Then and Now: The changing landscape of enteric disease surveillance, outbreak detection and response

Where are we going from here?

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Listeriosis Outbreaks and Incidence*, 1983-2016

**Pre-PulseNet**
- Outbreaks per year: 0.3
- Median cases per outbreak: 69

**Early PulseNet**
- Outbreaks per year: 2.3
- Median cases per outbreak: 11

**Listeria Initiative**
- Outbreaks per year: 2.6
- Median cases per outbreak: 5.5

**WGS**
- Outbreaks per year: 6.3
- Median cases per outbreak: 4

*2016 incidence rate preliminary data from FoodNet
Foods implicated in listeriosis outbreaks since 2013 in the United States (in the WGS era)

- **Expected foods:**
  - Raw milk
  - Soft cheeses
  - Mung bean sprouts
  - (Not processed meats)

- **Novel foods:**
  - Caramel-dipped apples
  - Ice cream
  - Packaged leafy green salads
  - Stone fruits (nectarines)
  - Frozen raw vegetables

Found as a result of multi-state investigations

Contamination often occurred at the packing shed or processing facility

Most investigations started with ill people. A few started with finding *Listeria* in a food, that matched strains from patients who ate that food

*New efforts in food industry now to reduce contamination with listeriosis*
Improving our ability to detect, solve and stop outbreaks

- Routine whole genome sequencing is swiftly becoming part of routine public health surveillance

- Now placing WGS capacity in state and city health departments
  - Starting with *Listeria*
  - Expanding to STEC, *Salmonella, Campylobacter, Shigella*…
  - Likely to start finding more clusters

- Expanding investigative capacity in states as well

*Anticipate using WGS as main subtyping method in 2019*
CDC Support for PulseNet WGS and expanded Food Safety Epidemiology as of November 2017

11-2017
50 states with support for sequencers
39 states PulseNet WGS certified
33 states have enhanced epi
6 states with Centers of Excellence

*PulseNet certified laboratories meet national testing standards and results from this testing are included in national surveillance and genome bank
Evolving paradigm for surveillance and investigation

- Testing all strains with standard molecular subtyping
- Interviewing all patients with standard questionnaire
- Reviewing strains from foods or food production environments also in PulseNet
- Multi-dimensional cluster detection – for similar
  - Molecular pattern/sequence type
  - Time/space
  - Demographic/ethic grouping
- Analyze epi data as soon as cluster identified

- With sequence, can predict antimicrobial resistance as soon as cluster identified, use to prioritize
The impact of finding more multi-jurisdiction clusters

- Finding more clusters that are
  - Multi-county
  - Multi-state
  - Multi-national

- Importance of standardized, harmonized approaches
  - IFORC (Interagency Foodborne Outbreak Response Collaboration)
  - Gen-FS (Interagency Collaboration on Genomics and Food Safety)
  - PulseNet International
  - CIFOR, and other collaborative groups

Making collaborative investigations a new norm
The impact of finding smaller clusters

- Increased subtyping precision means more confidence
- Finding clusters that are too small for traditional measures of statistical significance
- Growing potential of “rapid precision traceback”
  - Patient interviews including source of food
  - Loyalty card permissions
  - Retail logistic records
  - Blockchain

*Need great care in communicating results*
The impact of finding smaller clusters – cont’d

- Blurring the boundary between outbreaks and sporadic cases
- Changing interpretation of “baseline”
  - With PFGE, often defined background rate, and subtracted it from outbreak, assuming some cases in cluster represented unrelated background
  - With WGS, may look at cases in background, and wonder how they are related to current cluster

- Are there sustained points of harborage or reservoirs where a strain may be maintained for years, blooming periodically?
- Can identifying and controlling them prevent future disease?

*Chipping away at the baseline*
Vive la France

- Santé Publique France has been in the forefront
- Ran WGS (cgMLST) with PFGE for 2015-2016
- Now switched to WGS for Listeria, and applying to Salmonella and others pathogens.
- Changed their cluster definition for listeriosis:
  - ≥2 isolates of same cgMLST type in 2 years, of which
  - ≥1 is from a human

- Routinely sample suspect foods in
  - Refrigerators of patients with *Listeria* meningitis
  - Hospital kitchens of hospital-associated cases

What is next?

- WGS depends on
  - Isolating a pure culture in a clinical laboratory
  - Shipping it to the public health laboratory
  - Sequencing and interpreting
  - *Can take weeks*

- To make surveillance faster, public health will need more advanced molecular diagnostic tools for direct use on a clinical specimen to
  - Provide species identification
  - Predict serotype, subtype virulence, antimicrobial resistance
  - Report results in hours, rather than days

- Exploratory work
  - Amplifying around key gene targets, like Shiga toxin-coding phage genes
  - Using metagenomic approaches with long-read sequencing
  - Single cell sorting and sequencing

*The next generation of methods*
Future foodborne outbreaks more likely to be

- Dispersed in space: Multi-state, multi-national
- Dispersed in time: Multi-year
- Detected by sequence-based surveillance
- Detected as contaminated product first

- Associated with
  - fresh and minimally processed foods
  - imported foods
  - novel food vehicles
  - novel routes and pathways of contamination

More dispersed and smaller: “low and slow”
Foodborne diseases in the 21st century: A rapidly evolving public health approach

- Foodborne outbreak investigations are an important driver for improving food safety

- Whole genome sequence-based surveillance is a major evolutionary step forward in outbreak detection and investigation

- Combined with enhanced patient interviews and better traceback

- Improvement in subtype-based surveillance mean more outbreaks are detected and stopped while they are smaller, and more food safety gaps are identified and corrected

- Collaborative partnerships are vital to
  - Detect and investigate cross-border events
  - Focus improved control measures around the world
  - Reduce the number of foodborne infections, hospitalizations and deaths
Thank you

The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention.
E. coli:  
www.cdc.gov/ecoli

Salmonella:  
www.cdc.gov/salmonella

Listeria:  
www.cdc.gov/listeria

FoodNet:  
www.cdc.gov/foodnet

PulseNet:  
www.cdc.gov/pulsenet

Foodborne outbreak surveillance:  
www.cdc.gov/outbreaknet

Foodborne burden of illness:  
www.cdc.gov/foodborneburden

General Information About Foodborne Diseases:  
www.foodsafety.gov

http://www.cdc.gov/vitalsigns/foodsafety/

Our websites

And a May 25, 2017 Webcast
“How Deadly Burgers Made Food Safer – The Impact of the 1993 E. coli O157 Outbreak”

https://www.cdc.gov/od/science/wewerethere/