Norovirus and Food Safety: What Food Safety Professionals Need to Know

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Division of Viral Diseases, NCIRD, CDC

AFDO Just-In Time Refresher Webinar
November 8, 2019
Norovirus Headlines

‘We haven’t had anything like this before’: Norovirus has spread to at least 10 schools in Salt Lake County

The Salt Lake Tribune

Case count in Canadian oyster norovirus outbreak doubles

ET NEWS DESK | APRIL 18, 2018

Norway norovirus outbreaks linked to seaweed salad from China

By Joe Whitworth on September 3, 2019

THE NEW YORK POST

Chipotle says sick staffer spread norovirus, causing $1 billion market cap loss

Published: July 26, 2017 8:11 a.m. ET

Positive test result for norovirus spurs recall of frozen blackberries

Norovirus Outbreak Craps Up Track And Field World Championships

Patrick Redford
8:08:17 PM · Filed to: TRACK AND FIELD

A Possible Chink In The Armor Of Satan's Bioweapon: Norovirus
Classification of Noroviruses
Clinical Disease

- Incubation period: 12-48 hours
- Acute-onset vomiting and/or diarrhea
  - Watery, non-bloody stools
  - Abdominal cramps, nausea, low-grade fever
- Most recover after 12-72 hours
  - 10-12% seek medical attention; some require hospitalization and fluid therapy
  - More severe illness and death possible in elderly and those with other illnesses
- 30% of infections are asymptomatic

Hall 2011 EID
Phillips 2010 Am J Epid
de Wit 2001 Am J Epid
**Viral Shedding**

- Primarily in stool, but also vomitus
- Occurs for at least 2-3 weeks
- Peaks 4 days after exposure
  - $10^5$-$10^{11}$ viral copies/gram feces
  - May persist after resolution of symptoms
- Infectious dose: 18-2,800 viral particles
- Infectivity of prolonged viral shedding and role in transmission is unclear

Infectivity and Persistence

- Norovirus can remain infectious for $\geq 61$ days and detectable for $>3$ years in groundwater.
Immunity and Genetic Susceptibility

- Human volunteer studies demonstrated short-term homologous immunity (6–24 months)
- Mathematical modeling based on observed disease incidence suggests longer duration (4–8 years)
- Degree of cross-protection unclear
- Genetic correlates of susceptibility/resistance
  - Histo-blood group antigens
  - Secretor status (FUT2 gene)

Parrino 1977 NEJM
Johnson 1990 JID
Simmons 2013 EID
Lindesmith 2003 Nat Med
Norovirus Transmission Cycle

Transmission Vehicles
- Person-to-Person
- Environment & Fomites
- Water
- Food

Exposed Population
- Non-secretor (Innately Resistant)
- Secretor (Susceptible to Infection)

Previously Acquired Immunity
- Present (Protected)
- Absent (Susceptible to Infection)

Symptomatic \ Asymptomatic

Intestinal Pathology
- A
- B

Viral Shedding
- Stool
- Vomit

Secretor (Susceptible to infection)
Non-secretor (Innately Resistant)

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Annual Burden (Lifetime Risk) of Norovirus Disease in the United States

- 570–800 Deaths (1 in 5000–7000)
- 56,000–71,000 Hospitalizations (1 in 50–70)
- 400,000 Emergency Dept Visits (1 in 9)
- 1.7–1.9 million Outpatient Visits (1 in 2)
- 19–21 million Total Illnesses (~5)
Foodborne Norovirus in the United States

- #1 cause of foodborne disease outbreaks
- #1 cause of foodborne illnesses
- #4 cause of foodborne hospitalizations
- #5 cause of foodborne deaths
- Costs $2 billion annually in healthcare expenses and productivity losses

www.cdc.gov/norovirus
Scallan 2011 EID
Hoffmann 2012 JFP
Global Disease Burden of Norovirus

- WHO Foodborne Disease Burden Epidemiology Reference Group (FERG)
  - Global and regional age-stratified estimates of illnesses, deaths, and DALYs caused by specific foodborne hazards
  - Norovirus #1 cause of foodborne illness worldwide

- Total norovirus burden annually:
  - 685 million illnesses and 212,489 deaths
  - 29% of illnesses and 26% deaths in children <5
  - 85% of illnesses and 99% of deaths in developing countries
  - Costs $60 billion in medical expenses and lost productivity
U.S. Norovirus Outbreak Surveillance

- **NORS**
  - Comprehensive epidemiologic surveillance for all foodborne, waterborne, and enteric disease outbreaks
  - Data on setting, transmission mode, exposures, demographics, outcomes

- **CaliciNet**
  - Laboratory surveillance using molecular genotyping of outbreak-associated specimens
  - Data on genotypes to identify new strains and potentially link outbreaks
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- Systems integrated to exchange data on linked outbreaks

<table>
<thead>
<tr>
<th>Transmission Mode</th>
<th>GII.4 Outbreaks (n=2,353)</th>
<th>Non-GII.4 Outbreaks (n=1,396)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-to-person</td>
<td>60.5%</td>
<td>74.3%</td>
</tr>
<tr>
<td>Foodborne</td>
<td>14.8%</td>
<td>23.8%</td>
</tr>
<tr>
<td>Waterborne</td>
<td>0.3%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Environmental*</td>
<td>0.3%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>10.3%</td>
<td>13.9%</td>
</tr>
</tbody>
</table>

* Chi-square p=0.18 for difference between GII.4 and non-GII.4 outbreaks with environmental transmission; for all other transmission modes displayed, Chi-square p <0.001

For all settings displayed, difference between GII.4 and non-GII.4 outbreaks Chi-square p <0.001

# Other healthcare settings include: hospital, dialysis center, and “other healthcare facility”

+ Other settings include: private residence, prison/jail, office, hotel/motel, religious facility, grocery store, ship/boat, “other”
Predictors of Mortality Rate from Multivariable Analysis of Linked Norovirus Outbreaks, NORS and CaliciNet, 2009–2016

GII.4
Healthcare Settings
Foodborne Transmission
≥ 50% cases female
≥ 50% cases 75+ years old
≥ 75% cases with vomiting
≥ 25% cases with fever
Outbreak Nov. - Apr.

Rate ratio and 95% CI

Burke 2019 JID
Epidemiology of Foodborne Norovirus Outbreaks, NORS and CaliciNet, 2009–2015

- 493 foodborne norovirus outbreaks linked in NORS and CaliciNet
  - Most frequent genotypes: GII.4 (258, 52%), GII.6 (45, 9%), and GI.3 (38, 8%)
- GII.4 had higher hospitalization rate, compared to non-GII.4 (13 vs 5 per 1,000 cases)
- Food product implicated in 173 (35%) outbreaks
  - Molluscan shellfish more often implicated in non-GII.4 outbreaks
- 240 (49%) outbreaks with known contributing factor
  - Food workers implicated as source of contamination in 182 (76%) outbreaks
  - Bare hand contact with ready-to-eat food implicated in 99 (54%) food worker outbreaks

Proportion of implicated single food commodities among 101 GII.4 and 72 non-GII.4 foodborne norovirus outbreaks.
*Significantly different (p=0.04).
Key Recommendations for the Food Service Industry

- Underscore provisions in the FDA model Food Code and CDC guidelines
  - Practicing proper hand washing and using utensils and single-use disposable gloves to avoid touching ready-to-eat foods with bare hands
  - Certifying kitchen managers and training food service workers in food safety practices
  - Establishing policies that require food service workers to stay home when sick with vomiting and diarrhea and for at least 48 hours after symptoms stop
Assessment of State Food Safety Regulations for Norovirus Prevention

- Key norovirus recommendations for food service industry in 2013 FDA Food Code
  - Adoption of specific provisions at discretion of state and local governments
  - Detailed adoption not previously tracked by any federal agency

- Analyzed food codes of 50 states, DC, and Puerto Rico for 5 specific provisions:
  1. Require hand washing
  2. Prohibit bare-hand contact with RTE food
  3. Exclude ill staff until ≥24 hours after asymptomatic
  4. Require certified food protection manager
  5. Response plan to contamination events
Rate of Reported Foodborne Norovirus Outbreaks Among States Adopting Provisions

- Lower rates of reported outbreaks in states that adopted these provisions
- Suggests potential impact of adoption on reducing incidence of foodborne norovirus
- Many potential confounders and limitations of outbreak surveillance data

Kambhampati 2016 JFP
## Attribution of US Disease Burden to Infected Food Workers

<table>
<thead>
<tr>
<th>Scenario description</th>
<th>Proportion of symptomatic foodworkers excluded</th>
<th>Proportion of post-symptomatic foodworkers excluded (2 days)</th>
<th>No. symptomatic norovirus cases (million/year)</th>
<th>No. symptomatic norovirus cases averted (million/year)</th>
<th>% symptomatic norovirus cases averted</th>
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<tr>
<td>(i) No exclusion</td>
<td>0</td>
<td>0</td>
<td>30.4</td>
<td>-6.0</td>
<td>-24.2%</td>
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<tr>
<td>(ii) Referent</td>
<td>2/3</td>
<td>0</td>
<td>24.3</td>
<td>Referent</td>
<td>Referent</td>
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<tr>
<td>(iii) Referent and full post-symptomatic compliance</td>
<td>2/3</td>
<td>1</td>
<td>23.2</td>
<td>0.85</td>
<td>3.5%</td>
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<tr>
<td>(iv) Full symptomatic compliance</td>
<td>1</td>
<td>0</td>
<td>18.5</td>
<td>5.4</td>
<td>22.8%</td>
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<tr>
<td>(v) Full compliance</td>
<td>1</td>
<td>1</td>
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*Yang 2018 AJE*
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<td>(i) No exclusion</td>
<td>0</td>
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<td>30.4</td>
<td>15.3, 40.4</td>
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<td>17.2</td>
<td>10.5, 23.6</td>
<td>6.7</td>
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<td>Virus Like Particle (VLP)</td>
<td>Preclinical</td>
<td>Phase 1</td>
<td>Phase 2</td>
<td>Phase 2b</td>
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<tr>
<td>Daiichi Sankyo Company, Limited &amp; UMN Pharma Inc., Japan</td>
<td>• GI.3, GII.4, rotavirus VP6&lt;br&gt;• Intramuscular Injection&lt;br&gt;• Trials in mice</td>
<td>Takeda Pharmaceutical Company Limited</td>
<td>• GI.1/GII.4&lt;br&gt;• Intramuscular injection&lt;br&gt;• Trials in children 6 weeks through 8 years of age, adults, the elderly &gt;60 years, and military recruits</td>
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<td>Chinese Academy of Sciences</td>
<td>• GII.4, Enterovirus 71&lt;br&gt;• Intraperitoneal Injection&lt;br&gt;• Trials in mice</td>
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<td>Arizona State University</td>
<td>• GII.4&lt;br&gt;• Intranasal&lt;br&gt;• Trials in mice</td>
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<td>Vaxart, Inc.</td>
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<td>• GI.1&lt;br&gt;• Oral Pill&lt;br&gt;• Trials in healthy adults</td>
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<td>Cincinnati Children’s Hospital Medical Center &amp; University of Cincinnati</td>
<td>• GII.4, Hepatitis E, Astrovirus&lt;br&gt;• Intranasal&lt;br&gt;• Trials in mice</td>
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Conclusions

- Noroviruses are the leading cause of foodborne disease and acute gastroenteritis outbreaks in the U.S.
  - Pose substantial morbidity, mortality, and public health burden
  - Temporal and genotypic variations underscore need for ongoing surveillance

- Lessons learned from US norovirus outbreak surveillance
  - Infected food workers are the most common source of foodborne norovirus outbreaks, often by touching ready-to-eat foods in restaurants with bare hands
  - Continued need for technical and resource support for local public health agencies and coordination between epidemiology, laboratory, and environmental health

- Guide development, prioritization, and targeting of interventions
  - Improved food safety and infection control practices
  - Candidate vaccines for specific age groups, settings, and/or occupations
Acknowledgments

Norovirus Epidemiology Team
• Neha Balachandran
• Laura Calderwood
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• Ben Hallowell
• Anita Kambhampati
• Claire Mattison
• Mary Wikswo

Viral Gastroenteritis Branch
• Rachel Burke
• Umesh Parashar
• Jan Vinjé

Collaborating CDC Programs
State, Local, Regulatory Partners
USDA-NIFA Food Virology Collaborative (NoroCORE)

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348
www.cdc.gov/norovirus

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Extra Slides
Rapid reporting, response, and investigation
- Identify source and transmission mode
- Collect appropriate specimens

Promote appropriate hand hygiene
- Wash with soap and water ≥ 20 seconds
- Alcohol-based hand sanitizers?

Prompt and thorough disinfection
- Bleach solution for contaminated surfaces
- Other EPA-approved disinfectants?

Manage and exclude ill persons
- ≥ 24-72 hrs after symptom resolution
- Accommodating sick pay/leave policies
Chlorine Inactivation of Norovirus GII.4 Sydney Using Human Intestinal Enteroid Culture System

![Graph showing chlorine inactivation of Norovirus GII.4 Sydney using human intestinal enteroid culture system. The graph displays Norovirus RNA copies per well across different chlorine concentrations and time points (1 hpi and 3 dpi). The x-axis represents chlorine concentrations in ppm ranging from 5 to 5,000, and the y-axis represents Norovirus RNA copies per well ranging from $10^2$ to $10^7$. The graph includes bars for input, 1 hpi, and 3 dpi samples, with error bars indicating variability. The neutralization control is also shown.]