Multistate Outbreak of Shiga Toxin-producing *E. coli* O121 and O26 Infections Associated with Flour

Karen P. Neil MD, MSPH
Outbreak Response and Prevention Branch
Division of Foodborne, Waterborne, and Environmental Diseases

CDC Food Industry Safe Foods Forum
October 3, 2016
Shiga Toxin-producing *E. coli* (STEC)

- Colonizes intestinal tract of healthy ruminants (*e.g.*, cattle, deer)
- Causes diarrheal illness
  - Can be severe in children and older adults
  - HUS in ~11% of *E. coli* O157 infections and ~1% of non-O157 infections
- Non-O157 STEC outbreaks increasingly identified in United States
  - > 40 outbreaks since 1990
  - Ground beef, leafy vegetables, unpasteurized dairy common vehicles
  - Also person-to-person, animal, and environmental

http://www.cdc.gov/foodsafety/outbreaks/multistate-outbreaks/outbreaks-list.html
PulseNet

- National network of >85 public health and regulatory agency laboratories that conduct foodborne disease surveillance
- Perform molecular subtyping of foodborne disease-causing bacteria
- Current method is pulsed-field gel electrophoresis (PFGE)
- Create PFGE pattern or DNA fingerprint for each isolate
Whole Genome Sequencing (WGS)

- Analyzes entire DNA sequences of bacteria to identify differences
- High-quality single nucleotide polymorphism (SNP) analysis
  
  \[
  \text{ATGTT}_C\text{CTC} = \text{test sequence} \\
  \text{ATGTT}_G\text{CTC} = \text{reference sequence}
  \]

- Infer evolutionary relationships between a group of bacteria
- Identify how closely related bacteria are and whether they are likely part of an outbreak
Data Used During Outbreak Investigations

**Epidemiologic**
- Distribution of illnesses geographically & over time
- Exposures occurring more often in ill people than expected
- Illness subclusters

**Traceback**
- Identifying common point of contamination in distribution chain
- Environmental assessments

**Laboratory**
- Finding the bacteria in the food or production environment
- DNA fingerprint linking bacteria in food to bacteria in ill people
Outbreak Investigation
Outbreak Detection and Initial Investigation

- In February 2016, PulseNet identified cluster of *E.coli* O121 infections with the same, uncommon PFGE pattern
- Initial interviews suggested leafy greens
- As investigation continued leafy greens appeared less likely
  - Additional illnesses continued longer than expected
  - Signal less compelling as additional people interviewed
Open-Ended Interviews

- In mid-March, moved to open-ended hypothesis generating interviews
  - Can identify unusual or “stealth” exposures
  - Conversational style
  - All exposures in week before illness
  - Successful in solving other challenging outbreaks

- Single interviewer conducted 10 open-ended interviews
Open-Ended Interviews: Flour Hypothesis

- All 10 (100%) reported they or household member baked
- 8/10 (80%) specifically remembered baking something homemade in week before illness began (5 definite, 3 maybe)
- Of the 5 who definitely baked:
  - 4/5 ate or tasted the raw dough or batter
  - 3/4 used Gold Medal flour; the 4th used either Gold Medal or another brand
  - 2 still had the bags of Gold Medal flour used before illness
    - Both bags produced in same plant within one day
    - Both people reported eating raw cookie dough
Flour as a Vehicle for STEC

- Flour is a raw agricultural product
- Suspected but not proven in past STEC outbreaks
  - 2009 *E. coli* O157 outbreak linked to commercial unbaked cookie dough
  - 2012–2013 *E. coli* O121 outbreak linked to frozen food products
  - 2015 *E. coli* O157 outbreak linked to a dessert pizza at a pizza chain
- STEC had been isolated from dough and flour previously
Matched Case-Case Study

- Conducted in late April through June 2016
  - People with non-STEC enteric infections as comparison; sought 4 controls for each case
  - Matched on age group, gender, and state of residence

- Questionnaires focused on baking
  - Whether someone in household baked something homemade
  - Flour and baking mix brands used
  - Tasting or eating raw dough or batter
  - Other foods of interest

- Illness significantly associated with someone in the household baking something homemade with flour, using Gold Medal brand flour, and eating/tasting raw dough
Traceback Investigation

- Detailed product information from 3 ill people with leftover packages of Gold Medal flour

- Records collected from restaurants linked to ill people
  - In early May 2016, identified 3 young children exposed to raw dough at restaurants in several states
  - All played with the raw dough and some ate it

- *E. coli* O121 from ill people closely related genetically to outbreak strain

- Identified that flour was produced in the same week in November 2015 at the General Mills facility in Kansas City, Missouri
Initial Product Recall

- On May 31, 2016, General Mills recalled certain production dates of several sizes and varieties of Gold Medal Flour, Gold Medal Wondra Flour, and Signature Kitchens Flour.
- On June 1, CDC and FDA post initial investigation announcements.

Photos from: http://www.fda.gov/Safety/Recalls/ucm504235.htm
Product Testing

- State public health laboratories sent samples of leftover flour collected from ill people’s homes in several states to FDA for testing
  - Initial testing did not identify STEC O121
  - Testing procedure modified after delayed lactose fermentation noted in clinical isolates
    - Appeared lactose negative initially
    - Might not be further screened as this is atypical for *E. coli*

- General Mills also conducted flour testing
Product Testing

- In June, FDA isolated STEC O121 from leftover flour samples from Arizona, Colorado, and Oklahoma
  - Flour isolates closely related genetically by WGS to clinical isolates
  - Oklahoma sample from flour not included in the initial recall

- In July, FDA conducted WGS on an O26 isolate provided by General Mills
  - Flour isolate closely related genetically to a clinical O26 isolate
  - This ill person subsequently included in the investigation
  - Flour tested not covered under earlier recalls
Additional Recalls

- General Mills issued recall expansions on July 1 and July 25 to include additional production dates
- Downstream product recalls issued by companies that had used recalled flour to make their own products
  - Various baking mixes
  - Frozen entrees and snacks
- In total, over 200 products across ~30 brands recalled
People infected with the outbreak strains of *E. coli* O121 or *E. coli* O26, by state of residence, as of September 28, 2016 (n=63)
People infected with the outbreak strains of *E. coli* O121 or *E. coli* O26, by date of illness onset, September 28, 2016 (n=63)
Public Health Messaging

- It is not safe to taste or eat raw dough or batter
  - Flour or other ingredients used to make raw dough or batter can be contaminated
  - Always bake items made with raw dough or batter before eating them
  - Do not taste raw dough or batter

- Do not give playdough made with raw flour to children

- Restaurants and retailers should not serve raw dough to customers or provide raw dough for children and other guests to play with
Summary

- Epidemiologic, traceback, and laboratory investigations linked this outbreak of STEC O121 infections to flour produced at a single facility
- First time flour has been definitively implicated in any STEC outbreak
- Highlights the risks of consuming or handling raw dough
- Collaborative efforts of state, local, and federal public health and regulatory efforts key to successful investigation
# Acknowledgements

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.

## State and Local Health Departments and Regulatory Agencies

<table>
<thead>
<tr>
<th>Alabama</th>
<th>Massachusetts</th>
<th>Oklahoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arkansas</td>
<td>Maryland</td>
<td>Oregon</td>
</tr>
<tr>
<td>Arizona</td>
<td>Michigan</td>
<td>Pennsylvania</td>
</tr>
<tr>
<td>California</td>
<td>Minnesota</td>
<td>Tennessee</td>
</tr>
<tr>
<td>Colorado</td>
<td>Missouri</td>
<td>Texas</td>
</tr>
<tr>
<td>Iowa</td>
<td>Montana</td>
<td>Virginia</td>
</tr>
<tr>
<td>Illinois</td>
<td>Nebraska</td>
<td>Washington</td>
</tr>
<tr>
<td>Indiana</td>
<td>New York</td>
<td>Wisconsin</td>
</tr>
</tbody>
</table>

## Federal Partners

- U.S. Food and Drug Administration
  - Core Response Team 3
  - Pacific Regional Laboratory NW
  - District Offices
- CDC Enteric Diseases Laboratory Branch
- CDC Outbreak Response and Prevention Branch
  - Lyndsay Bottichio
  - Laura Burnworth
  - Sam Crowe
  - Ian Williams
  - Matt Wise
Questions?