KEY POINTS
for Successful Foodborne Outbreak Detection and Investigation

PRIORITIZATION OF PULSED-FIELD GEL ELECTROPHORESIS CLUSTERS FOR INVESTIGATION

Pulsed-field gel electrophoresis (PFGE) will still be an important molecular subtyping tool in the United States, until whole genome sequencing (WGS) becomes fully implemented. It can be challenging to determine which PFGE clusters should be investigated, and once initiated, how aggressively they should be pursued. Epidemiologists have to balance preserving scarce public health resources by avoiding or minimizing investigations of clusters that likely do not have a common source, with the goal of identifiying as many outbreaks as possible. Here are some key points for determining how to prioritize *Salmonella* and *E. coli* O157 PFGE clusters for investigation and how hard to pursue them, based on Minnesota Department of Health's (MDH) research.

Cluster definition

- To study proportions of clusters that are solved, MDH has used a cluster definition of ≥2 cases in different housholds with isolates of the same PFGE pattern and with specimen collection dates within 2 weeks. (Note: investigations aren't limited to clusters with this definition, but for the purpose of measuring investigation success it is necessary to have one objective definition).

Certain characteristics of PFGE clusters can be used to predict which clusters are more likely to be solved (and by extension, which represent common source outbreaks vs. unrelated sporadic cases):

- Cluster size (number of cases)
  - For *Salmonella* and *E. coli* O157, clusters of 3 cases, of 4 cases, and of ≥5 cases are more likely to be solved than clusters of 2 cases (with the proportion solved generally increasing with the size of the cluster).
- Cluster density (over what time frame the initial cases occurred)
  - For *E. coli* O157, clusters are more likely to be solved if the first 2 isolates are received in the public health lab on the same day. Clusters are also more likely to be solved if the second case isolate was received within 1-7 days of the first case isolate (compared to ≥15 days apart).
  - For *Salmonella*, clusters are more likely to be solved if the first 3 isolates are received on the same day, and if the third case isolate in the cluster is received within 1-7 days of the first case isolate (compared to ≥15 days apart). Clusters **are** also more likley to be solved if the third case isolate was received within 8-14 days of the first case isolate.
- Commonality of the PFGE subtype
  - In general, a new or rare PFGE subtype suggests that a cluster is more likely to represent a common source outbreak.

- *Salmonella* clusters of very common subtypes are less likely to represent a common source outbreak (compared to common or uncommon subtypes).
  i. However, common subtypes do cause outbreaks commonly, so do not dismiss them out of hand. Rather, use the other cluster characteristics.
  ii. Increased subtype discrimination, such as that provided by a second restriction enzyme, or, ideally, whole genome sequencing, is tremendously helpful in this situation.
  iii. When evaluating how common a particular subtype is, it is best to use state rather than national PFGE data, as some subtypes are very common in some regions but rare or absent in others.
- Subtype commonality has little effect on likelihood of *E. coli* O157 clusters beng solved.

Additional questions to consider when deciding how to prioritize a PFGE cluster

- Are cases share geographically related cases?
- Are the cases distinct demographically?
- Do any of the cases have a "red flag" exposure like sprouts or unpasturized milk?

If any of these are true, this argues for prioritizing clusters higher.

Often the decision isn't if you should investigate a cluster or not but how aggressive you should be

- If there are only 2-3 cases, compare routine interviews to identify potential common exposures
- As additional cases occur, the next step is to identify specific exposures which you will use to re-interview older cases and incorporate into the initial interviews of newer cases.
  - Create a short supplemental questionnaire.
  - Ask specifically about all of the restaurants mentioned by all of the cases.
  - Ask about interesting exposures mentioned by other cases.
  - Get additional details on suspect foods like brand or variety.

Impact of whole genome sequencing (WGS)

- We don't yet know the exact impact WGS will have, but our experience with *S.* Enteritidis and *S.* Typhimurium indicates that:
  - Cases within an outbreak typically fall within 5 single nucleotide polymorphisms (SNPs) of each other (but, how all serotypes behave remains to be determined).
  - The number of clusters compared to PFGE will depend on the serotype (increase for *S.* Enteritidis and decrease for *S*. Typhimurium).
  - But, many clusters will have fewer cases than when based on PFGE.
  - Investigators can have more confidence that WGS clusters truly represent a common source outbreak and that investigation efforts will be worthwhile, or that food isolates that match a cluster are meaningful.

Additional Resources:

http://mnfoodsafetycoe.umn.edu/cluster-investigations/
MN Systems: Cluster Investigations

http://mnfoodsafetycoe.umn.edu/salmonella-cluster-investigation/
Evaluation of PFGE Cluster Investigations: *Salmonella*

http://mnfoodsafetycoe.umn.edu/e-coli-o157h7-investigation/
Evaluation of PFGE Cluster Investigations: *E. coli* O157

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