<td>5</td>
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</table>
**Identified Enteropathogens: 107 Facility-Based Studies**

- Percentage identification of selected enteropathogens from children with diarrhea in 107 health facility-based studies

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<thead>
<tr>
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<tr>
<td>Rotavirus</td>
<td>25</td>
</tr>
<tr>
<td>Enteropathogenic <em>E. coli</em></td>
<td>16</td>
</tr>
<tr>
<td>Enterotoxigenic <em>E. coli</em></td>
<td>10</td>
</tr>
<tr>
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<td>Campylobacter</td>
<td>5</td>
</tr>
<tr>
<td>Salmonella</td>
<td>4</td>
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</table>
Dehydrated Under-Fives with Diarrhea: Bangladesh

- Percentage of children less than five years old experiencing dehydration during diarrheal episodes, by enteropathogen, in community-based studies in rural Bangladesh

<table>
<thead>
<tr>
<th>Enteropathogen</th>
<th>No. of episodes</th>
<th>No. with dehydration</th>
<th>Percentage with dehydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus</td>
<td>78</td>
<td>28</td>
<td>36</td>
</tr>
<tr>
<td>Enterotoxigenic E. coli</td>
<td>322</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td>843</td>
<td>17</td>
<td>2</td>
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</table>
Comparison of viral etiologic agents of diarrhea in developing countries and the United States

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<tr>
<th>Etiologic agent</th>
<th>Developing country</th>
<th>U.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus</td>
<td>Important</td>
<td>Very important</td>
</tr>
<tr>
<td>Noroviruses</td>
<td>Probably important</td>
<td>Important</td>
</tr>
<tr>
<td>Enteric adenoviruses</td>
<td>Minor</td>
<td>Probably important</td>
</tr>
</tbody>
</table>
Comparison of bacterial etiologic agents of diarrhea in developing countries and the United States

<table>
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</thead>
<tbody>
<tr>
<td>Enterotox. <em>E. Coli</em></td>
<td>Very important</td>
<td>Minor</td>
</tr>
<tr>
<td>Campylobacter</td>
<td>Important</td>
<td>Important</td>
</tr>
<tr>
<td>Shigella</td>
<td>Important</td>
<td>Minor</td>
</tr>
<tr>
<td>Salmonella</td>
<td>Variable</td>
<td>Important</td>
</tr>
<tr>
<td>Enterohem. <em>E. Coli</em></td>
<td>Minor</td>
<td>Important</td>
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Comparison of parasitic etiologic agents of diarrhea in developing countries and the United States

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</thead>
<tbody>
<tr>
<td>Cryptosporidium</td>
<td>Important</td>
<td>Minor</td>
</tr>
<tr>
<td>Giardia</td>
<td>Minor</td>
<td>Minor</td>
</tr>
<tr>
<td>Strongyloides</td>
<td>Minor</td>
<td>Minor</td>
</tr>
<tr>
<td><em>E. histolytica</em></td>
<td>Minor</td>
<td>Minor</td>
</tr>
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</table>
Section C

Risk Factors, Transmission, and Prevention in Developing Countries
Seasonality in Developing Countries

- Bacterial diarrheas usually peak in hot months
- Viral diarrheas may have some peak in cooler months, but transmission continues year round
Seasonality of Diarrhea in Bangladesh

Matlab Treatment Center Visits for Diarrhea Associated with Enterotoxigenic *Escherichia coli*, *Vibrio cholerae*, and Rotavirus, February 1977–January 1979

![Graph showing the number of cases of diarrhea associated with different causative agents over time. The graph indicates peaks and troughs in cases throughout the year, with different colored lines representing different agents.](image)
Co-infection

- Percentage of diarrhea cases with co-infection (i.e., two or more enteric pathogens)
  - Community-based studies: 11%
  - Hospital-based studies: 12%
Incidence of *Campylobacter* Infections at Increasing Age Groups, in a Cohort of 179 Mexican Children
Transmission of Infectious Agents Causing Diarrhea

- “Fecal–oral” via
  - Food
  - Water
  - Hands
Infectious Dose Affects Transmission

- **Low infectious dose** (e.g., shigella, giardia, rotavirus, cryptosporidium) can be transmitted by person-to-person contact.
- **High infectious dose** (e.g., salmonella, *E. coli*, vibrios) usually transmitted by water or food.
Preventive Interventions for Diarrhea Mortality

- Breastfeeding and complementary feeding
- Improving food safety, water, sanitation, and hygiene
- Vitamin A
- Zinc
- Measles immunization
- Future—specific vaccines, e.g., for rotavirus, ETEC (enterotoxigenic *Escherichia coli*), shigella
Risk Factors for Childhood Diarrhea

- Suboptimal breastfeeding
- Contaminated complementary foods
- Poor quality of water
- Poor sanitation and hygiene
- Malnutrition and micronutrient deficiencies
  - vitamin A deficiency
  - zinc deficiency
Prevention of Childhood Diarrhea

- Breastfeeding
- Safe complementary feeding
- Latrines and hand washing
- Water supply and quality
Prevention of Childhood Diarrhea

- Correcting Vitamin A deficiency—reduces mortality, but not incidence
- Correcting zinc deficiency—reduces mortality and incidence
- Preventing stunting—reduces mortality and incidence