Detecting and Investigating More and Smaller Outbreaks using WGS

“Food Safety and High-Throughput Sequencing – What does the Future Hold?”

Government Agencies
Institute for Food Safety and Health
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Health burden of infection from contaminated foods

- Each year, 48 million people become sick (1 in 6 Americans), 128,000 are hospitalized, and 3,000 die

- Major pathogens: $3 billion US in health-related costs each year

- ~ 800 foodborne outbreaks are reported annually

- Finding, investigating and stopping outbreaks is a major driver for improving prevention

Many steps along the food chain

Many points for
- Contamination
- Control
- Prevention

Contamination in final kitchen:
- Localized outbreak

Contamination further upstream of a widely distributed product:
- Dispersed outbreak

What we detect depends on the methods we use
The PulseNet surveillance network combines strain subtyping and patient interviews

- Detecting 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
  - Network of state and big city public health labs
  - Subtyping all clinical strains across network in real time
  - Making subtyping data available to all participants
  - Interviewing all patients
  - Detailed follow-up of clusters of related isolates

- Subtyping food and animal isolates, combined in same database

- Focus on STEC, *Salmonella, Listeria*

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
1990 - Hubble Space Telescope
PulseNet increased the number of multistate foodborne outbreaks reported to CDC: 1973-2010
The median size of multistate foodborne outbreaks reported to CDC decreased 1973-2010.

- **72 cases** before PulseNet begins
- **35 cases** after PulseNet begins

**Campylobacter, E. coli O157 and Listeria** incidence drops by 30-40%.

**Cost-benefit analysis at state level**:
- 270,000 fewer illnesses/year
- $507 million saved/year
- ROI = 70/1

FoodNet USA, Scharff 2016 Am J Prev Med
2020 - James Webb Space Telescope
The next generation
2013-2016 Pilot project: Does WGS technology improve listeriosis surveillance?

- In 2013, collaborative multiagency effort began sequencing isolates of *L. monocytogenes* as part of routine surveillance
  - Clinical isolates at CDC (~800/year)
  - Food isolates at FDA, USDA
  - Whole genome sequence data stored at NIH
  - BioNumerics data platform reversioned
  - Centralized data analysis

- State health departments interview all listeriosis cases
  - Case-case comparison when clusters are found

- Coordination with collaborators in Canada, UK, France, Denmark, Australia

Surveillance based on DNA Sequencing: Solving more foodborne listeriosis outbreaks

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 at packing shed or processing facility

Some investigations started with finding *Listeria* in food or a food environment

*New efforts in many parts of food industry now to reduce contamination with listeriosis*
**Listeria and raw milk, 2014-2016**

- November 2015: FDA collected sample at a raw milk conference in CA, from a PA farm
- January 2016: *Listeria* isolated from raw milk, WGS matched 2 infections from 2014
- Patients in FL and CA
- Mean age 77: both hospitalized, 1 died
- PFGE: Two different patterns
- WGS: Extremely close: Within 2 SNPs

Both drank raw milk
- One reported to get raw milk online from same PA farm
- Source of other unclear
- PA farm sold milk interstate over the web
- Private membership organization
- March 18: CDC warned public

www.cdc.gov/listeria/outbreaks/
**Listeria and Ice Cream, 2015**

- **Cluster #1**: Feb 2015. Local health lab found *L mono* in Blue Bell Ice Cream, many PFGE patterns
  - PulseNet: 5 cases, 4 patterns in patients at one hospital over 1 year
  - All highly similar by WGS
  - All had eaten one product from Texas plant, same strain found there
  - All product from that line recalled

- **Cluster #2**: Other BB ice cream in that hospital’s freezer yields *L mono*.
  - Rare PFGE, match with 5 hospital acquired cases over 5 years in 3 other states (‘10 – ‘14)
  - Made at a second BB plant, served at those hospitals
  - WGS matched patients, ice cream and many isolates from plant

10 cases, in 4 states, 3 deaths, in two clusters

Novel food vehicle: Ice cream industry now implementing rigorous prevention
**Listeria and bagged salads, US and Canada: 2015-2016**

- July 2015 - Jan 2016
- 19 cases in US, 14 in Canada (33 total)
- Closely related by WGS
- 9 states, 5 provinces
- All hospitalized, 4 died
- Median age 64 years, 74% female
- 13/14 ate bagged salad, 9 named 1 brand

- WGS match to *Listeria* from same brand
  - regulatory salad sample in Ohio
  - bagged salad tested in Canada

- Multiple products from one packaging plant
- CDC and FDA shared information with company
- Halted production, and recalled product
- Plant closed for 4 months
- Intensive assessment, sanitation
- New program of in-plant monitoring
- No further cases

www.cdc.gov/listeria/outbreaks/
Salmonella Enteritidis (SE) and frozen stuffed breaded raw chicken products – Minnesota, 2015

- Minnesota DOH began sequencing SE
  - 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 patients knew the product was raw, and followed cooking instructions
- Some even checked the internal temperature
- USDA now considering further standards for products like this

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

Regulatory action for SE in eggs is focused on farms with ≥ 3000 hens

- DOH began sequencing SE prospectively in 2016, found 1st outbreak
- 6 cases from Restaurant A: Cohort study - Steak with Bernaise sauce (made with eggs)
- Eggs from “small” local Farm X (<3000 hens)
- Env cultures on Farm X negative for SE

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

- Salmonella Enteritidis is our most common serotype
- A few common PFGE types makes cluster detection difficult
- WGS promising in finding small outbreaks, undetected sources
- Time to review small farm exception?

[https://cste.confex.com/cste/2017/webprogram/Paper7567.html](https://cste.confex.com/cste/2017/webprogram/Paper7567.html) and thanks to Steffany Cavallo
Value added by whole genome sequencing at state and national levels

- More confidence that a cluster of infections are related, so more focus
  - Split up common PFGE patterns into more specific subgroups
  - Join strains with different PFGE types
  - Compare strains from foods, animals, and production environments
  - Finding and solving more and smaller clusters

- Empowering epidemiologists, in close partnership with labs
  - Better definition of which cases to interview, which to exclude
  - Still must find out what patients ate that others did not, and trace suspect foods to their source

- With whole genome sequencing platform we can
  - Quickly know serotype, virulence type (STEC), antibiotic resistance
  - Help prioritize investigations
  - Use same data platform for other pathogens: Norovirus, Cryptosporidium, Mycobacterium tuberculosis, Legionella.
Finding matching strains does not by itself prove that infections came from the same food

- It certainly increases the probability, but by itself is not certainty
- Multiple foods can be contaminated with the same strain
- Detect complex contamination events
- Need careful interviews of the patients, to see what exposures they have in common
- Need swift traceback of a suspect food through supply chain
- Need more field epidemiologists, not fewer
  - Supporting enhanced epidemiological teams in 33 states to work on the increasing number of clusters detected
What is the next generation of methods?

- WGS can take a week or more to
  - Ship specimen or pure culture to the public health laboratory
  - Sequence and interpret

- Clinical laboratories now are adopting culture-independent diagnostic tests
  - We still need cultures in public health for detecting outbreaks
  - Also for tracking trends, excluding people from work or daycare
  - Now asking clinical labs to do reflex cultures on positive specimens
  - OR ship specimen to state public health lab and do reflex culture there

- Public health needs more advanced molecular diagnostic tools for direct use on the clinical specimen without going through culture step for
  - Species identification
  - Predicting serotype, subtype, virulence, antimicrobial resistance
  - Reporting results in hours, rather than days
Foodborne outbreaks more likely to be

- Dispersed in space: Multi-state, multi-national
- Dispersed in time: “Low and slow” profile
- Smaller when detected
- First detected as contaminated product or place

Associated with
  - novel food vehicles
  - novel routes and pathways of contamination

More that are dispersed and smaller
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 traceback
- More outbreaks can be detected and stopped while they are smaller, and more food safety gaps can be identified and corrected
- This is the year of changeover – using both PFGE and WGS
- Collaborative partnerships are vital to
  - Detect and investigate cross-border events
  - Focus improved control measures
  - Reduce the burden of foodborne infections
  - Improve confidence in safety of food supply
Thank you

See 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/

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
Our websites

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

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

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