Impact of Culture Independent Diagnostic Tests on Enteric Disease Outbreak Detection and Response: Nebraska, 2015–2017

Anna V. Carlson, MS, PhD
Foodborne and Waterborne Disease Epidemiologist
Nebraska Department of Health and Human Services
University of Nebraska Lincoln

Co-author: Bryan F. Buss, DVM, MPH
Nebraska State Public Health Veterinarian
Culture Independent Diagnostic Testing (CIDT) in Nebraska

• Before 2015, no labs in Nebraska used Gastrointestinal PCR Panels (GIPs)

• GIPs becoming more widely used over more traditional diagnostic testing methods such as culture
  ▪ 36/57 NE labs (capable of testing for enteric pathogens) have GIPs, to date
    – Some are labs having never performed microbiology or familiar with reporting

• Impacts on communicable disease surveillance
  ▪ Unforeseen informatics challenges
    – 88% of labs on Electronic Lab Reporting (ELR)
  ▪ Change in baseline levels of disease for some pathogens

• Impacts in ability to detect and respond to outbreaks
Yersiniosis outbreak? Or False alarm?

- November 2015, observed a substantial increase in reports of *Yersinia enterocolitica* infections
  - Suspected this was result of increased use of GIP
  - But, all laboratory reports were positive cultures

- Investigation initiated to establish if outbreak occurred
  - No common exposures identified

- Verified GIP used as initial diagnostic test at front-line laboratories; however, GIP reports not provided to the State

- ELR “filters” in hospital labs missing GIP tests & lab staff unaware of lapses in reporting
  - Only receiving positive reflex culture results
Number of yersiniosis laboratory reports in Nebraska 2015, by quarter

- 8 labs using GIPs during 2015
- 6 implemented GIPs September or later
- 25% (2/8) detected by culture alone
- 75% (6/8) first detected by GIP

Case count (n)

<table>
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<th>Month</th>
<th>Case Count</th>
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<tr>
<td>JAN-MARCH</td>
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<td>OCT-DEC</td>
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Yersiniosis in Nebraska

Mean number of yersiniosis infections reported/year = 4.3 (range, 3–7)

1,069% increase above baseline annual number of infections (p-value = <0.001)

395% increase above baseline annual number of infections (p-value = <0.001)

*Baseline annual number of reported infections during 2005–2014
Yersiniosis in Nebraska 2015 & 2016, by testing method

During 2016, an additional 22 Nebraska laboratories implemented GIPs (2016 total; n=30)

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<tr>
<th>Month</th>
<th>GIP only</th>
<th>GIP + Culture</th>
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During 2016, an additional 22 Nebraska laboratories implemented GIPs (2016 total; n=30)
HIGHLIGHTING CIDT UTILITY IN OUTBREAK DETECTION & INVESTIGATION
Campylobacter Outbreak Investigation
Nebraska, March 2017
The Call

Friday, March 10\textsuperscript{th}, 2017

- 6 lab reported cases of \textit{Campylobacter} in $<$ 1 week
  - 2 by culture, 4 by the GIP

- City A population $<$1,000 residents

- Average number \textit{Campylobacter} cases in this community previously (one every 3 years)

- Developed Hypothesis Generating Questionnaire
  - Info on exposures – raw milk, animal contact, restaurants, large town events, poultry and ground beef sources, water source
  - 9 additional probable cases identified
City A Site-Visit Investigation

Tuesday March 14\textsuperscript{th} 2017

- Recreate distribution of poultry/ground beef to local grocery store, bar and restaurant
  - No shared ground beef or poultry source
  - No raw poultry at grocery store, no evidence of possible routes for cross contamination
  - Told about standing “livestock” water seen in road ditch

- Identified additional probable cases
  - \textit{Campylobacter} outbreaks this size are historically associated with contaminated water
  - Nursing home had no cases and has R/O water system
  - Only cases at the tri-county high school were City A residents

- Visited City A water operators
  - Pump records
  - Well locations
  - Gathered details of standing water in road ditch
Well #4 with #3 in background

Details from DNR records of total well depths, pumping water depths, and static water levels:

- Well 4 has static water level of 21 feet, pumping level of 25 feet and total well depth of 43 feet.
- Well 3 has a static water level of 22 feet, pumping level of 26 feet and total well depth of 46 feet.
Number of confirmed (n=6) and probable (n=33) campylobacteriosis cases (N=39) among persons by date of onset and stratified by self-reported City A tap water exposure

City A tap water; Odds Ratio = 7.84 (95% CI 1.69-36.36)

For municipal tap water exposure, we assessed both in-home and possible out-of-home exposures. Water treatment (e.g., reverse osmosis, filtration) reported at home, work, or other out-of-home settings was considered protective (i.e., no exposure).
**Campylobacter Cluster Detection aided by CIDT**

- 2 detected by culture - both patients resided in same community BUT:
  - Different ordering providers
  - One patient unwilling to be interviewed & other had live poultry exposure

- 4 other cases detected by GIP only, from 3 different labs, in relatively small hospitals
  - Follow-up cultures all **negative**

- Had CIDT not been implemented by these rural Nebraska facilities, this outbreak might have been missed or not investigated thoroughly
Nebraska *Salmonella Enteritidis* Outbreak Investigation, June 2017
Monday, June 19th, 2017

- Notified of apparent outbreak of gastroenteritis among wedding attendees in Northeast Nebraska in June 2017

- Concerned attendee who had developed illness reported event since others at event had also mentioned being ill

- Survey sent to 239 families who attended wedding
It’s the Chicken!

- Total number of completed responses = 175 persons

- Odds ratio = 11.4 (95% CI 2.6-49.1)

- Of 175 questionnaires, 30 individual comments/observations provided concerning food items or food service
  - 7 people reported chicken as “cold” or “not hot”
  - 8 stated chicken was “raw” or “undercooked”
  - 3 said chicken was “rubbery”
  - 5 - “did not like the chicken” or “didn’t taste right” or “had a funny taste”

- Chicken prepared by licensed caterer who took no temperatures during preparation or serving
Survey Results

• Symptoms consistent with Salmonellosis
• Sought medical care = 16 (36.3%)
• 8 persons had stool tested
  ▪ 3 NE cases listed local clinic physician in survey
    – 2 physicians, 2 different LHD jurisdictions, 2 separate labs did testing
    – Called labs and each patient was NEGATIVE for:
      • Stool culture (Salmonella, STEC, Shigella, Campy)
      • Norovirus, Rotavirus, Crypto/Giardia

• NO ETIOLOGIC AGENT IDENTIFIED…….
Geographic Complications

- The test type and geographic distribution of confirmed cases would have made timely detection of this outbreak challenging had it not been reported.....
  - 3 initial negative stool cultures on NE cases in 2 LHD jurisdictions
  - 4 positive cultures residing in 2 states and 3 different LHD jurisdictions with testing done in South Dakota
  - 1 NE case with GIP testing requested at a later date by public health

- Obtain 1 original stool & 2 new stool samples from these 3 cases
  - >1 week later
- Run the GIP @ NPHL
- All 3 positive for *Salmonella*
CIDT highlights in this outbreak

• GIP identified 3 positive cases originally negative by culture
  ▪ Reflex culture at NPHL successful for isolation and subsequent serotyping/PFGE
    – *Salmonella* Enteritidis XbaI JEGX01.0021, JEGA26.0005
  ▪ Highlights importance to engage PHL in process to detect pathogens from CIDT positives

• Without investigation & use of GIP..... only 4 cases would have been identified
  ▪ Because they resided in 2 states & 3 different LHD jurisdictions, cluster detection would likely have been delayed or completely missed

• GIP as first-line test aids in more cases detected
  ▪ More cases identified early on, facilitates more timely outbreak detection
Nebraska *Salmonella* Enteritidis Outbreak Investigation, July 2017
Outbreak Timeline – CIDT allows for rapid response

Friday/Saturday  
July 28th/29th
- 7 ill persons sought health care @ local hospital
- Tested with GIP, results within 2 hours
- All + for Salmonella

Sunday  
July 30th
+ Salmonella results in NEDSS through ELR
- Physician called LHD to report commonality of restaurant A exposure

Monday  
July 31st
- LHD calls NDHHS
- Department of Ag on site for inspection
- Case interviews completed, all report restaurant A
- 3 employees + for Salmonella

Tuesday  
August 1st
- NDHHS on site investigation
- Identified 2 ill food handlers
- Took rectal swabs on all employees
CIDT allows for rapid public health intervention

• Within 3 days of doctors visit, we had a likely source identified

• Ill food handlers immediately excluded from work

• Restaurant stopped serving high risk food items

• No additional cases with exposure date after public health intervention

• Clinic continued to use GIP as frontline test for patients who presented with a syndrome compatible with GI illness
  ▪ 25 people sought medical care; tested with GIP independently of public health
Survey – rapidly target the correct population

• Large confirmed case population facilitated use of extended questionnaire immediately
  ▪ 25/25 cases ate at this restaurant! #epidreamcometrue

• Enabled us to narrow intervention and narrow survey target
  ▪ Media release of survey link for anyone who had dined at restaurant A
  ▪ Survey results analyzed and answer for restaurant within 1 week time frame

• Survey Results
  ▪ Total number of survey responses = 178
  ▪ Number of cases that met the case definition = 51
  ▪ Females = 40 (78 %) and Males = 11 (22%)
  ▪ Median Age = 41.5 years (Range = 7 to 73 years)
  ▪ 29 (57%) sought medical care and 2 were hospitalized
Number of confirmed (n=25) and probable (n=26) cases by date of meal and date of onset among people who ate at restaurant A

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Days sick workers worked

Legend:
- Meal date
- Illness onset date
- Confirmed salmonellosis by GPL/culture

Date of Illness Onset (July 2017)
Discussion & Conclusion

• As GIP use increases, comparison of incidence to pre-GIP numbers for enteric diseases will be challenging as new baselines emerge
  ▪ Analyze surveillance data to determine whether observed changes in incidence are true increases or changes in diagnostic methodology

• Wide-spread use of CIDT as first-line diagnostic test aids in cluster/outbreak detection
  ▪ Detect cases we weren’t able to before
  ▪ Detect large numbers of cases rapidly = fast public health action

• Targeted use of CIDT in outbreak settings appears to be beneficial
  ▪ Several reasons why GIP has/might be a headache....
  ▪ For outbreaks, it aids in quickly orienting the person/place/time that is required for determining the presence of an outbreak
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• South Dakota Public Health Laboratory
Anna Carlson, MS, PhD
Foodborne & Waterborne Disease Epidemiologist

DHHS Division of Public Health
Epidemiology and Informatics Unit

Anna.carlson@nebraska.gov
402-471-7012