Introduction
This series focuses on investigations of outbreaks caused by commercially distributed food items and detected through pathogen-specific surveillance. The etiologic agents often are *Salmonella*, Shiga toxin-producing *E. coli* (STEC), or *Listeria monocytogenes*, but other pathogens are sometimes responsible. The primary target audience is foodborne disease epidemiologists who investigate (or are training to do so) these types of outbreaks, but others might find this series informative as well.

The primary focus of this series is methods used by epidemiologists (in concert with their co-investigators) to generate, develop, and confirm hypotheses about the outbreak vehicle. Descriptions will generally begin with the detection of a cluster (typically by molecular subtyping of submitted clinical isolates at a public health lab) and end when the food source is identified to a level of certainty/confidence that public health interventions are implemented. While this outbreak occurred when pulsed field gel electrophoresis was the subtyping method used by public health laboratories, the lessons are still applicable now that whole genome sequencing is the subtyping method.

From an epidemiologist’s perspective, the overall goal in these types of investigations is to document a sufficiently specific food exposure in a sufficiently high proportion of cases that one can confidently conclude that the food item of interest is the outbreak vehicle. This series will use outbreak examples that detail the exact process and methods that led investigators to that “threshold of confidence” that prompted them to take action. What were the epidemiologists thinking and doing day-by-day, case-by-case, and step-by-step as the investigation progressed, leading up to the attainment of that threshold of confidence? How were leads identified, and how did investigators decide when and how aggressively to follow a particular lead? The nuances, complexities, obstacles, and decision nodes involved in these types of investigations are nearly impossible to fully describe in the limited space of a peer-reviewed manuscript (plus, many excellent investigations are never published). It is our objective to capture all of the important methodological intricacies of selected particularly speedy or effective investigations using a detailed timeline format. We strongly encourage our audience to read the published investigation manuscript (when one exists) before going through our description. We hope that our descriptions will be a useful, educational supplement to the characterization of the investigation.
E. coli O157:H7 - American Chef’s Selection
Angus Beef Patties, 2007
SEPTEMBER 17 (DAY 1 OF INVESTIGATION)

This story starts with receipt of a clinical E. coli O157:H7 (O157) isolate at the Minnesota Department of Health (MDH) Public Health Laboratory (PHL) on September 17, 2007 (submission of clinical O157 isolates to MDH is mandatory in Minnesota). That same day, a health care provider notified MDH that the case (Case 1, a 4 year-old girl) had illness onset on September 10, presented to an ER with bloody diarrhea on September 13, and had developed hemolytic uremic syndrome (HUS).

On the day of the report (September 17), an MDH epidemiologist interviewed the mother of Case 1 by telephone using the MDH Standard Questionnaire for STEC and Salmonella Cases.

- The case had consumed a hamburger, reportedly pink in the middle, at a high school football game tailgating event 3 days prior to illness onset (see interview excerpts below).
- The burgers had been brought by another person, but the case’s mother reported that the source hamburgers were pre-made, frozen, 1/3-pound patties, and had been purchased at a Sam’s Club store in Eagan (a suburb of St. Paul).
- Queries of the mother and high school staff revealed that there were no other known illnesses among event attendees.

What are you thinking at this point?
Move to the next page to see what the investigators were thinking...

<table>
<thead>
<tr>
<th>Date of Isolate Receipt at MDH PHL</th>
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<tr>
<td>17 18 19 20 21 22 23 24 25 26 27 28 29 30</td>
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<tr>
<td>September October</td>
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19. Did you attend any large gatherings the week before your illness (wedding, receptions, showers, parties, festivals, fairs, etc.)? Yes [ ] No [x] 
- if yes, when: 9/17/2007
- what type of event: Tailgating party before 1st football game - Eagan HS, Faculty + Staff + Family, Ate hamburgers + hot dogs - noticed they were pink - came from Sam's Club Eagan 3rd pound pre-frozen patties - none left.
CASE 1

Assessment: The reported consumption of an undercooked hamburger (classic vehicle for O157) 3 days before illness onset (classic incubation for O157) vaults the hamburger patties to the top of the list of suspected vehicles. Because the hamburger patties were a commercially distributed product, and as such we could expect more cases to come through surveillance in the near future if they really were the vehicle, we immediately contacted the person who had brought the patties to initiate collection and testing of remaining patties. However, no product remained, and the packaging had been discarded.
September 21 (DAY 5)

Subtyping of Case 1’s O157 isolate by pulsed-field gel electrophoresis (PFGE) at the MDH PHL was completed on September 21. 2 enzymes are used routinely on O157 isolates in Minnesota. The isolate was given the Minnesota 2-enzyme subtype designation MN744ECB13 (national PulseNet designation EXHX01.00560/EXHA26.0015).

- The first enzyme (XbaI) pattern, MN744, was very rare in Minnesota, having been seen only three other times in the previous 12 years.
  - However, the XbaI pattern was similar to MN179, the most common XbaI pattern in Minnesota (see PFGE image below).
- The second enzyme (BlnI) pattern, ECB13, was the most common BlnI pattern in Minnesota, and occurred commonly in conjunction with MN179.

![PFGE-XbaI](image)

- E2007001378  MN179
- E2007002470  MN744
October 1 – 3 (DAYS 15-17)

On October 1, MDH received 2 additional O157 isolates through routine surveillance that, when subtyping was completed on October 3, were also PFGE subtype MN744ECB13.

- One isolate was from a sibling (Case 2) of Case 1.
  - Because illness onset was 4 days after onset of Case 1, Case 2 was classified as a potential secondary case; therefore, an exposure history was not taken.
- The other isolate was from a 9 year-old HUS case (Case 3).
  - The mother of Case 3 was interviewed with the MDH standard O157 questionnaire on October 3 and reported that the case had consumed a grilled hamburger 2-3 days before illness onset on September 20, and that the burger was made from a frozen, pre-made hamburger patty purchased from a Sam’s Club store in White Bear Lake (also a suburb of St. Paul). See interview excerpts below. Note that there were 2 distinct sources of hamburger reported.
  - The mother’s Sam’s club membership card number was collected.
  - The mother also reported that leftover product and packaging were available, and we made arrangements to collect them the next day (October 4).

5. Where and when did you purchase any hamburger you ate the week before your illness? 

   Sam’s Club - frozen, pre-made patties - Still have some.

6. What type of hamburger was it (extra lean, lean, 9% fat, etc.)?

   What size package? ½ lb. □ 1 lb. □ 2 lb. □ Other □

   Angus Meats - Maplewood (Butcher Shop).

   3 x 1 lb packs packaged “prime” hamburgers. 95% lean.

   still have some.

   a. Hamburger as an ingredient: type of dish caserole
   b. Hamburger raw Y N U
   medium (pink in middle) Y N U
   well done (no pink) Y N U
   c. Hamburger patty-grilled

   01/17/07
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  - The mother also reported that leftover product and packaging were available, and we made arrangements to collect them the next day (October 4).

**Assessment:**
Case 2 is inconsequential in the investigation, but Case 3 represents a second case household. The fact that Case 1 and Case 3 have isolates with the same very rare XbaI PFGE pattern, and no obvious connection (i.e., they did not know each other, did not attend the same day care, did not visit the same restaurant, did not visit the same petting zoo or attend the same gathering, etc.) indicates that a common source outbreak due to a commercially distributed food product is almost certainly happening. Case 3’s history of consuming a hamburger of a description and source that sound much like that of Case 1’s hamburger makes us fairly certain we have identified the vehicle. However, we need more product detail and evidence to confirm the Sam’s Club frozen, pre-made hamburger patty hypothesis and reach that “threshold of confidence” that prompts us to implement an intervention. As we really believe there are contaminated hamburger patties in people’s freezers, we act as fast as we can to acquire that evidence.
October 4 (DAY 18)

MDH visited Case 3’s household and collected the remaining hamburger patties and packaging.

- The brand was American Chef’s Selection Angus Beef Patties (see image below), and there were numerous patties left in the box. The patties were submitted to the Minnesota Department of Agriculture (MDA) Laboratory for O157 testing. But testing takes time, and we can stop this outbreak even before the results come back.

Sam’s Club membership card numbers were acquired for Case 1 and Case 3 (for Case 1, this required calling the person who purchased the burgers for the tailgating event at which Case 1 was exposed). The numbers were provided to MDA, which passed them along to a Sam’s Club representative along with a request for purchase histories in the weeks before illness onset.

- For Case 1, Sam’s Club produced the information only 3 hours after it was requested (fantastic response time), and it showed that “American Chef’s Angus Burgers” were purchased on September 7.

- We were confident that this was the same product consumed by Case 3, but this needed verification.

![Image of American Chef's Selection Angus Beef Patties]

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**Case 1**

**Case 2**

**Case 3**
October 4 (DAY 18) continued

A fourth cluster case was identified through routine surveillance.

- The O157 isolate was received by MDH on October 2, and on October 4 PFGE subtyping determined that the isolate matched the outbreak PFGE pattern.
- The case (Case 4) was a 12 year-old boy with onset on September 26.
- Case 4’s father was interviewed on October 4 with the MDH standard O157 questionnaire (although we were confident we knew the vehicle, we wanted to be systematic and make sure there weren’t other commonalities between the cases).
- The father reported that the boy had eaten a hamburger during the week before illness onset.
  - The burgers were reported to have been made from frozen pre-made patties, brand name American Chef’s Selection Angus Burgers, and purchased at Sam’s Club in Maple Grove (a suburb of Minneapolis).
- The mother had a Sam’s Club membership card, but she was not home at the time.

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• The mother had a Sam’s Club membership card, but she was not home at the time.

Assessment:
One more day has passed, and we are very confident that we know what the vehicle is. A fourth case (representing a third case household) was identified and reported consumption of burgers described much like the burgers consumed by Cases 1 and 3. We feel like we are almost there, and just need to tie up a few loose ends before we go public.
October 5  (DAY 19)

MDH was notified by MDA at 8:05 a.m. that info from the Sam’s Club membership card number query confirmed that the burgers consumed by Case 1 and Case 3 were indeed the same product (same product name, Item #, and UPC #).

Case 4’s household was called back, and specific product information on the box of American Chef’s Selection Angus Burgers was obtained (and the box itself was ultimately obtained), and compared to the same information on the box from Case 3’s household.

- The results were striking: the 2 different boxes of burgers were produced on the same date (as indicated by the same Best if Used By date), on the same production line, 1 minute apart.
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**Assessment:**

Now we have reached that “threshold of confidence” that prompts a public health intervention. What is the probability that 3 temporally associated cases with the same rare PFGE subtype of O157 would have consumed the same specific brand of hamburger patties purchased from 3 separate Sam’s Club locations, if those burgers were not the source of the outbreak (furthermore, 2 of the boxes of product were produced 1 minute apart)? We deemed a community case-control study to be completely unnecessary. Although we didn’t know the background rate of consumption of this brand of hamburger patties, experience made it obvious to us that the chance that this was a coincidence was extremely low. Even though preliminary lab testing results of ground beef patties were not yet available, the epidemiology was so strong that we felt we had no choice but to go public. Thus, a press release was issued the afternoon of October 5. Most of our cases still had leftover patties in their freezers, which meant that many other people did as well; risk to the public was clearly ongoing.

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**Minnesota Department of Health**

**News Release**

October 5, 2007

Contact information

E. coli O157:H7 cases linked to frozen ground beef patties purchased at Sam’s Club stores in August and September

Product removed from store shelves; customers asked to return or destroy
The outbreak PFGE subtype of O157 was ultimately cultured from raw patties from all six boxes of product recovered from cases’ homes and tested at the Minnesota Department of Agriculture. Product was heavily contaminated - 13 of 13 subsamples taken from each box were positive. Waiting for product testing results would certainly have resulted in unnecessary additional exposure to the product among the public. In the end, 11 outbreak cases were identified in Minnesota, including 4 HUS cases (HUS occurred in all 3 female Minnesota cases). This is a very high percentage of HUS, suggesting a particularly virulent strain (and/or a heavy dose). Thirty-six additional O157 isolates with the outbreak PFGE pattern were reported from 14 other states. The outbreak subtype of O157 was isolated from implicated product in California, South Carolina, Tennessee, and Wisconsin. Two additional HUS cases were identified in Tennessee. All in all, the rapid epidemiologic investigation (and not waiting for food testing results or an unnecessary analytic study) undoubtedly prevented much morbidity, and probably mortality as well.

Summary of Key Investigation Lessons:

- The **PFGE subtype** of isolates in this cluster was **very rare**, which **indicated** that this cluster indeed represented a **common source outbreak**, thus warranting aggressive follow-up.
  
  See: [CIFOR Guidelines for Foodborne Disease Outbreak Response Chapter 4.2.9.2](http://mnfoodsafetycoe.umn.edu/)

- The **cluster cases had no obvious commonalities**, indicating a strong likelihood that the **outbreak vehicle was a commercially distributed food item**; again, this warranted aggressive follow-up.
  
  See: [CIFOR Guidelines for Foodborne Disease Outbreak Response Chapter 5.2.2.2](http://mnfoodsafetycoe.umn.edu/)

- It is usually **worthwhile to be aggressive in following up on high risk exposures** – in this case, an undercooked hamburger reported by the first case.

- **Obtaining detailed product information (e.g., brand, type, purchase location) up front**, during initial surveillance interviews, was critical in rapid identification of the vehicle. This is especially true for commonly eaten foods like ground beef. The vehicle was suspected with just one case, we were pretty sure of it after the second primary case, and we confirmed it with the third primary case.
  
  See: [CIFOR Guidelines for Foodborne Disease Outbreak Response Chapter 4.2.9.3.2](http://mnfoodsafetycoe.umn.edu/)
  
  See: [CIFOR Guidelines for Foodborne Disease Outbreak Response Chapter 4.2.10.3](http://mnfoodsafetycoe.umn.edu/)

- **Outbreaks can be solved with very few cases, using epidemiologic methods alone.** To do this, very specific exposure details need to be obtained (see previous bullet).

- **Epidemiologic data often are sufficiently strong to implicate an outbreak vehicle and implement a public health intervention.** In addition, epidemiologic methods often can identify an outbreak vehicle more rapidly than laboratory testing of food.

- **Analytic studies may not be needed to identify an outbreak vehicle – if sufficiently specific product information can be obtained for cases.**

Acknowledgments:

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