Detecting and Investigating Enteric Disease Outbreaks

Tess Gorden, MPH
Enteric Epidemiologist
Indiana State Department of Health
Objectives

• Understand how outbreaks and clusters are detected through pathogen-specific surveillance.
• Describe the role of local public health in national pathogen-specific surveillance.
• Interpret results from clinical specimen testing.
• Explain how subtyping of the causative agent can be used in an outbreak investigation.
• Discuss recent shifts in the nature of foodborne disease outbreaks.
Pathogen-specific Surveillance

Also called “reportable diseases,” “notifiable diseases,” or “laboratory-based reporting”

• Reports of individual laboratory-confirmed cases of foodborne disease by medical and laboratory staff
  – Submission of clinical isolates, upon request
• Only covers diseases specified by public health agency
• Cases linked to each other by common pathogen
Steps in Pathogen-specific Surveillance

1. Illness in individual
2. Individual seeks health care
3. Specimen collected
4. Diagnosis by health-care provider/laboratory
5. Initial report to health department
6. Submission of isolate to public health laboratory
7. Further characterization
8. Entry into electronic database
9. Forward to CDC
10. Follow-up interview of case
11. Analysis of cases for clusters/outbreaks

Common pathogen links cases over time

Starts with positive lab result
Initial Report

- From health-care provider or laboratory
- Standardized form
- Information of interest
  - Patient identifiers
  - Basic demographic information
  - Clinical information
  - Laboratory results

http://www.in.gov/isdh/25366.htm
Follow-up Case Interview

• To identify potential exposures leading to illness
• Similar to interview for complaint system but *tailored* to specific pathogen
  – High-risk food exposures for agent
  – Other exposures related to agent (e.g., contact with ill people, animals, water)
• Often occurs weeks after exposure leading to
  – more illness
  – poor recall
Laboratory Characterization of Pathogen

- Submission of patient isolate to public health laboratory for confirmation and subtyping
- Increased detail about the pathogen (e.g., serotyping, PFGE) improves
  - Recognition of clusters
  - Linking a cluster with an exposure
- Most critical with common pathogens
Analysis for Clusters

• Examine cases by pathogen over time using
  – Different levels of specificity of pathogen (e.g., species, selected subtypes)
  – Subgroups of population (certain time, place, or person characteristics)

• Look for increase in number of cases over expected or baseline, indicating a cluster
  – Exact # not defined
    • Regionality
  – Time/Place/Person
Analysis by Causative Agent

Lab-confirmed salmonellosis cases by month of diagnosis, 2010.

Month of Diagnosis

Number of Cases

All *Salmonella*
Analysis by Causative Subtype

Lab-confirmed salmonellosis cases by month of diagnosis, 2010.
Analysis with Age Group

Lab-confirmed salmonellosis cases by month of diagnosis, 2010.

- All *Salmonella*
- *Salmonella* Javiana among persons <5 yrs.

Month of Diagnosis

Number of Cases

Indiana State Department of Health
Strengths of Pathogen-specific Surveillance

Primary means to detect outbreaks that are

- Wide-spread (i.e., multijurisdictional),
  - Due to prolonged low-level food contamination,
    - Intermittent/over time
  - Due to diseases with a long incubation (e.g., hepatitis A)
Pathogen-specific Surveillance Issues

- Incomplete detection and reporting
Pathogen-specific Surveillance Issues

- Incomplete detection and reporting
- Elapsed time
Pathogen-specific Surveillance Issues

- Incomplete detection and reporting
- Elapsed time
- Availability of isolate for further characterization
Laboratory Characterization
Isolate vs. Specimen

- An isolate is the microbial strain that has already been grown in a culture.
- A specimen is the raw clinical material.
- Isolates are preferred:
  - Saves time and resources by not needing to grow the culture first.
  - Clinical material samples degrade in quality and can make it more difficult to identify the microorganism.
Laboratory Characterization of Pathogen

• Submission of patient isolate to public health laboratory for confirmation and subtyping

• Increased detail about the pathogen (e.g., serotyping, PFGE) improves
  – Recognition of clusters
  – Linking a cluster with an exposure

• Most critical with common pathogens
Subtyping of Causative Agent

• Characterization of microorganisms below the species level using characteristics that
  – Differ between strains
  – Are same among isolates with common origin

• Variety of subtyping methods (e.g., serotyping, phage typing, antibiotic susceptibility, pulsed field gel electrophoresis [PFGE], multiple-locus variable number tandem repeat analysis [MLVA]), not all of which are available for all organisms

• Not all methods equally discriminatory
Uses of Subtyping in Outbreak Investigation

• Usefulness based on presumption
  – Isolates in an outbreak have a common origin
  – Single strain will be the culprit in most outbreaks

• Uses
  – Link cases together
  – Link foods with outbreaks
  – Refine case definition decreasing misclassification in epidemiologic studies
  – Link clusters in different locations
Pulsed Field Gel Electrophoresis (PFGE)

- Separation of DNA fragments in a gel using a pulsing electric field
- Creates visual banding pattern unique for isolate
- Different DNA composition → different PFGE
- Indistinguishable patterns suggest similar origin of isolates

Cluster of indistinguishable patterns
PulseNet Laboratory Network

Participating Laboratories

PFGE Patterns

Patterns uploaded by testing laboratory

PulseNet National Database (CDC)

• Monitors for similar patterns
• Notifications of clusters
• Can be queried

Standardized testing of
• *E. coli* O157:H7,
• *Salmonella*,
• *Shigella*,
• *Listeria*, and
• *Campylobacter*
Subtyping Issues

- Matching of subtypes not proof of common exposure
- Association of multiple subtypes with one outbreak
- Need for routine subtyping (in real time)
- Limited ability of available methods to distinguish between strains
- Patient isolate not available if rapid diagnostic testing used
National Pathogen-Specific Surveillance Systems
National Pathogen-specific Surveillance

- NNDSS: National Notifiable Disease Surveillance System
  - Data from pathogen-specific surveillance forwarded to CDC (minimal case information)
  - Statistical algorithm used to identify increases
National Pathogen-specific Surveillance

- PulseNet: National Molecular Subtyping Network for Foodborne Disease Surveillance
  - Laboratory network using standardized Pulsed Field Gel Electrophoresis (PFGE) methods
  - PFGE patterns uploaded by labs for STEC, *Salmonella, Shigella, Listeria, Campylobacter*
  - Comparisons of patterns to identify clusters
National Pathogen-specific Surveillance

- CaliciNet: National Electronic Norovirus Outbreak Network
  - Laboratory network that subtypes/sequences norovirus isolates related to outbreaks
  - Data uploaded to CDC allows linkage of outbreaks and identification of new variants
National Pathogen-specific Surveillance

- NARMS: National Antimicrobial Resistance Monitoring System—enteric bacteria
  - Submission of *Salmonella, Shigella, E. coli* O157, *Campylobacter*, and non-cholerae *Vibrio* to CDC
  - Determines trends in antimicrobial resistance
Local Public Health Role in National Pathogen-Specific Surveillance

• Local pathogen-specific case reports and laboratory results feed into national surveillance

• Important for local health departments to
  – Collect data in format consistent with other investigators.
  – Streamline reporting and isolate submission.
  – Share case reports with state and submit patient isolates as quickly as possible.
  – Use national systems to learn about outbreaks in other jurisdictions.
What difference does one local case make?

- Two *E. coli* O157:H7 infections in MN with same PFGE pattern; both ate tenderized steaks
- Through PulseNet, single cases identified in KS and MI; both ate tenderized steaks
- Steaks eaten by cases from same plant
- Recall of 739,000 lbs. of beef
- Outbreak generated high levels of concern about needle/blade tenderized steaks
Tenderized Beef

• June 11, 2003, the Minnesota Department of Health (MDH) identified two *E coli* O157:H7 cases (same PFGE subtype).
  – Both had consumed Brand A vacuum packed frozen steaks sold by door-to-door vendors.

• June 17, a message encouraging states to share info on any PFGE matches posted on PulseNet.

• MDH epidemiologists contacted epidemiologists at MI and KS. One isolate from each state had an indistinguishable PFGE pattern from the MN isolates.
Tenderized Beef

- Both MI and KS case patients consumed steaks purchased from door-to-door vendors.
- Based on USDA numbers on product labels, the steaks consumed in MN, MI, and KS originated from the same processing plant in Illinois.
  - The steak consumed by the KS case was a different brand.
- June 29, implicated processing plant voluntarily recalling 739,000 lbs. of frozen beef products
Tenderized Beef

• Investigation generated concern about the safety of needle/blade tenderized steaks.
• This outbreak ultimately resulted in
  – 6-confirmed O157 cases in MN
  – 1-confirmed case in MI, KS, IA, and ND
• Product had been distributed nationwide to restaurants, institutions, and retailers under several different brand names.
• The single cases from MI and KS were critical in allowing officials to take action.
Multijurisdictional Outbreak Investigations
And how they differ from the “Traditional” Outbreak Investigation Model
Traditional Outbreak Scenario

Focal outbreak

- Caused by local food handling error (endpoint contamination event)
- Large number of cases in one jurisdiction
- Detected by affected group
- Local investigation
- Local solution
Traditional Outbreak Scenario

Production

Processing

Distribution

Final preparation and cooking

Farm

Localized cases

Problematic food safety practices
Newly Identified Outbreak Scenario

Dispersed outbreak

- Caused by industrial contamination event (during production, processing, or distribution) with a widely distributed food
- Small numbers of cases in many jurisdictions
- Detected by pathogen-specific surveillance with subtyping
- Multijurisdictional investigation
- Solution that has broad implications
Newly Identified Outbreak Scenario

Production

Processing

Distribution

Final preparation and cooking

Farm

Problematic food safety practices

Dispersed cases

39
Significance of Multijurisdictional Outbreaks

- Small proportion (2%) of reported foodborne outbreaks are multistate
- Disproportionate public health impact
  - 7% of outbreak-related illnesses
  - 31% of outbreak-related hospitalizations
  - 34% of outbreak-related deaths
  - 40% of E. coli O157:H7 and 25% of Salmonella and hepatitis A outbreaks

Significance of Multijurisdictional Outbreaks

Multistate foodborne outbreaks, 1989-2008

Year of Report

Number of outbreaks

Source: CDC, National Foodborne Disease Outbreak Surveillance System
Reasons for Increase

• Centralized production and wide distribution of food products
• Globalization of food supply
• Increased detection of outbreaks through
  – Improved surveillance efforts
  – Subtyping of causative agents
  – Information sharing
Local Significance of Multijurisdictional Outbreaks

• “Local” outbreak may herald a national or international event.
Multijurisdictional Outbreak Indicators

• Implicated food contaminated before point of service and is
  – Commercially distributed, processed, or ready-to-eat item
  – Fresh produce item
  – Ground beef in *E. coli* O157:H7 outbreak

• Illnesses linked to multiple food-service establishments

• Molecular subtype of causative agent matches agent associated with outbreaks in other locations

• Exposed persons have subsequently dispersed
Which of the following outbreaks are likely to involve cases residing in multiple jurisdictions?

- Illness linked to food safety problem at elementary school cafeteria: No
- Outbreak associated with national brand food; no local contributing factors identified: Yes
- Cases linked to food purchased from several different restaurants in one city: Yes
- Outbreak linked to food on airline flight: Yes
Local Significance of Multijurisdictional Outbreaks

- “Local” outbreak may herald a national or international event.
- Local jurisdictions will need to coordinate investigation efforts with other local, state, and federal partners.
Federal Public Health Agencies

- Centers for Disease Control and Prevention (CDC)
  - Non-regulatory agency that focuses on disease surveillance, outbreak detection, and investigation
- U.S. Department of Agriculture/Food Safety and Inspection Service (USDA/FSIS)
  - Regulatory agency that oversees safety of meat, poultry, pasteurized egg products
- U.S. Food and Drug Administration (FDA)
  - Regulatory agency that oversees safety of most foods except meat, poultry, and pasteurized egg products
Federal Agency Contributions to Outbreak Investigation

- Leadership and coordination
- Expertise and experience
- Laboratory testing
- Other resources (e.g., manpower, educational materials)
- Public health regulatory authority over certain control measures (e.g., ability to recall food items)
When to Involve Federal Agencies

- Outbreaks associated with
  - Cases from multiple states (or countries)
  - Commercially distributed food contaminated before point of service
  - Highly pathogenic or unusual causative agent
  - Large numbers of cases
  - Intentional contamination suspected

- Request federal assistance through State
- Be prepared to provide outbreak information
Local Significance of Multijurisdictional Outbreaks

• “Local” outbreak may herald a national or international event.

• Local jurisdictions will need to coordinate investigation efforts with other local, state, and federal partners.

• Local jurisdictions may be asked to urgently investigate one or a few cases that are part of a larger outbreak despite their apparently small local impact.
Role of State and Local Jurisdictions in Multijurisdictional Outbreaks

- Notify other jurisdictions of local outbreaks.
- Be aware of outbreaks in other jurisdictions.
- Search for local cases/clusters associated with multijurisdictional outbreak.
- Participate in hypothesis generation.
- Perform tasks as agreed upon.
- Collect data to support traceback investigations by federal agencies.
Shigellosis Outbreak – Central Indiana, 2014

Treatment Policies and Implications for Antibiotic Resistance
Shigellosis

- Shigellosis is a bacterial infection that is transmitted via the fecal-oral route and causes acute gastrointestinal illness (Figure 1).

- From 2009 – 2013, the annual average number of confirmed shigellosis cases in Indiana was 97.
Antimicrobial Resistance

- The American Academy of Pediatrics recommends antibiotic therapy only for severe cases.
- Antimicrobial susceptibility testing is needed because resistance to antimicrobials is common.
- Ampicillin and trimethoprim-sulfamethoxazole (TMP/SMX) are recommended treatments.
- Azithromycin and ceftriaxones are recommended for TMP/SMX or ampicillin-resistant strains.
2014 Exclusion Policies

- In Indiana, confirmed cases of shigellosis are excluded from attending daycare or school until they have satisfied release of exclusion criteria.
- Indiana’s exclusion criteria encouraged the use of antibiotic therapy and are inconsistent with national recommendations.
Outbreak Investigation

- Public health staff from eight affected counties interviewed a total of 862 outbreak-associated culture-confirmed *S. sonnei* cases using a standardized case investigation form.
- Demographic and clinical data were then compared between severe cases and mild cases.
Case Definitions

• **A severe case** was defined as a person with shigellosis and exhibiting bloody stool and/or fever.

• **Confirmed cases** were defined as people who lived or attended school, daycare, or work in central Indiana with clinically compatible symptoms starting between MMWR weeks 10 and 53 of 2014 and testing positive for *S. sonnei*.
Investigation Findings

- 862 laboratory-confirmed cases in Central Indiana were associated with this outbreak.
- Of the confirmed cases, 64% (555) were considered “severe”:
  - The most commonly reported symptom was diarrhea, followed by abdominal cramping.
  - Approximately two-thirds of cases reported either bloody stools and/or fever, which classifies them as “severe” cases.
Investigation Findings

- Children aged 1-9 years (68%) and women aged 20-49 years (82%) were disproportionately affected by the outbreak.
- The incidence of outbreak-associated shigellosis cases increased during MMWR weeks 20-28 (May-July) and again during MMWR weeks 38-42 (Sept-Oct), which corresponds with times of student congregation during the school year.
Persons infected with *S. sonnei*, by Date of Illness Onset and Severity

![Bar chart showing number of cases for mild and severe infections by MMWR week.](image-url)

- **Mild** (n = 307)
- **Severe** (n = 555)
Antibiotic Treatment

- 80% of cases had a *S. sonnei* strain that was resistant to TMP/SMX
  - Most cases (58.9%) were prescribed azithromycin, despite severity status.
  - Nearly 8% of cases were prescribed amoxicillin, an antibiotic that is not recommended per national guidelines.
  - Nearly 90% of mild cases were prescribed antibiotics, which is not recommended per national guidelines.
# Treatment Prescribed to Shigellosis Cases by Severity

<table>
<thead>
<tr>
<th>Prescribed Treatment</th>
<th>Mild Cases(^\d) (n = 307)</th>
<th>Severe Cases (n = 555)</th>
<th>Total Cases (n = 862)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin(^\d)</td>
<td>7.8%</td>
<td>7.9%</td>
<td>7.9%</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>4.6%</td>
<td>3.6%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>60.6%</td>
<td>58.0%</td>
<td>58.9%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>11.7%</td>
<td>15.9%</td>
<td>14.4%</td>
</tr>
<tr>
<td>Other*</td>
<td>2.6%</td>
<td>4.3%</td>
<td>3.7%</td>
</tr>
<tr>
<td>No Antibiotics Prescribed</td>
<td>4.9%</td>
<td>6.7%</td>
<td>6.0%</td>
</tr>
<tr>
<td>No Data/Unknown</td>
<td>7.8%</td>
<td>3.6%</td>
<td>5.1%</td>
</tr>
<tr>
<td><strong>Total Prescribed Antibiotics(^\d)</strong></td>
<td><strong>87.3%</strong></td>
<td><strong>89.7%</strong></td>
<td><strong>88.1%</strong></td>
</tr>
</tbody>
</table>

\(^\d\) Not recommended for treatment per national guidelines  
*Includes multiple antibiotics prescribed  
\(^\d\) Sum of amoxicillin, ampicillin, azithromycin, ciprofloxacin, and “other” categories  
Totals may not equal 100% due to rounding
Investigation Findings

- Cases with a severe infection reported shorter median symptom duration and shorter time between first symptom onset and first dose of prescribed antibiotic.
- Duration of treatment for severe cases was similar to duration of treatment for mild cases.
Conclusions

- Most outbreak cases were between the ages of 1 and 9 years and impacted by the state’s school/daycare exclusion policy, which prohibited them from returning to school or daycare without appropriate antimicrobial therapy or negative stool samples.
- Nearly 90% of the mild cases were inappropriately prescribed antibiotics, most likely to comply with the state exclusion policy.
Communicable Disease Rule

- Data from this outbreak influenced the ISDH to revise the state’s exclusion policy to correspond with national treatment guidelines.

   Exclude preschool or day care attendee until **one all** of the following has occurred:
   - Asymptomatic for ≥ 48 hours
   - Completed effective antibiotic therapy OR have **one two** negative stool

   Exclude school attendee until **one all** of the following has occurred:
   - Asymptomatic for ≥ 24 hours
   - Initiated effective antibiotic therapy for ≥ 48 hours OR have **one two** negative stool
Questions?
Tess Gorden
Enteric Epidemiologist
Indiana State Department of Health
tgorden@isdh.in.gov
317-234-2808