Norovirus Epidemiology and Food Safety

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Noroviruses: The Perfect Human Pathogens?

- Highly contagious
- Rapidly and prolifically shed
- Diverse and constantly evolving
- Evoking limited immunity
- Moderately virulent

Hall 2012 JID
Classification of Noroviruses

Genogroup VII
- canine

Genogroup III
- bovine

Genogroup II
- human, porcine

Genogroup VI
- canine

Genogroup IV
- human, feline/canine

Genogroup V
- murine

Vinje 2015 JCM
<table>
<thead>
<tr>
<th>Norovirus Strain</th>
<th>Years of Circulation</th>
<th>Increased Number of US Outbreaks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bristol</td>
<td>1987–1994</td>
<td>None</td>
</tr>
<tr>
<td>Henry</td>
<td>2000–2002</td>
<td>None</td>
</tr>
<tr>
<td>Hunter</td>
<td>2003–2006</td>
<td>None</td>
</tr>
<tr>
<td>Asia</td>
<td>2004–2006</td>
<td>None</td>
</tr>
<tr>
<td>Osaka</td>
<td>2005–2007</td>
<td>None</td>
</tr>
<tr>
<td>New Orleans</td>
<td>2009–present</td>
<td>None</td>
</tr>
<tr>
<td>Sydney</td>
<td>2012–present</td>
<td>None</td>
</tr>
</tbody>
</table>

Pringle 2015 Future Micro
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)

Hall 2013 EID
Burden of Foodborne Norovirus in the United States

• Causes 58% of all domestically-acquired foodborne illness from known agents
  – #1 cause of illness
  – #2 cause of hospitalization
  – #4 cause of death

• Costs $2 billion per year in medical care services and lost productivity

Scallan 2011 EID
Hoffmann 2012 JFP
Global Burden of Norovirus

- WHO Foodborne Disease Burden Epidemiology Reference Group (FERG)
- Global and regional age-stratified estimates of illnesses, deaths, and DALYs
- Norovirus ranking as foodborne hazard:
  - #1 cause of foodborne illness
  - #4 cause of foodborne deaths
  - #5 cause of foodborne DALYs
- Total norovirus burden annually:
  - 685 million cases; 200 million in children <5
  - 212,489 deaths; 54,214 in children <5
  - 85% of illnesses and 99% of deaths occur in developing countries
  - $60 billion in direct health system costs and productivity loses

Pires 2015 PLoS One
Kirk 2015 PLoS Med
Bartsch 2016 PLoS One
Hall 2016 Exp Rev Vac
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% seek medical attention; some require hospitalization and fluid therapy
  – More severe disease in elderly, young children, and immune compromised
• 30% of infections are asymptomatic

de Wit 2001 AJE
Phillips 2010 AJE
Hall 2011 EID
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 unknown

Atmar 2008 EID
Aoki 2010 J Hosp Infect
Teunis 2008 J Med Virol
Atmar 2014 JID
Norovirus can remain infectious for ≥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

Symptomatic

Asymptomatic

Infected

Exposed Population

Previously Acquired Immunity

Present

Absent

(Susceptible to Infection)

(Susceptible to infection)

Non-secretor

Secretor

(Innately Resistant)

(Susceptible to infection)

Viral Shedding

Infecting Pathology

A

B

Transmission Vehicles

Person-to-Person

Environment & Fomites

Water

Food

Hall 2012 PPPID
U.S. Norovirus Outbreak Surveillance

• **NORS**
  - Epidemiologic surveillance for all 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
Norovirus Outbreaks by Month, NORS, 2009-2012 (N=4,318)

Hall 2014 MMWR
Setting of Norovirus Outbreaks, NORS, 2009-2012 (N=3,243)

- Long-Term Care Facilities: 59%
- Restaurants: 17%
- Schools: 5%
- Caterer/Banquet Facility: 5%
- Hospitals: 3%
- Private Residence: 2%
- Daycares: 2%
- Other/Multiple: 7%

Note: Does not include 44 (1%) norovirus outbreaks meeting VSP posting criteria

Hall 2014 MMWR
Transmission Mode of Norovirus Outbreaks, NORS, 2009-2012 (N=4,318)

- Person-to-person: 69%
- Foodborne: 23%
- Unknown: 7%
- Waterborne: 0.3%
- Environmental: 0.3%

Hall 2014 MMWR
Norovirus Genotype Distribution by Transmission Route, CaliciNet, 2009-2013

Foodborne Outbreaks (n=449)

- GI.3 4%
- GI.4 1%
- GI.6 8%
- GI.7 2%
- GI.1 8%
- GI.2 3%
- GI.12 5%
- GI.7 3%
- GI.6 3%

Person-to-Person Outbreaks (n=2371)

- GI.4 78%
- GI.6 4%
- GI.3 1%
- GI.7 1%
- GI.12 1%
- GI.3 2%
- GI.4 1%
- GI.6 5%
- GI.7 1%
- GI.1 6%

Non-GI.4 genotypes 3x more likely to be foodborne

Vega 2014 JCM
# Predominant Epidemiologic Characteristics of Norovirus Outbreaks by Genotype

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>GII.4</th>
<th>Non-GII.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seasonality</td>
<td>Winter</td>
<td>Spring-summer or non-seasonal</td>
</tr>
<tr>
<td>Setting</td>
<td>Healthcare facilities</td>
<td>Non-health care (restaurants, schools, etc.)</td>
</tr>
<tr>
<td>Transmission</td>
<td>Person-to-person</td>
<td>Foodborne</td>
</tr>
<tr>
<td>Ages affected</td>
<td>≥65 years</td>
<td>&lt;65 years</td>
</tr>
<tr>
<td>Severity</td>
<td>Elevated rates of hospitalization and death</td>
<td>Lower rates of severe outcomes</td>
</tr>
</tbody>
</table>

Vega 2014 JCM  
Leshem 2013 EID  
Desai 2012 CID  
Matthews E&I 2012
Foodborne Norovirus Outbreaks by State, NORS, 2009–2012

- 1,008 outbreaks reported by 43 states
- Median outbreaks per state: 9 (range 1–117)
- Median reporting rate per million person-years: 0.6 (range 0.05–5.5)

*Legend indicates rate ranges divided by quartile.*

Hall 2014 MMWR
Settings of Foodborne Norovirus Outbreaks, NORS, 2009–2012

- Restaurant: 64%
- Catering or Banquet facility: 17%
- Sit-Down: 77%
- Fast Food: 13%
- Other/multiple: 13%
- Other: 10%
- Private Residence: 4%
- Health Care Facilities: 1%
- Schools and Daycare: 1%

Hall 2014 MMWR
Contributing Factors and Foods Implicated in Foodborne Norovirus Outbreaks, NORS, 2009–2012

- Factors contributing to contamination reported in 520 (52%) outbreaks
  - 70% implicated infectious food worker as source
    - 54% involved bare-hand contact with ready-to-eat foods

- Specific food item in 324 (32%) outbreaks
  - 92% implicated foods contaminated during final preparation; 75% were foods eaten raw
  - Single food category identified in only 21%
    - Vegetable row crops (30%)
    - Fruits (21%),
    - Mollusks (19%)
Environmental Health Specialists Network (EHS-Net) Studies on Restaurant Food Safety

• Ill food worker study
  – 1 in 5 food workers report working while sick with diarrhea and vomiting
  – Significant factors in their decision were fear of job loss and concerns about leaving coworkers short staffed

• Hand hygiene study
  – Food workers practice proper hand hygiene only 27% of the time recommended
  – Less frequently (16%) when gloves were used

Carpenter 2013 JFP
Green 2006 JFP
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

Kambhampati 2016 JFP
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
Conclusions and Public Health Implications

- Noroviruses are the leading cause of reported foodborne disease outbreaks in the United States.
- Infected food workers are the most common source of foodborne norovirus outbreaks, often by touching ready-to-eat foods in restaurants with bare hands.
- Food service industry can help foster an environment that promotes food safety and ensures that food service workers adhere to recommended practices.
- Continued need for capacity of state and local health departments to investigate and report outbreaks.
• 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
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

Hall 2014 MMWR
Norovirus Vaccine Development

• Two randomized double blind placebo-controlled multicenter trials with healthy adults 18-50 years old:
  1. Intranasally delivered Norwalk virus (genotype GI.1) VLP vaccine followed by homologous challenge
     – Vaccine protected against illness (~50%) and decreased infection frequency (~25%)
     – First demonstration that a norovirus vaccine can prevent disease
  2. Intramuscular bivalent (GI.1 and consensus GII.4) VLP vaccine followed by GII.4 challenge
     – Did not significantly reduce illness or infection, but did reduce disease severity and decreased viral shedding
     – Hampered by low disease rate from challenge and high baseline infection rate in control group

• Key questions remaining: duration of immunity, cross-protection, other formulations, target populations

Atmar 2011 NEJM
Bernstein 2014 JID
Aliabadi 2015 ERV
Norovirus Vital Signs Report
www.cdc.gov/vitalsigns/norovirus/

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 63
June 3, 2014


Compute Hall, DVM1, Mary E. Winnie, MPH2, Kimberly Pringle, MD2, L. Hannah Gould, PhD, Ursula D. Parashar, MD, MPH1

Author affiliations at end of text

Introduction
Norovirus is the leading cause of acute gastroenteritis and foodborne disease in the United States, causing an estimated 15 U.S. residents to become ill each year as well as 6,000–71,000 hospitalizations and 370–800 deaths, predominantly among young children and the elderly. Whereas noroviruses often spread through person-to-person contact, foodborne transmission can cause widespread exposure and presents important prevention opportunities.

Methods
CDC analyzed 2009–2012 data on suspected and confirmed norovirus outbreaks reported by state, local, and territorial health departments through the National Outbreak Reporting System (NORS) to characterize the epidemiology of foodborne norovirus outbreaks.

Results
During 2009–2012, a total of 1,000 foodborne norovirus outbreaks were reported to NORS, constituting 48% of all foodborne outbreaks with a single known cause. Outbreaks were reported by 43 states and occurred year-round. Restaurants were the most common setting (64% of food preparation reported in outbreaks). Of 520 outbreaks with factors contributing to contamination reported, food workers were implicated as the source in 70%. Of 524 outbreaks with an implicated food, most resulted from food contaminated during preparation (92%) and food consumed raw (75%). Specific food categories implicated in only 67 outbreaks; the most frequently implicated were vegetable-row crops (e.g., leafy vegetables) (30%), fruits (21%), and mollusks (19%).

Conclusions
Noroviruses are the leading cause of foodborne disease outbreaks and are most often associated with contamination of food in restaurants during preparation by infected food workers.

Implications for Public Health Practice
Improving adherence to appropriate hand hygiene, excluding ill staff members from working until 48 hours after symptom resolution, and supervision by certified kitchen managers are all recommended to reduce the incidence of foodborne norovirus disease.

Preventing Norovirus Outbreaks
Food service has a key role.

Norovirus often gets attention for outbreaks on cruise ships, but those account for only about 1% of all reported norovirus outbreaks. Norovirus is very contagious, and outbreaks can occur anywhere people gather or food is served. People with norovirus usually vomit and have diarrhea. Some may need to be hospitalized and can even die. Infected people can spread norovirus to others through close contact or by contaminating food and surfaces. Food service workers who have norovirus can contaminate food and make many people sick. In norovirus outbreaks, for which investigators reported the source of contamination, 70% are caused by infected food workers.

The food service industry can help prevent norovirus outbreaks by:

- Making sure that food service workers practice proper hand washing and avoid touching ready-to-eat foods, such as raw fruits and vegetables, with their bare hands before serving them.
- Certifying kitchen managers and training food service workers in food safety practices.
- Requiring sick food workers to stay home, and considering use of paid sick leave and on-call staffing, to support compliance.

Want to learn more? Visit:

www.cdc.gov/vitalsigns

Norovirus Vital Signs Report
www.cdc.gov/vitalsigns/norovirus/
Norovirus is a very contagious virus that can infect anyone. You can get it from an infected person, contaminated food or water, or by touching contaminated surfaces. The virus causes your stomach or intestines or both to get inflamed. This leads you to have stomach pain, nausea and diarrhea and to throw up. These symptoms can be serious for some people, especially young children and older adults...

Have You Ever Heard of Norovirus?

This PLOS norovirus collection fills critical knowledge gaps and provides key information for the development of a much-needed vaccine. This is a "living collection" and more articles will be added over time.

Protect Yourself from Norovirus!

Wash your hands often
Thank You… Questions?

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

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

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.
HAVE YOU EVER HEARD OF NOROVIRUS?