Beyond the Cruise Ship: Norovirus Gastroenteritis

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Disclosures

• Clinical investigator on trials funded by Pfizer
• I WILL mention the off-label use of a drug

Learning Objectives

• Describe the epidemiology and clinical manifestations of norovirus gastroenteritis
• Understand when norovirus testing is indicated

Norovirus

Norovirus: A Bit of History

Norovirus Outbreak Forces Closure Of Three Yala County Schools

Norovirus: A Bit of History
Norovirus: A Bit of History

1968 → 1971 → 1972

Norovirus: Epidemiology

https://www.cdc.gov/norovirus/php/illness-outbreaks-figure.html
**Norovirus: Perfect Outbreak Pathogen**

- Short incubation time
- Low infective dose (18 viral particles!)
- Resistance to common disinfectants
- Persistence on surfaces
- Prolonged shedding of virus 1-2 months
- Susceptibility to re-infection

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**Norovirus: Perfect Outbreak Pathogen**

<table>
<thead>
<tr>
<th>Exposure Setting</th>
<th>Outbreaks</th>
<th>Outbreaks (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare facility</td>
<td>2389</td>
<td>62.7</td>
</tr>
<tr>
<td>Restaurant/transport facility</td>
<td>771</td>
<td>22.1</td>
</tr>
<tr>
<td>School or daycare</td>
<td>214</td>
<td>6.1</td>
</tr>
<tr>
<td>Private residence</td>
<td>69</td>
<td>1.9</td>
</tr>
<tr>
<td>Other/multiple settings</td>
<td>251</td>
<td>7.2</td>
</tr>
</tbody>
</table>

Reported through the National Outbreak Reporting System (NORS), 2009-2012

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**Norovirus: Perfect Outbreak Pathogen**

- Infected food workers cause 70% of food-related outbreaks
- ~50% outbreaks related to touching ready-to-eat food with bare hands
- 20% food workers report working with diarrhea
- Hand hygiene among food workers sub-optimal

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**Norovirus: Biology**

- Caliciviridae
- Non-enveloped, single-stranded RNA viruses
- Genetically and antigenically diverse
- 6 genogroups
  - GI, GII and GIV cause human infections
  - GII.4 most common cause of outbreaks
Norovirus: Biology

Norovirus: Susceptibility

Norovirus: Transmission

Norovirus: Clinical Manifestations
Norovirus: Clinical Manifestations

- Less common
  - Low grade fever
  - Myalgias
  - Headaches
- Prolonged, severe symptoms in immunocompromised

Norovirus: Diagnosis

- History and Physical Exam
- Virology Culture

Norovirus: Kaplan Criteria

- Used by public health to determine if outbreak likely cause by norovirus
  - Mean (or median) illness duration of 12-60 hours
  - Mean (or median) incubation period of 24-48 hours
  - >50% of people affected with vomiting
  - No bacterial agent found
- 30% of outbreaks do not meet these criteria
Norovirus: Treatment

- Supportive care
- No FDA approved antiviral
- Case reports describe use of nitazoxanide (immunocompromised hosts)

Norovirus: Challenges to Vaccine Development

- Genetically and antigenically diverse group of viruses
- Virus not readily cultured
- Immunity to natural infection is complex
  - Strain- or genotype-specific (no protection across genogroups)
  - Not life-long after natural infection
  - Influenced by host genetics of glycan expression
- Need for polyvalent vaccine likely

Norovirus: Candidate Vaccines

<table>
<thead>
<tr>
<th>Vaccine Antigens</th>
<th>Stage of Development</th>
<th>Route of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norovirus VLPs GI.1 and GII.4</td>
<td>Clinical: Phase I and II in adults completed, phase III trials in adults and children planned</td>
<td>Intranasal and Intramuscular</td>
</tr>
<tr>
<td>Norovirus VLPs GI.1, GI.3, GII.4 and GII.12</td>
<td>Pre-clinical</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Norovirus VLPs GI.3 and GII.4 and Rotavirus rVP6</td>
<td>Pre-clinical</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Norovirus VLPs GII.4 and Enterovirus 71</td>
<td>Pre-clinical</td>
<td>Intrapartional (mouse model)</td>
</tr>
</tbody>
</table>

Norovirus: Candidate Vaccines

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<th>Vaccine Antigens</th>
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<tr>
<td>Norovirus P-particles</td>
<td>Pre-clinical</td>
<td>Intranasal</td>
</tr>
<tr>
<td>Norovirus GII.4 P-particle enhanced by adjuvant FlaB</td>
<td>Pre-clinical</td>
<td>Intranasal and Sublingual</td>
</tr>
<tr>
<td>Norovirus, Hepatitis E and Astrovirus P-particles</td>
<td>Pre-clinical</td>
<td>Intranasal</td>
</tr>
<tr>
<td>Virus replicon particles including Norovirus P-domain</td>
<td>Pre-clinical</td>
<td>Intranasal</td>
</tr>
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