CDC Update on Food Safety: Whole Genome Sequencing and Other Advances

123rd Association of Food and Drug Officials Annual Education Conference
Atlanta, Georgia

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Division of Foodborne, Waterborne, and Environmental Diseases
Foodborne illnesses in the United States

- 48 million people become sick, 128,000 are hospitalized, and 3,000 die
- Estimated annual cost of foodborne illness: $15.6 billion
- Prevention: Understanding transmission well enough to prevent it
- Result of actions by regulators, public health, industry, consumers
- Progress often driven by foodborne outbreaks, that changes in industry practices and regulatory policies
- 1996-2007: Important progress made
- Little further progress has been made since in reducing incidence
Selected 2018 Multi-state Outbreaks

1. **Kratom linked to multistate Salmonella outbreak**
   - By Joseph James Whitworth

2. **Shredded coconut causes widespread salmonella outbreak**
   - By Wendy Heine

3. **Jimmy John's sprouts linked to multistate salmonella outbreak**
   - By Joseph James Whitworth

4. **CDC: Five states hit by Salmonella outbreak linked to chicken salad**

5. **Pre-Cut Melon in 10 More States Linked to Salmonella Outbreak**

6. **Vibrio outbreak linked to crab meat imported from Venezuela**

7. **Multistate E. coli outbreak traced to romaine lettuce from Arizona**

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**America**

207 Million Eggs Are Recalled due to Salmonella Fears

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**USA Today**

**26 states where cases were reported:**

Outline of Food Safety Activities at CDC

- Conduct national surveillance for infections often transmitted by food
- Investigate and control outbreaks to stop them and prevent future illness
- Drive illness prevention policy with data, analyses, and partnerships
- Innovate by applying advanced technologies to improve surveillance and to address diagnostic challenges
- Support state and local health departments, global and other partners to fulfill their primary roles in addressing the above goals
Surveillance and investigation are multi-agency efforts

- Caregivers and clinical labs
  - Make the diagnoses, and report the specific illnesses

- State and local health departments: epi, lab, and food safety officials
  - Receive reports of specific diseases
  - Interview people
  - Subtype pathogens in the public health labs
  - Traceback, assess and control within state events

- CDC is lead national public health agency
  - National disease surveillance and multistate outbreak detection
  - Epidemiologic investigation

- FDA (most foods) and USDA/FSIS (meat and poultry), as regulatory agencies
  - Trace suspected foods back to source
  - Assess production and processing facilities
How do we determine a food is the source of an outbreak?

- Three types of evidence:
  - **Epidemiologic**: association between illness and exposure
  - **Traceback**: suspected food item traced back to a common source of contamination
  - **Microbiologic**: same pathogen found in the food, farm or facility as in the ill people

*Methods for all three are evolving*

Standard PFGE method
Results in CDC database
All participants can use

87 labs participate:
– All state health departments
– City health departments
– FDA laboratories
– USDA laboratories

50,000 bacteria/year from
– ill people
– foods
– animals

Links with:
• PulseNet Canada
• PulseNet International
The PulseNet surveillance network combines strain subtyping and patient interviews

- Detecting and investigating a dispersed outbreak can
  - Stop an ongoing hazard
  - Identify food safety gaps early in food production chain
  - Drive improvements in prevention across the system

- Detection depends on finding a signal in the background noise
  - Subtyping clinical strains in state and local public health labs
  - Sharing subtype data with all participants
  - Interviewing patients
  - Detailed follow-up of clusters of related isolates

- Subtyping food and animal isolates, combined in same database

- Focus on STEC, *Salmonella, Listeria*
Onset dates of *Escherichia coli* O157:H7 cases submitted to MDH Clinical Laboratory Section, Minnesota, 1995 (n=183)
Onset dates of *Escherichia coli* O157:H7 cases submitted to MDH Clinical Laboratory Section, Minnesota, 1995 (n=183)
PulseNet increased the number of multistate foodborne outbreaks reported to CDC: 1973-2010

PulseNet begins
Incidence of diagnosed cases, by pathogen — FoodNet, 2018

- Active surveillance, part of Emerging Infections Program
- Collaboration among CDC, 10 FoodNet sites, FDA, USDA/FSIS
- 8 infections often spread through food
- Reliable and up-to-date data on illness trends

- **E. coli O157**
  - 49% decrease

- **Campylobacter**
  - 43% decrease

- **Listeria**
  - 43% decrease

- **Salmonella**
  - 7% increase

Confirmed only
Food Safety Goals for 2020 and 2030

- Healthy People 2020: From baseline in 2006-2008:
  - 33% reduction in *Campylobacter* infections
  - 50% reduction in *E. coli* O157 infections
  - 33% reduction in *Listeria monocytogenes* infections
  - 25% reduction in *Salmonella* infections
  - 33% reduction in *Vibrio* infection
  - 50% reduction in hemolytic uremic syndrome in children <5 years of age

- Healthy People 2030 goals: From baseline in 2016-2018: Under development
  - Fewer targets for reducing incidence
  - More modest reductions in incidence

2020: https://www.healthypeople.gov/2020/
Expanding efforts at CDC to meet Food Safety Goals

- Make surveillance and investigations more powerful
  - Implement whole genome sequencing for routine PulseNet subtyping
  - Detect and control outbreaks we may be missing now
  - To identify emerging problems

- Use our surveillance to target interventions
  - Attribute illnesses to specific food categories
  - Account for changing diagnostic tests that affect surveillance

- Stay on the cutting edge as new laboratory diagnostic methods arise.
  - The challenge of culture–independent diagnostic tests
  - Metagenomic tools for public health are coming

2020: https://www.healthypeople.gov/2020/
Whole genome sequencing and routine public health surveillance – Big data meets microbiology

- PulseNet: National subtyping network since 1996, using pulsed-field gel electrophoresis (PFGE). 50,000 strains/yr
- Cost and speed of sequencing bacteria has dropped
- Reading and interpreting sequence faster
- 3M base pairs = 1800 pages of text (2 Moby Dick volumes)
- Comparing whole genomes give vastly more information
  - Strains are closely related (same source?)
  - Strains from patients related to strains from foods
  - Predict antibiotic resistance, many other features
- What happens if we try it in PulseNet?
Applying whole genome sequencing to surveillance
Listeriosis Pilot Project 2013-2016

- **Listeria**: severe, but rare illness in elderly, immunocompromised or pregnant (800 cases/year)
- 2013: Pilot project with WGS
  - Began sequencing all clinical, food, and environmental *Listeria* isolates
  - FDA, and FSIS/USDA partners
- Solved outbreaks increased 3x
- Size of outbreaks decreased
- Identified new and unsuspected risks

Surveillance based on DNA Sequencing: Solving more foodborne listeriosis outbreaks

Salmonella Enteritidis (SE) and frozen stuffed breaded raw chicken products – Minnesota, 2015

- For SE: PFGE has too few types to easily find clusters
- Minnesota DOH began sequencing SE in 2015
- Found 2 clusters in summer of 2015

Cluster #1: 5 illnesses
- Ate one brand of frozen stuffed breaded raw chicken entrée
- Same strain found in product
- Product distributed to many states
- 2.4 M pounds recalled

Cluster #2: 15 illnesses (including 7 in other states)
- Ate a different brand of frozen stuffed breaded chicken products
- Same strain found in frozen product
- Product distributed to many states
- 1.7 M pounds recalled

Most knew the product was raw, and followed cooking instructions
- Some checked the internal temperature
- USDA now considering further standards for products like this

www.fsis.usda.gov

www.cdc.gov/salmonella/outbreaks/
Salmonella Enteritidis (SE) and eggs from a small farm – Tennessee, 2016

- For SE: PFGE has too few types to easily find clusters
- 2016: TDOH began sequencing SE, found an outbreak
- 6 cases from Restaurant A: Steak with Bernaise sauce, made with raw eggs
- Eggs from local Farm X (<3000 hens)
- Env cultures on Farm X negative for SE

- A month later, found 2nd outbreak. WGS, within 3 SNPs of first outbreak
- 9 cases from Restaurant B: ate mayo made with raw eggs at Restaurant B;
- Eggs also from farm X
- Reinvestigation of farm X: SE in chicken litter
- Restaurant B changed egg suppliers
- All receiving eggs educated not to use them raw

Salmonella Enteritidis is about 20% of all salmonellosis
- Limited number of PFGE types makes cluster detection difficult
- WGS looks promising in finding small outbreaks, and undetected sources
- Regulations for SE in eggs covers farms with ≥ 3000 hens

Implementing whole genome sequencing as PulseNet standard – 2017-2019

- **2017-2019**
  - Built state lab and epi capacity
  - Trained and certified staff in all 50 states
  - Built data infrastructure
  - Partner with FDA Genome TrakR labs, and FSIS labs
  - PulseNet transition to WGS (end of June 2019)

- **Expect PulseNet with WGS to find more:**
  - Clusters that are truly genetically related
  - Successful epidemiologic investigations
  - Gaps in food safety and targets for prevention
“Clade of concern”: MDR *E. coli* O157:H7 and Romaine

- Large outbreak in spring of 2018, linked to Romaine
  - 210 cases, 36 states, 96 hospitalized, 27 HUS, 5 deaths
  - Largest O157 outbreak in last decade
  - 87% said they ate Romaine lettuce, more than baseline
  - Traced to ~ 23 fields, across span of ~ 50 miles in Yuma Growing area
  - Ended after repeated warnings, end of harvest

WGS defined one main clade, one second clade
- WGS: Main clade has a history:
  - Mid 2017: 11 cases, Lake Wildwood in California
  - Late 2017: 17 cases, salad suspected in Midwest

Need heightened surveillance, prevention research

Thanks to Matt Wise, CDC
WGS is already making investigations more powerful

- **2018: E. coli O157 infections and Romaine Lettuce - Yuma Growing Area**
- WGS linked together 22 different PFGE patterns into 2 main clades
- Confidence that two dozen farms were all related, reflecting a widespread contamination
- *E. coli* O157 isolated from the irrigation canal matched the main outbreak clades
- Linked this outbreak with events in preceding year.

- **4/19/2019: Leafy Greens Marketing Agreement**
  Requires farmers to sanitize surface waters sprayed onto leafy greens
“Clade of concern”: Sustained event traced to a complex source: MDR *Salmonella* Infantis and poultry

- MDR strain first seen in travelers to Peru in 2012
- Rare ESBL resistance gene (defined by PFGE)
- Resistant/Decreased susceptibility to 10 agents, including Amp, Cipro, Ceftriaxone, and Tmp/Sxt
- Difficult to treat with commonly used antibiotics
- First non travel-associated US case in 2014
- Increasing rapidly in 2017-2018
- Multiple PFGE types – all related by WGS

Now represents 30% of all *S* Infantis in humans, 573 in 2018
- USDA/FSIS isolates: In chicken since 2013, rapid increase in 2017
- In 2018: 495 isolates from chicken, 53 isolates from turkey
- Met with National Chicken Council several times in last year, Jan 2019
- Preharvest investigations and interventions needed

Case map: *Salmonella* Infantis MDR strains 2012-2019 (n = 1246)

Thanks to Louise Francois Watkins
WGS is defining “Clades of Concern”

- Groups of closely-related strains that
  - Cause repeated outbreaks
  - Emerging in people and in specific food commodities
  - May be multi-drug resistant

- Examples of current “clades of concern”
  - *E. coli* O157:H7 in Southwest (e.g. the “Yuma” strains) – recurrent outbreaks
  - MDR *Salmonella* Infantis, emerging in chickens from many processors
  - MDR *Salmonella* Reading, related to turkeys in many processors

- Need to address with
  - Sustained investigation and traceback
  - Concerted broad prevention strategies
Using surveillance to help target interventions

- Interagency Food Safety Analytics Consortium (IFSAC): CDC, FDA, FSIS work together to summarize information on sources of foodborne infections

- Have constructed a model based on reported foodborne outbreaks over the last 18 years, giving more weight to most recent 5 years

- Attributed cases of illness across 17 major food categories, by pathogen

- Most recent summary based on 1998 – 2016

- Repeat and update annually

https://www.cdc.gov/foodsafety/ifSac/annual-reports.html
Using surveillance to target interventions
IFSAC Attribution: *Salmonella* infections for 2016

Salmonella

<table>
<thead>
<tr>
<th>Category</th>
<th>% Attribution</th>
<th>Cumulative Attribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seeded vegetables</td>
<td>19.3</td>
<td><strong>76.2%</strong></td>
</tr>
<tr>
<td>Chicken</td>
<td>12.7</td>
<td></td>
</tr>
<tr>
<td>Pork</td>
<td>10.8</td>
<td></td>
</tr>
<tr>
<td>Fruits</td>
<td>9.9</td>
<td></td>
</tr>
<tr>
<td>Other Produce</td>
<td>8.7</td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td>7.9</td>
<td></td>
</tr>
<tr>
<td>Beef</td>
<td>6.9</td>
<td></td>
</tr>
<tr>
<td>Sprouts</td>
<td>5.6</td>
<td></td>
</tr>
<tr>
<td>Turkey</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td>Dairy</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>Vegetable Row Crops</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td>1.6</td>
<td><strong>23.8%</strong></td>
</tr>
<tr>
<td>Other Seafood</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Other Meat/Poultry</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Grains Beans</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Oils Sugars</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Game</td>
<td>0.1</td>
<td></td>
</tr>
</tbody>
</table>

https://www.cdc.gov/foodsafety/ifsac/annual-reports.html
Using surveillance to target interventions

IFSAC Attribution: *E. coli* O157 for 2016

*E. coli* O157

https://www.cdc.gov/foodsafety/ifsac/annual-reports.html
Summary of biggest targets for prevention

- **FDA regulated foods**
  - Fresh produce: *Salmonella* and STEC*
    - Leafy greens and STEC*
    - Seeded vegetables and *Salmonella*
  - Eggs: *Salmonella*
  - Cheese and other RTE foods: *Listeria*

- **FSIS regulated foods**
  - Chicken: *Salmonella* and *Campylobacter*
  - Ground beef: *Salmonella* and STEC*
  - Pork: *Salmonella* and *Yersinia*

*Shiga toxin–producing *E. coli*, such as *E. coli* O157
Accounting for impact of changing diagnostic methods on case surveillance – culture-independent diagnostic panels

- Since 2015, use of rapid multi-pathogen diagnostic panels increasing in clinical laboratories

- Can diagnose up to 22 different infections, with results available in hours

- More people are being tested for more pathogens, including some that could not be routinely diagnosed before

- Tests do not yield a living bacterial isolate, unless the specimen that was positive is then cultured for that organism. **Isolate needed for PulseNet subtyping**

- Insurance may not cover cost of doing this “reflex culture”

- Labs are starting to send the positive specimens to the public health laboratories for culture
CIDT uptake and infections detected, FoodNet, 2012–2018*

*STEC excluded due to diagnostic differences, 2018 results preliminary

Dr. Aimee Geissler, CDC
Culturing CIDT positive specimens in a state public health laboratory can recover an isolate (Minnesota)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Recovery Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter</td>
<td>74%</td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>95%</td>
</tr>
<tr>
<td>Cyclospora</td>
<td>86%</td>
</tr>
<tr>
<td>EAEC</td>
<td>76%</td>
</tr>
<tr>
<td>EIEC/Shigella</td>
<td>55%</td>
</tr>
<tr>
<td>EPEC</td>
<td>59%</td>
</tr>
<tr>
<td>ETEC</td>
<td>48%</td>
</tr>
<tr>
<td>Salmonella</td>
<td>89%</td>
</tr>
<tr>
<td>STEC</td>
<td>73%</td>
</tr>
<tr>
<td>Vibrio</td>
<td>40%</td>
</tr>
<tr>
<td>Vibrio cholerae</td>
<td>0%</td>
</tr>
<tr>
<td>Yersinia</td>
<td>66%</td>
</tr>
</tbody>
</table>

David Boxrud, MDH
Including CIDT+ cases, cases are up. Are more infections truly happening, or they more likely to be diagnosed?

- FoodNet Active Surveillance (Collaboration of CDC, FDA, FSIS and 10 states)
- Tracking CIDTs since 2015

As microbiologic and diagnostic methods march forward, what will keep us on the cutting edge?

- Whole genome sequencing currently can take two weeks to turn around and requires an isolate.

- Public health will need more advanced molecular diagnostic tools for direct use on clinical specimens to get results in hours and provide information public health needs.

- Clinical researchers are exploring metagenomic methods now.

- Work at CDC has begun as well, and will be a growing focus in the future.

http://www.biken.osaka-u.ac.jp/act/act_imet-horii_e.php
Implementing whole genome sequencing - Challenges

- The clinical world is using more culture-independent diagnostic tests (CIDTs) that do not yield a living bacterial isolate.
- Sequencing requires an isolate, so need “reflex culture” on CIDT+ specimens
- “Big data” puts strain on IT infrastructure at CDC and in state health departments
- Changes in laboratory workflow and workforce
- Expecting a surge in detected clusters = more investigations (need more epidemiologists and environmental specialists)
Implementing whole genome sequencing - Opportunities

- Better target and accelerate prevention strategies
- Public health epi and lab on common network platform in each state
- Value beyond foodborne outbreak detection and investigation; can be used for other pathogens
- Bridge to the future – developing new metagenomic methods will depend on DNA sequence data
Foodborne disease prevention in the 21st century: An evolving public health approach

- Whole genome sequence-based surveillance is an evolutionary step forward:
  - More precise subtyping, combined with enhanced patient interviews and traceback
  - More outbreaks and sources detected and controlled
  - More food safety gaps found and corrected
  - Applicable to many other infections as well as the enteric ones

- A step towards the future, when Public Health will have culture-independent tools providing needed information rapidly

- Better approaches to defining the targets for prevention

- Long term effect: Impact on industry, regulators, and consumers to drive down incidence of foodborne infections
Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)

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.