Proceedings of
The Institute of Food Technologists'
First Annual Food Protection & Defense
Research Conference
November 3-4, 2005
Atlanta, Georgia

[Session: **Public Health and Response Coordination]**

Public Health and Response Coordination: the State of the Art

DR. CRAIG HEDBERG
UNIV. OF MINNESOTA

Thank you everybody for attending this session. What I want to do today is give you some perspectives both on my work over the years investigating food borne outbreaks and work that is being done in collaboration with the National Center for Food Protection and Defense and some other organizations to start to systematically evaluate our public health system for how we do our job of foodborne disease surveillance, with the idea that systems research should provide us insights that we need to do a better and more timely job of foodborne disease surveillance.

I'll get right to the conclusions; this slide is a depiction of the state-of-the-art of food borne disease surveillance. An outbreak you should all be familiar with, *E. coli* 157H7 associated with Dole, pre-packed lettuce. This was an outbreak which was identified in Minnesota. You can see a cluster of cases in red; people bought lettuce from the 13th through the 16th of September. The first flurry of cases occurred from the 16th to the 18th of September. The first was submitted to the State Health Dept. in Minnesota on the 22nd and by October 1, preparations were in place for a press release and recall of the specific product. That's a period of about two weeks from when the first illnesses occurred until we had a public health intervention. For foodborne pathogens like Salmonella and *E. Coli* 157, this is about as good as we can currently expect our system to perform.

Now when we start thinking about the challenges that intentional contamination events and bioterrorism pose, to the extent that some of these same agents may be potential weapons it creates some serious limitations on our ability to respond. That is one of the other aspects of our program in the National Center, to do some predictive modeling of foodborne disease events and public health responses. The data that I'm about to show you is all data that has been developed in part to feed into these models, that we've looked at over the past day or 2, to help us understand better how the public health system works and how it will relate to the distribution of illnesses in the event of an outbreak. Now just a little bit of background, the whole process of evaluating our public health surveillance system has not been going on very long.

CDC and CSTE, the Council of State and Territorial Epidemiologists has for several years been looking at elements of our national capacity for epidemiology and food borne response. That has led to a series of evaluations. The most recent being an enteric disease investigation timeline study which was designed to help quantify the time elements involved in our surveillance systems. This project looked at time intervals from the onset of symptoms until when a stool sample gets collected, when that stool sample gets submitted to the public health laboratory and eventually gets sub-typed and the information can then be linked with the epidemiology data. Similarly, on the left side the stream of information related to that single case—case report from a clinician to a health department, leading to an interview and then again providing us an opportunity to link the epidemiologic and the laboratory data.

This is a flow of information which is typical for most state health departments in the US. I'll jump to sort of the median values and inter-quartile ranges by state for onset of symptoms to timeline events. So, on this table we have salmonella and *E. Coli* 157 data on the median interval from onset of symptoms until collection of stool; four days for salmonella and three days for *E. Coli.* It took 9 d from onset of symptoms to report cases of salmonella to the health department, 7 d on average to report cases of 0157 and you can follow down to the bottom. The time element for PFGE sub-typing which increasingly is an important tool for us to identify clusters of cases and is the raw material that feeds into our national surveillance system such as Pulse Net. On average, it takes 18 d after onset of symptoms for salmonella and 15 d from onset of symptoms for *E. Coli* 157. So we can see a couple of things in this data. One is that the process of moving information throughout clinical and public health systems is a little bit slow but we can see that it moves a little bit faster on average for *E. Coli* 157 infections than it does for salmonella.

Now those are the medians, and one of the things that is actually important for us when we start looking at the response to massive events, that we might expect with a bioterrorism outbreak, is how quickly the early cases begin to get in to see a physician. This is data looking at onset of symptoms to collection of stool sample for several pathogens, *E. Coli*, salmonella, shigella, campylobacter and actually over this period of the 1st week, there's not a lot of difference. The behavior of people with these gastrointestinal illness looks like it's fairly consistent; median intervals being in the 3 to 4 d range after onset of symptoms. Again, following the distributions we see the median for *E. Coli* 157 and salmonella being in the 7 to 9 d range. But if we were looking at potential to detect the really big event it might be detectable if even 10% of cases get into see a physician within 2 or 3 d following onset of symptoms. So even though this data is derived from sporadic infections we can begin to use it in ways that help us model potential responses to big events.

This is data looking similarly at timeline to getting specimens into the public health laboratory, again 8 to 10 d and *E. Coli* 157 isolates coming

in a little quicker with the earliest possible time in the range of 3 to 4 d. We also looked at how public health systems are organized to see what impact that had on the timeliness of the surveillance data. This is data for *E. Coli* 157 and it compares states where reporting to a local health department, which is the most common mode of public health response in this country, to states with highly centralized surveillance systems. What we can see here is actually that local heath departments are actually quite effective at getting back to the patient and interviewing them very quickly. In fact, on average they're 5 d earlier than in centralized reporting systems. Conversely, the states with the centralized and heavily lab-based systems were actually much quicker to do the sub-typing on the isolets. So we have very different streams of response that are tied to the structure of the public health system that have some big implications for our ability to detect and respond to outbreaks.

These are some conclusions that can be drawn from the data; states with cases reported initially to the local health department were quicker to interview cases but slower to sub-type the isolates. They were faster response times for 0157 compared to salmonella which appears to be due to the higher value we put on following up on a 157 case. Primary differences for the timeline appear to relate to actions at the local or state health department following the report of the case. Now those are for individual sporadic cases; we also have data on outbreaks that were detected during this timeframe in this study state. This looks at onset, the number of days from onset of symptoms to the outbreak complaint or recognition for different pathogens.

The group of cream-colored bars, in this slide, represents outbreaks of bacterial toxins. These are typically recognized and recorded within 2 to 3 d following onset of symptoms or they are not recognized at all. The green bars represent outbreaks of neuron-virus and neuron-virus typically has a little longer incubation period and so the cases tend to be a little farther away from the point of exposure when they get sick, that leads to a little bit of a delay in recognition of those. When we get out to red being *E. Coli* and blue being salmonella, we are out now in the range of one to two weeks before most of these are being detected. When we look back at the added status this is consistent with these cases being clinically diagnosed with a laboratory confirmation leading to the detection of the outbreak. We can see evidence of this when we collapse all of our outbreaks by pathogen type; *E. Coli* 157 and salmonella are bacterial pathogens and look at how the outbreak was detected. We had 2 cases early on, where providers reported to the public health department that they thought something was going on. These correspond to when patients are actually in the physician's office and the physician stimulates a report. Most of our cases are reported in the time period that corresponds to a laboratory diagnosis even when that is a complaint coming in from the patient. These are complaints that're really driven by the fact that they have just been diagnosed as having salmonella. On this slide, on the far end we have outbreaks which are identified because of cluster analysis. Most of those are recognized more than three weeks following the onset of the event. I think this has some really strong implications for us in terms of how we want to work with our system to try to improve reporting. This is some summary data; you will get this but I'm going to skip over it right now.

In our food protection and defense project we wanted specifically to look at multi-state outbreaks as a class of important potential models for bioterrorism events if you attack a food item early in the distribution system. We wanted to look at the processes and decision making structures in multi-state outbreak investigations to see what impact that would have one the timeliness of the response. We began to look at outbreaks reported to CDC following improvements made in the reporting system in 1998. So essentially we reviewed outbreaks that were reported from 1998 through 2003; there are a total of 56 that we tried to look at in this review. A little over half of those are due to salmonella and that reflects a bias in what gets reported to the health system; 18% were due to *E. Coli* 157. This is data very similar to the data that we showed from the EDITS project looking at intervals from onset of symptoms to outbreak recognition or complaint. However, these are from multi-state outbreak investigations. There was one noroviral outbreak that was detected right away because of multiple related outbreaks; a couple shigella outbreaks, some *E. Coli* 157 and salmonella. Again, we're in the range now of 2 wk going out to 3 wk and 4 wk for most of these to be reported. This corresponds again to when cases are being confirmed in the laboratory and when subtype analysis can detect those cases.

This slide shows that same data array now by type of report, whether it was a complaint, a report from a provider, increased incidence in a specific type of salmonella or a PFGE sub-typing. You can see again that we tend to hear about outbreaks earlier when we have complaint and provider reporting than when we have detection because of cluster analysis. Those medians were 18 d for *E. Coli* O157, 23 d for salmonella and what is really critical for us, when we begin to look at the response of our public health system though, even in multi-state outbreak investigations; when a single state takes the lead in the investigation, very much like the state-of-the-art picture I showed you from Minnesota, those outbreaks are more likely to get a rapid response and determination of the source. A lot of the outbreaks that are detected because of multi-state clusters of pulse field patterns produce investigations that are very difficult to coordinate and don't yield satisfying results very rapidly.

This slide shows summary data for outbreaks investigated by a single state. The median interval from recognition to intervention was 7 d, 18 d for multi-state outbreak investigations. For interventions that were made within 8 d, three quarters of those were led by individual investigations. So this is data which is consistent with our EDITS results and it's apparent that multi-state outbreaks detected by case reports and follow-ups are recognized sooner than outbreaks identified by PFGE cluster evaluation. In addition, public health interventions are made more quickly in multi-state outbreaks investigated primarily by single states. This has some important implications. Strong state and local food borne disease surveillance programs are necessary for effective national responses. Strong state and local food borne disease surveillances are really the key to our effective national responses. Rapid and thorough investigation of outbreaks and clusters by individual state and health departments should be encouraged even if a multi-state outbreak is suspected.

This is very consistent with CDC's evaluation of pulse field clusters. CDC found that they were more likely to detect a source for a cluster if there was an unusual exposure suspected or if a subset of cases were linked. This is what happens when you have states looking directly at their cases in real time. You begin to develop those links that then allow for the detection of the source. This is consistent with other previous reports; this is data from Minnesota back in '94 and '95 when we started looking at PFGI routinely for a 157; we found that if we had a cluster involving 5 or more cases, two thirds of the time we were able to identify the source, very infrequently when clusters were smaller than that. So it suggests to us that we really need to be changing the emphasis of how we pursue these outbreak investigations.

I want to just briefly talk about botulism because this is obviously the single food borne disease that is the greatest concern to us regarding intentional contamination. This has been very nicely reviewed by Jeremy Sobel colleagues at CDC, published in EID. This is an epidemic curve showing a number of cases from 1990 to 2000; you can see the range is from about 20 to 50. Botulism is not a common disease in the United States. One of the ways that we will detect an outbreak or an intentional event with botulism is that clinicians have

some awareness. Because it is such an uncommon disease even one or two cases will prompt a very strong public health response.

In looking at those cases, 102 events, 160 cases in the lower 48 states, most of those were associated with noncommercial products, 2 events in restaurants and 5 events associated with some other noncommercial product. So the current background information we have with botulism creates the conditions where any occurrence of botulism will lead to a rapid detection. I want to focus on a couple of outbreaks that were published in the literature to highlight that. The first is an outbreak that occurred in Texas; most of the cases were associated with a church supper on August 25th. Four days later the event was recognized. This slide shows case onsets for individual patients. It took 4 d following the event before the nature of the event was recognized.

We also have a lot of experience with botulism up in Alaska where Native Americans are frequently exposed to botulism as a result of eating fermented foods. In this case there was an outbreak associated with people eating parts of a dead whale. Exposures occurred over a period of 3 d and again within 4 d of the onset of the event, physician reported three suspect cases and a public health response followed. So the response to outbreaks of botulism is based on levels of awareness, previous experience in the outbreak setting. Interestingly in a survey of physicians that was recently published in the archives of internal medicine; about half of physicians surveyed could correctly diagnose botulism. So even given that relatively low level of correct diagnosis, if we had very many cases at all, somebody is going to see it, recognize it and initiate a response. So I think the outbreaks we looked at in these previous slides really define for us what the bottom line is in terms of how rapidly a large outbreak of botulism would be detected.

So within the Center we are working with the public health community to establish a public health work group to help provide critical expertise, guidance and feedback on our public health system capabilities and to help us look at this data and begin to translate the results of this data into improved performance of our public health surveillance system.

What I want to get out of this is that we have many more public health responses, such as depicted in this slide, so that it becomes not only the state-of-the-art but a representation of the state of our practice.

Public Health and Response Coordination

The State of the Art

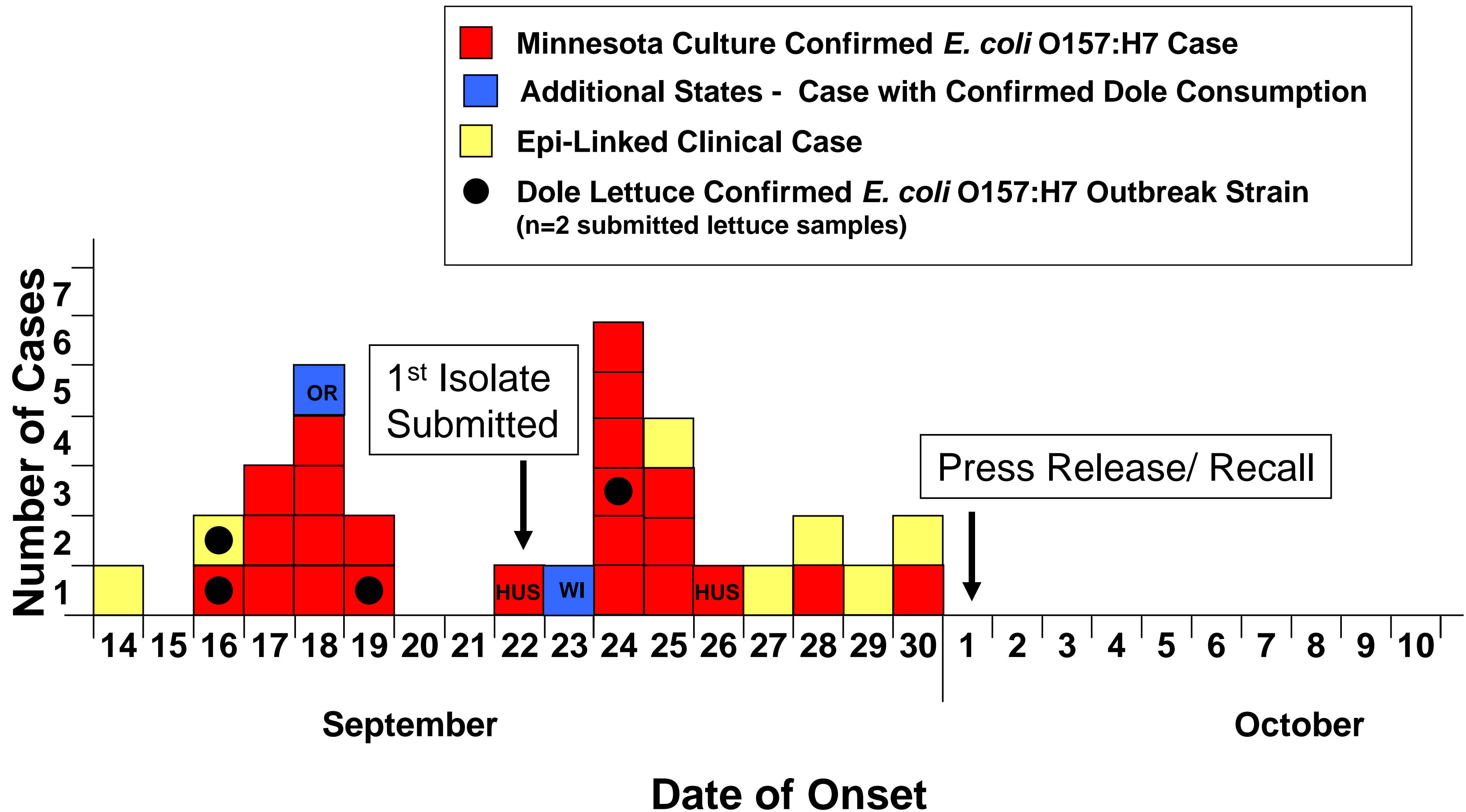
Craig Hedberg
University of Minnesota
NCFPD

UNIVERSITY OF MINNESOTA

NATIONAL CENTER FOR
FOOD PROTECTION AND DEFENSE
A HOMELAND SECURITY CENTER OF EXCELLENCE

PRIMARY PRODUCTION ➤ HARVEST ➤ TRANSPORTATION ➤ STORAGE ➤ PROCESSING ➤ DISTRIBUTION ➤ RETAIL/FOOD SERVICE ➤ CONSUMER

E. coli O157:H7 Cases Associated with Dole Prepackaged Lettuce



Public Health Response and Epidemiology

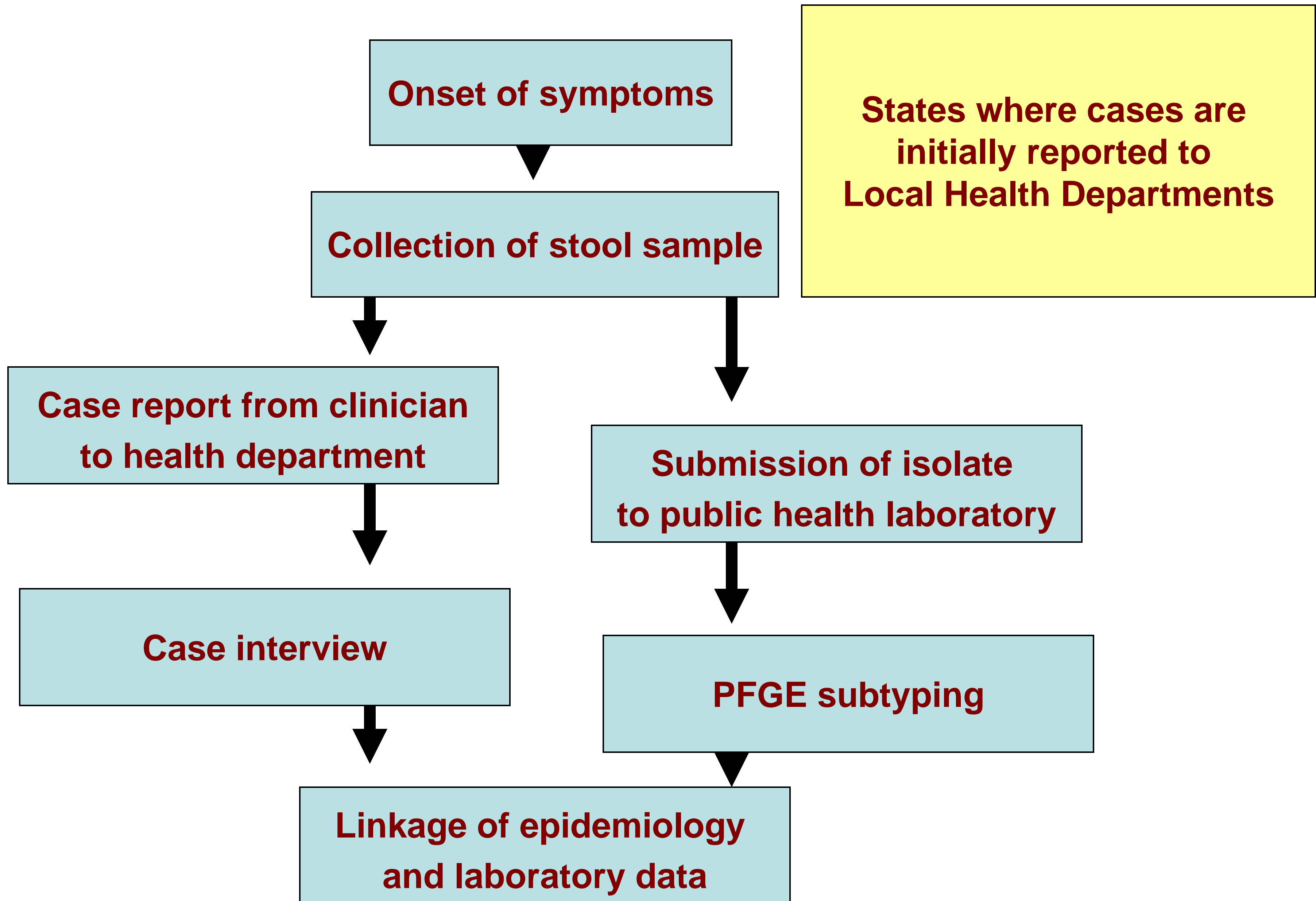
- Predictive Modeling and Decision Making Tool To Limit the Impact of Attacks on the Food System
- Modeling Public Health Response and Remediation Strategies
  - Processes and Decision Making Structures in Multi-State Outbreak Investigations
  - Diagnosis, Reporting & Investigating Botulism Outbreaks
- Public Health Core

Public Health Response and Epidemiology

- Backround:

  Enteric Disease Investigation Timeline Study

  – Assess time intervals from disease onset to reporting to CDC
  – Follow-up to National Assessment of Epidemiology Capacity in Food Safety Programs 2002 (http://:www.cste.org)
  – CDC Cooperative Agreement with CSTE

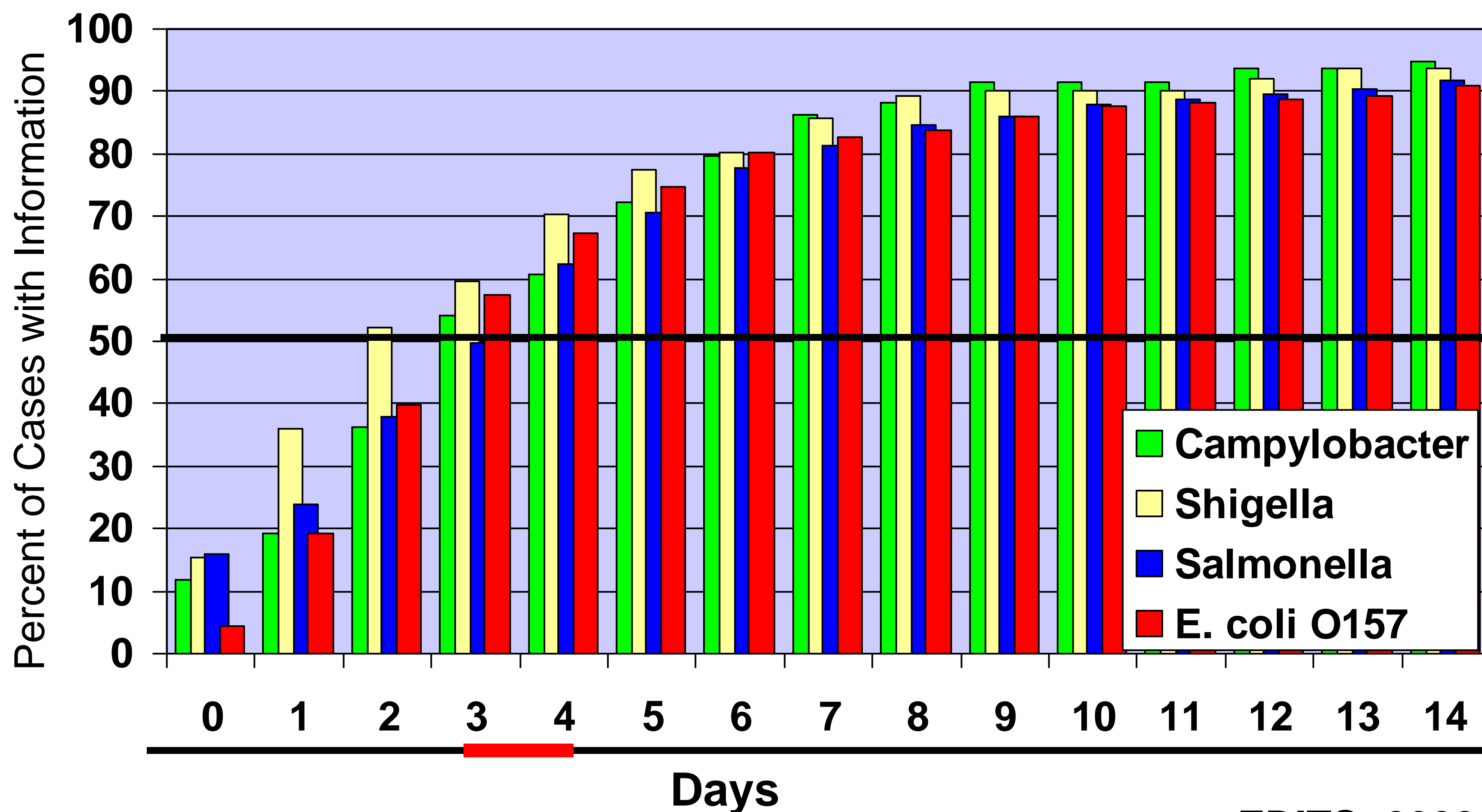

Onset of symptoms
Collection of stool sample
States where cases are initially reported to Local Health Departments
Case report from clinician to health department
Submission of isolate to public health laboratory
Case interview
PFGE subtyping
Linkage of epidemiology and laboratory data

Median Intervals (days) and Range (by state) from Onset of Symptoms to Timeline Event

Timeline Event	*Salmonella*	*E. coli* O157
Collection of stool sample	4 (2, 4)	3 (2, 6)
Case report from clinician to health department	9 (8, 11)	7 (6, 7)
Submission of isolate to public health laboratory	10 (8, 11)	8 (5, 9)
Case interview	14 (14, 22)	12 (9, 16)
PFGE subtyping	18 (15, 28)	15 (11, 22)

Onset of Symptoms to Collection of Stool Sample

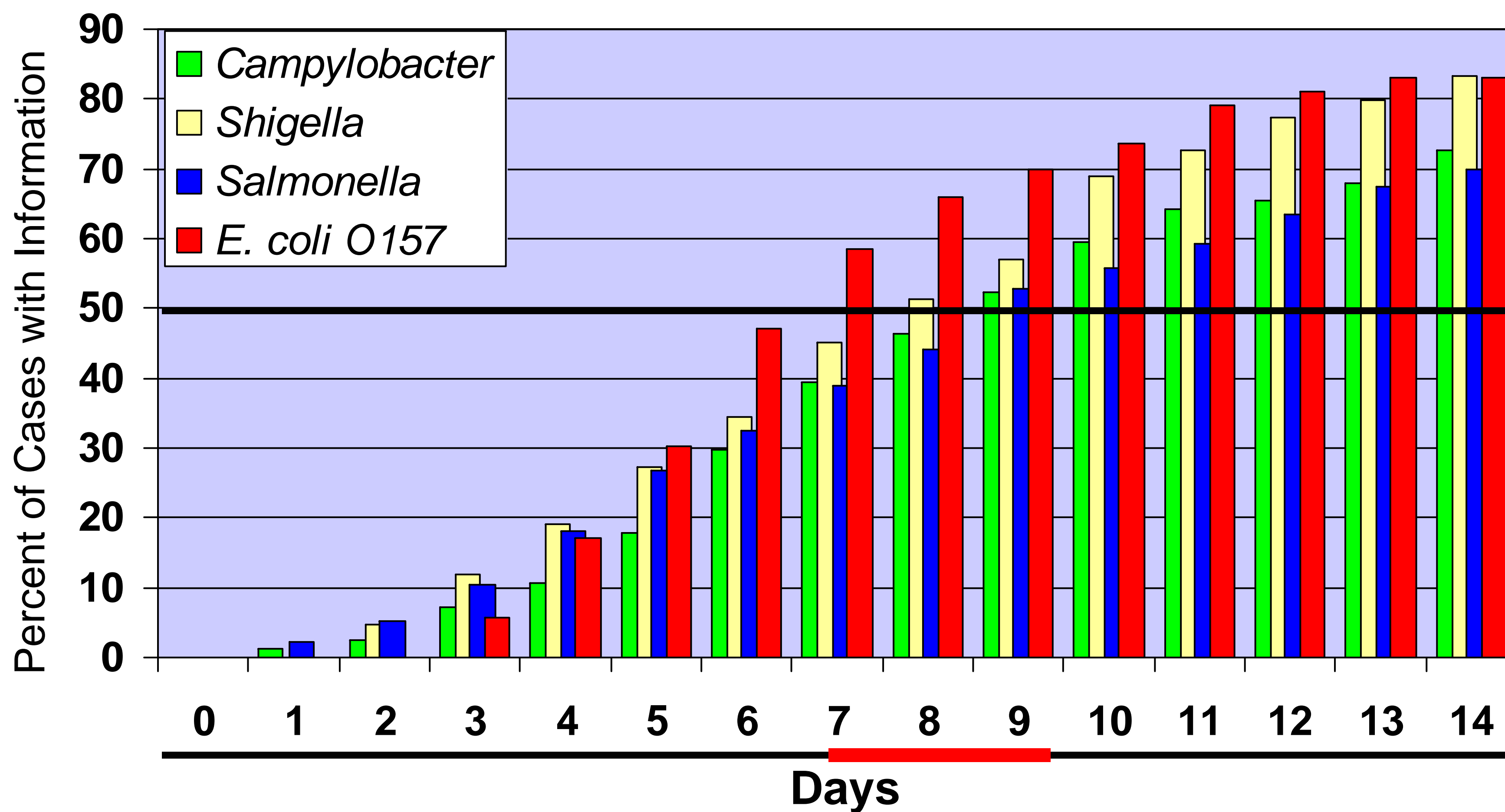
Timing of health care seeking behavior consistent across pathogens



EDITS: 2002

Onset of Symptoms to Case Report by Clinician

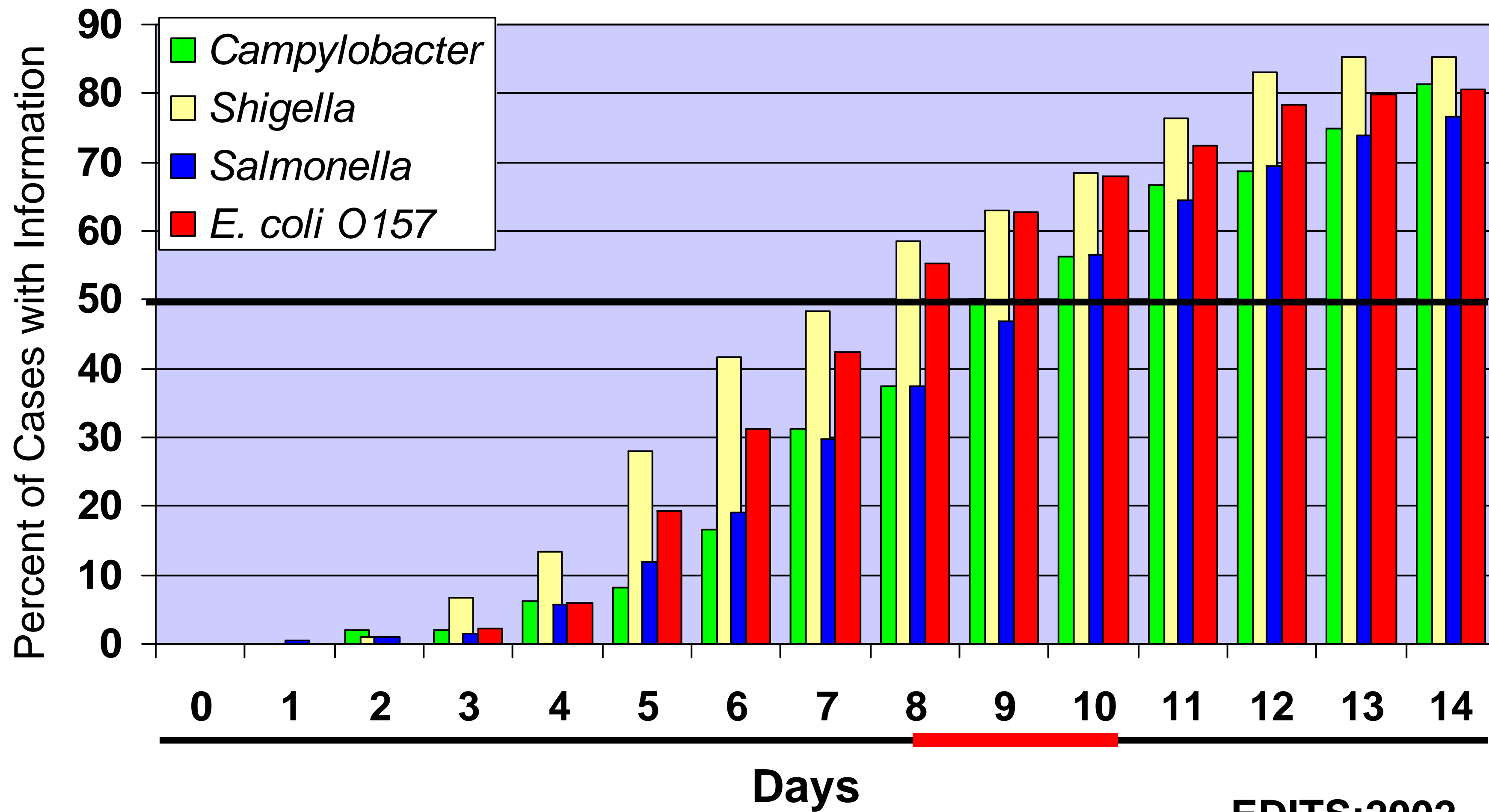
E. coli O157 cases <u>2 days</u> earlier than Salmonella



EDITS: 2002

Onset of Symptoms to Submission of Isolate to Public Health Laboratory (PHL)

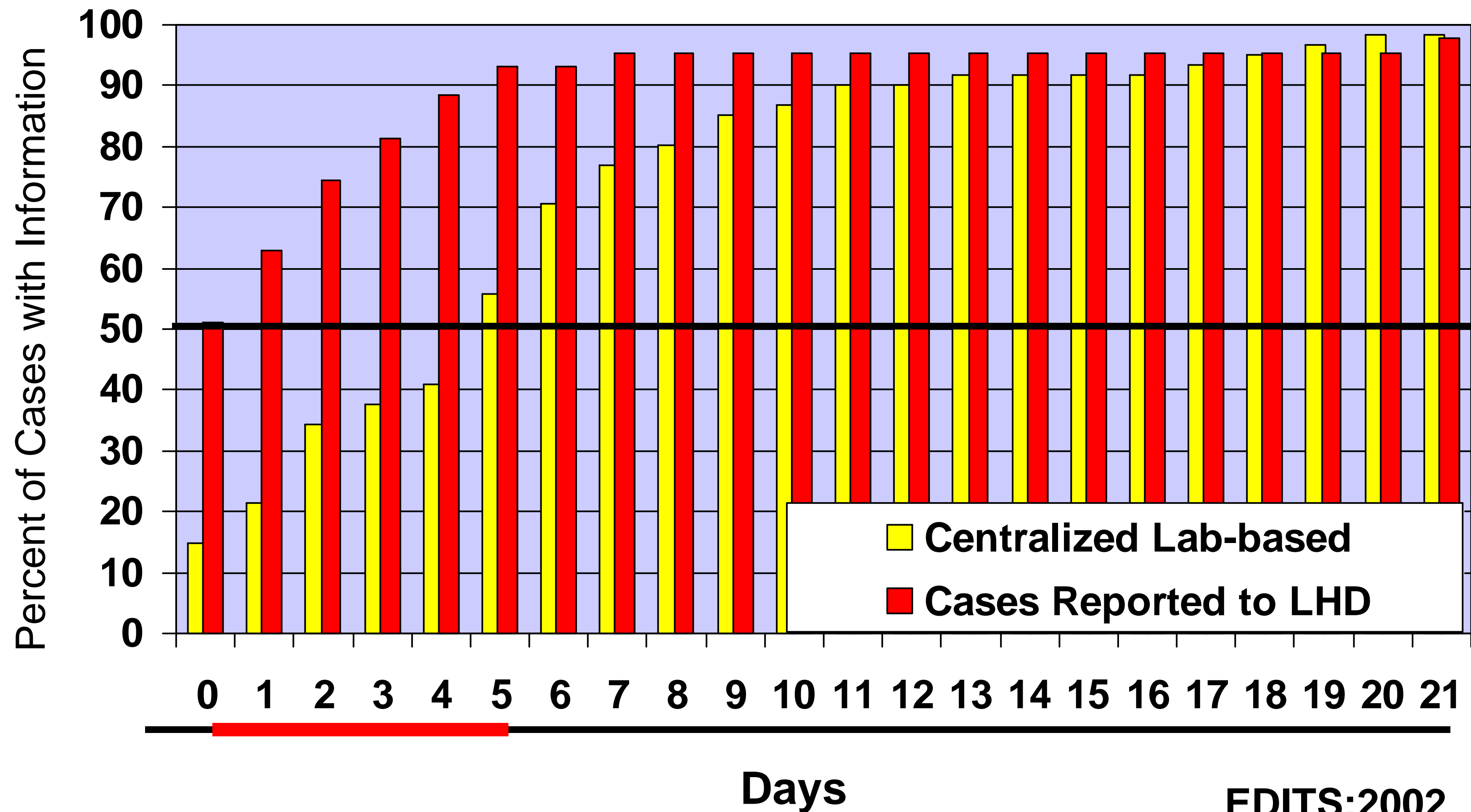
E. coli O157 cases 2 days earlier than Salmonella



EDITS:2002

Case Report to Case Interview
E. coli O157:H7

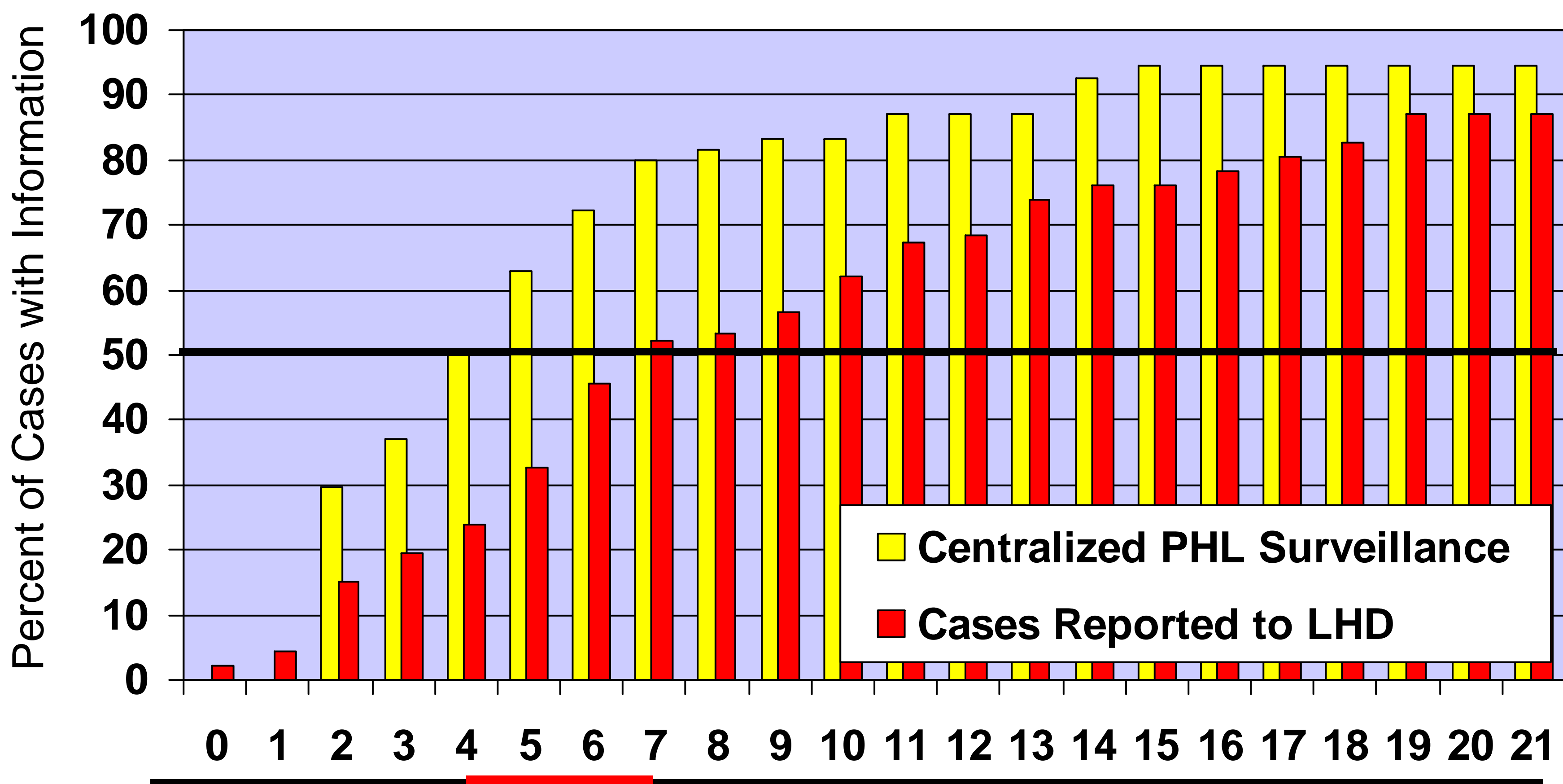
***5 days** earlier in states with reporting to Local HD*



EDITS:2002

Submission *E. coli* O157:H7 Isolate PHL to PFGE

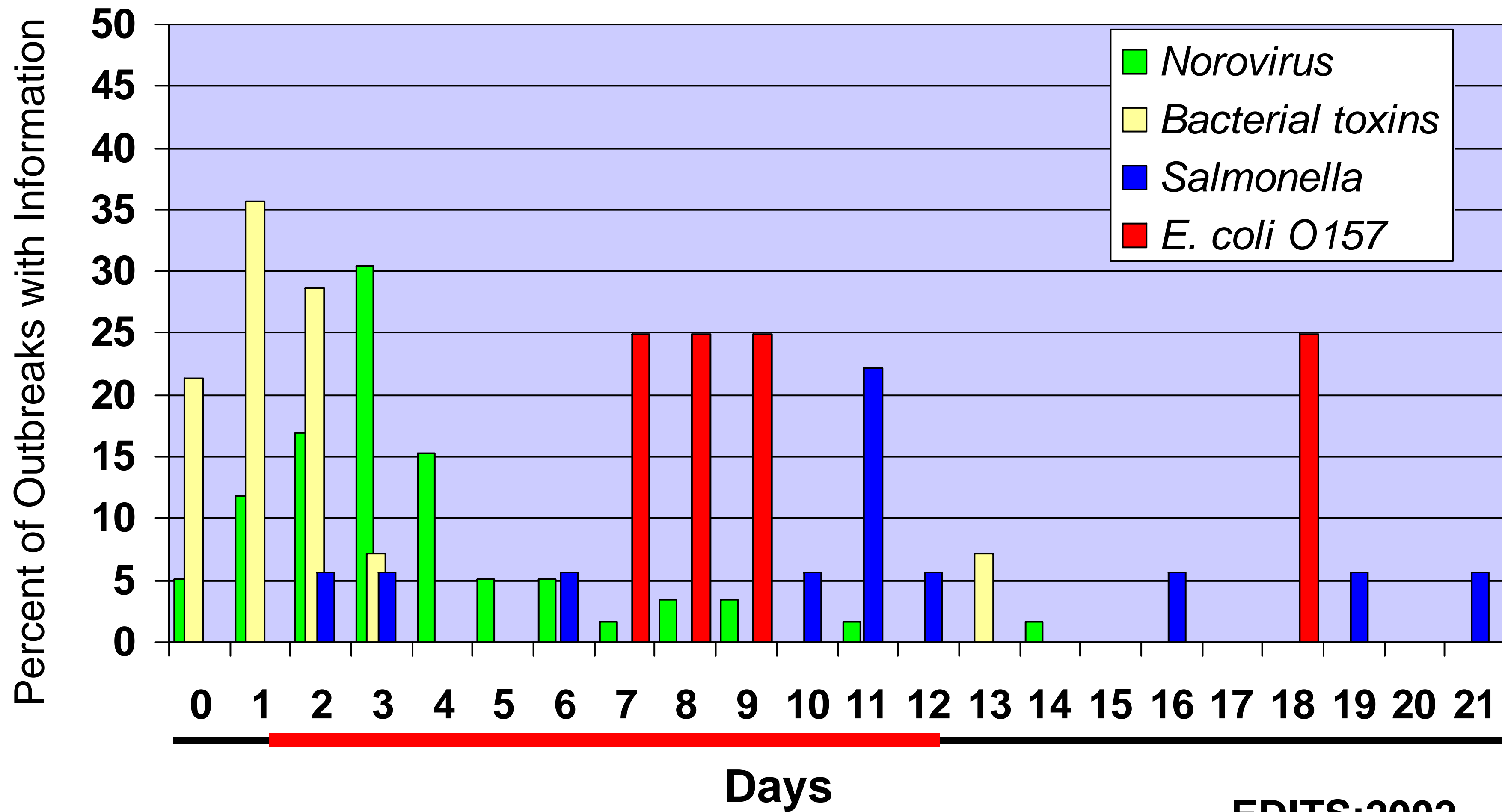
***3 days** earlier in states with centralized PHL surveillance*



EDITS: Data Analysis

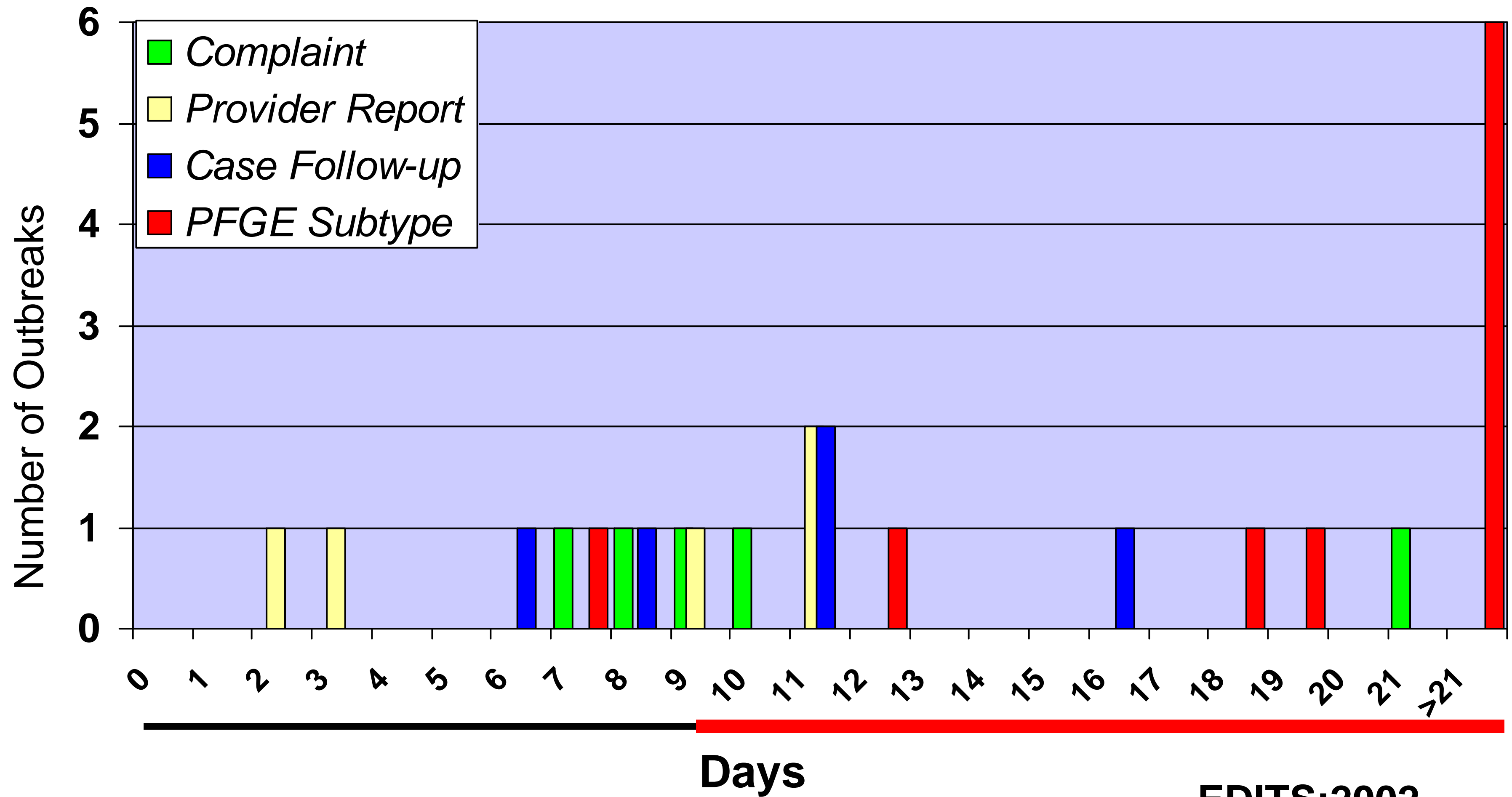
- **Conclusions:**
  - States with cases reported initially to LHD, quicker to interview cases, but states with centralized PHL laboratory surveillance quicker to subtype the isolates.
  - Faster response time for *E. coli* O157:H7 compared to *Salmonella*.
  - Primary differences for timelines appear to relate to actions of Local or State HD following report of case and submission of isolate.
  - Isolate submission requirement affected percentage of isolates submitted, but not timelines.

Onset of Symptoms to Outbreak Complaint or Recognition



EDITS:2002

Onset of Symptoms to Outbreak Recognition, *Campylobacter*, *E. coli* O157:H7, & *Salmonella*



EDITS: Data Analysis

- **Results:**
  - **Median intervals from onset to outbreak complaint or recognition ranged from:**
    - 1-3 days for bacterial toxins and norovirus
    - 8-10 days for *E. coli* O157:H7 and *Salmonella*

  For outbreaks caused by *Campylobacter*, *E. coli* O157:H7, and *Salmonella*:

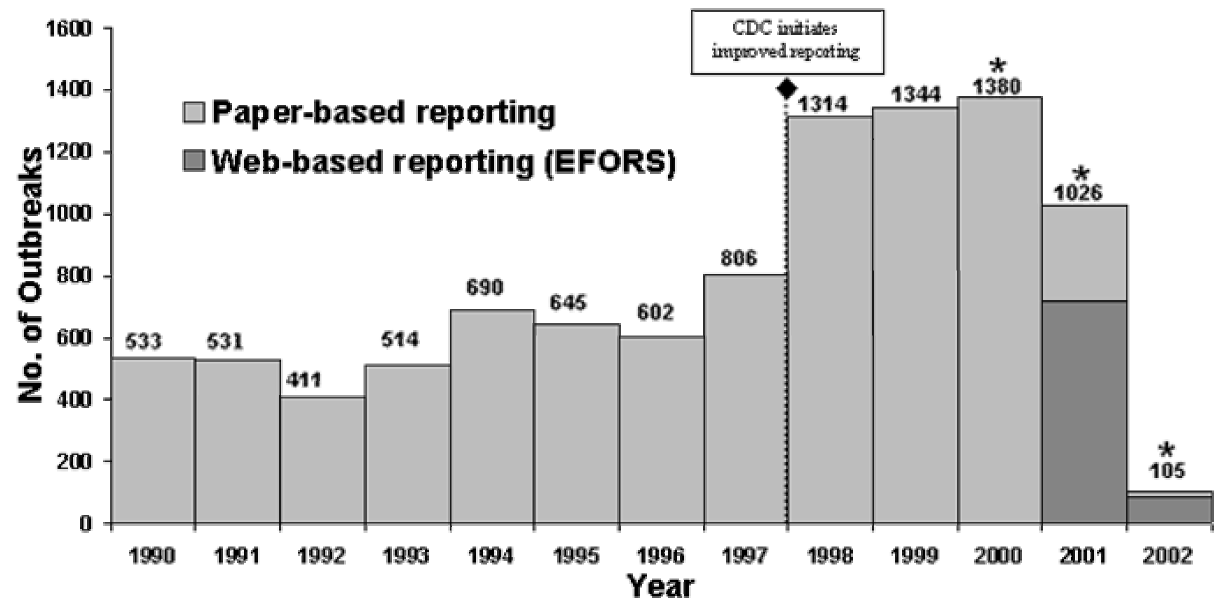
  - **Median intervals from onset to outbreak recognition were:**
    - 9 days for complaint and provider report
    - 12 days for case follow-up
    - >21 days for PFGE subtype
  - **A small number of outbreaks were reported by providers, 2-3 days after onset and before confirmation of etiology**

Public Health Response and Epidemiology

- Predictive Modeling and Decision Making Tool To Limit the Impact of Attacks on the Food System
- Modeling Public Health Response and Remediation Strategies
  - Processes and Decision Making Structures in Multi-State Outbreak Investigations
  - Diagnosis, Reporting & Investigating Botulism Outbreaks
- Public Health Core

Preliminary Assessment:
Onset of Symptoms to Outbreak Complaint or Recognition, Multistate Outbreaks, 1998-2003

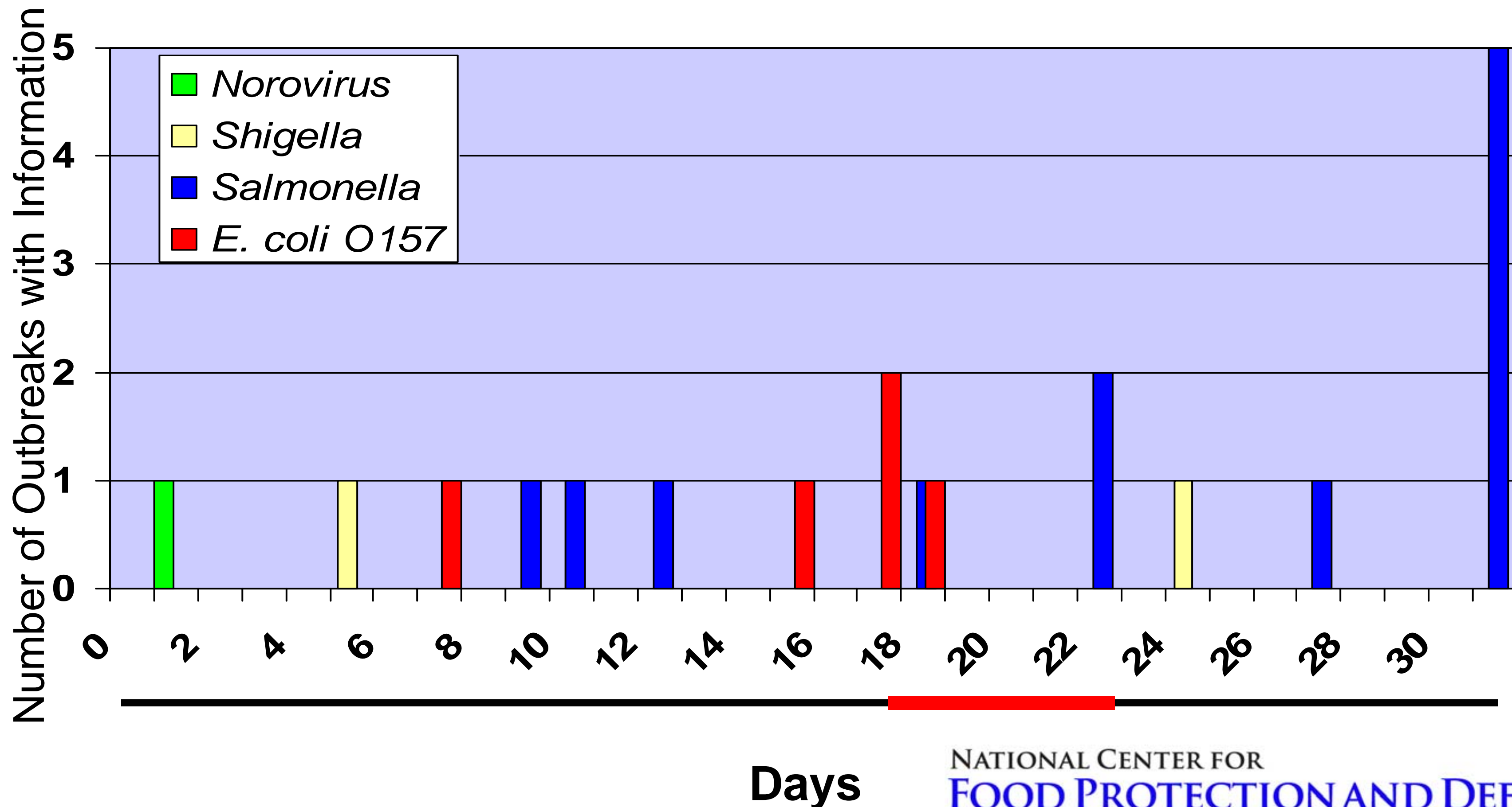
- Based on timeline parameters identified in EDITS, evaluate how surveillance processes and decision making structures affect the initiation and outcome of multistate outbreak investigations.
- Multistate outbreak investigations from 1998-2003 chosen to correspond to improved reporting to CDC.



Preliminary Assessment:
Onset of Symptoms to Outbreak Complaint or Recognition, Multistate Outbreaks, 1998-2003

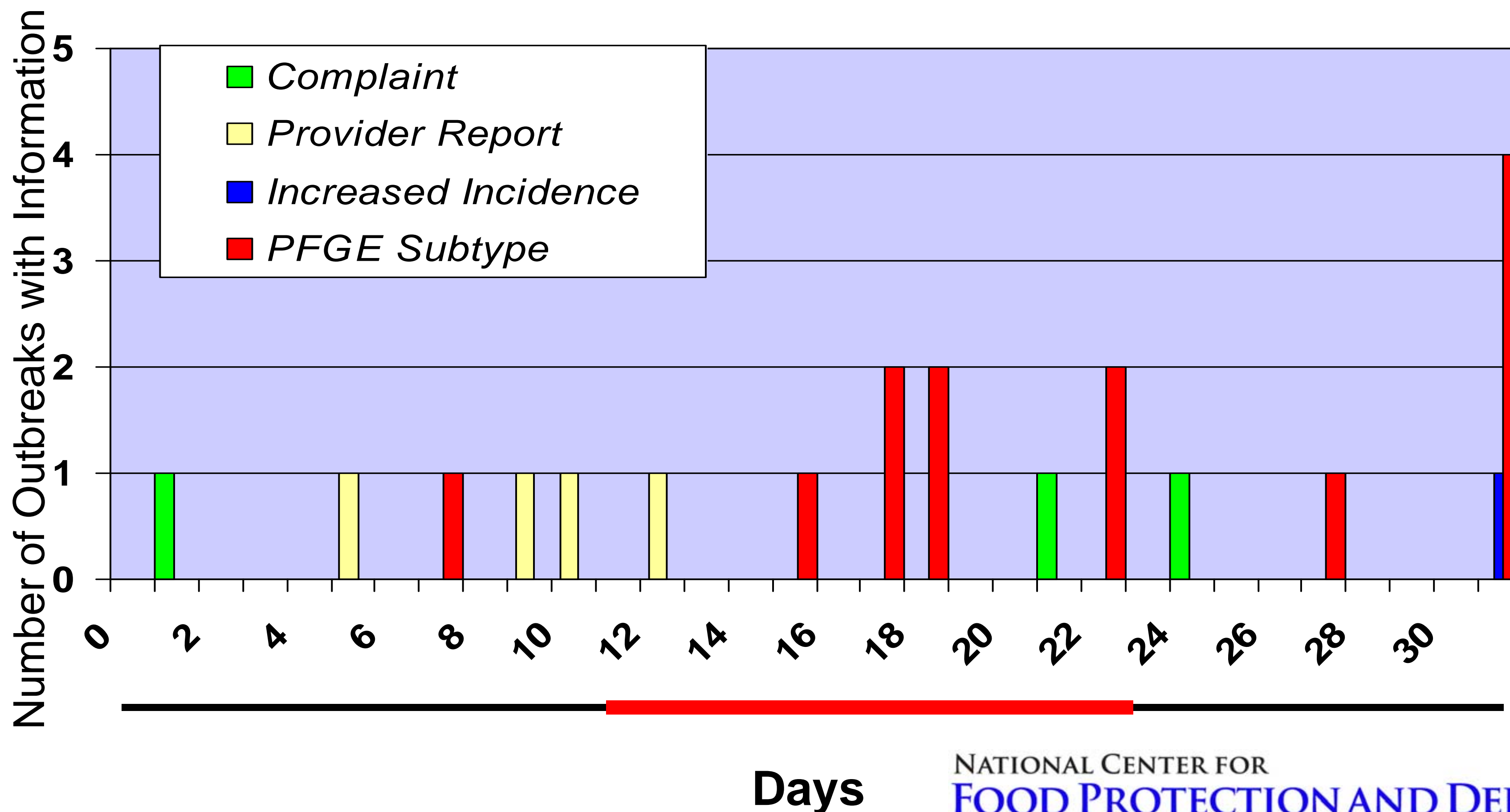
- 53 multistate outbreak with known etiology identified in annual listings of Foodborne Outbreak Response and Surveillance Unit (http://www.cdc.gov/foodborneoutbreaks/report_pub.htm)
- 3 additional multistate outbreaks identified by publication
- 56 multistate outbreaks:
  - 31 (55%) due to *Salmonella*
  - 10 (18%) due to *E. coli* O157:H7
- 27/56 (48%) warranted publication in MMWR or peer-reviewed journal

Preliminary Assessment:
Onset of Symptoms to Outbreak Complaint or Recognition, Multistate Outbreaks, 1998-2003



NATIONAL CENTER FOR
FOOD PROTECTION AND DEFENSE
A HOMELAND SECURITY CENTER OF EXCELLENCE

Preliminary Assessment: Onset of Symptoms to Outbreak Complaint or Recognition, Multistate Outbreaks, 1998-2003

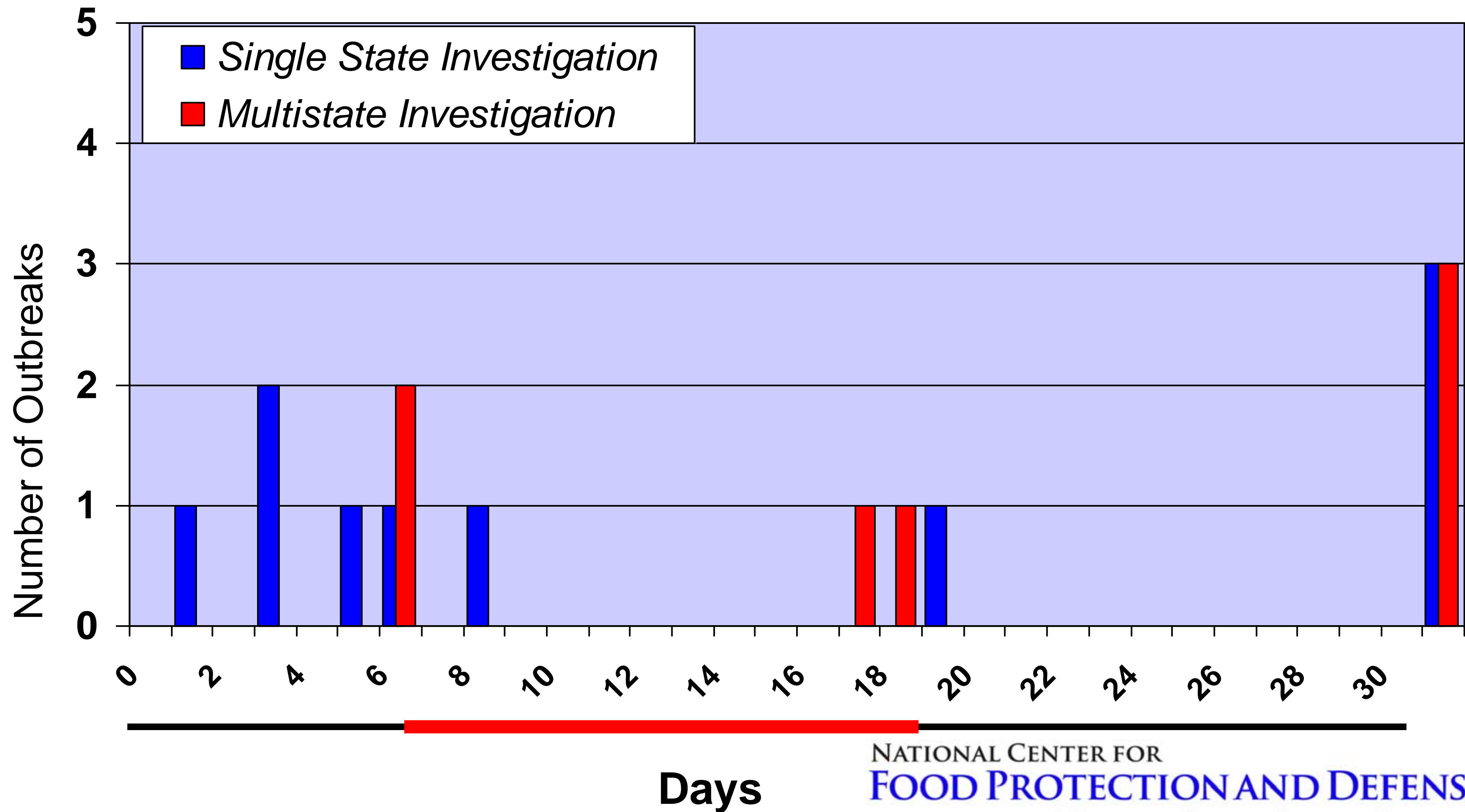


NATIONAL CENTER FOR FOOD PROTECTION AND DEFENSE
A HOMELAND SECURITY CENTER OF EXCELLENCE

Preliminary Assessment: Onset of Symptoms to Outbreak Complaint or Recognition, Multistate Outbreaks, 1998-2003

- Median intervals (and ranges) from onset to outbreak recognition:
  - 18 (8-19) days for *E. coli* O157:H7
  - 23 (10-48) days for *Salmonella*
- Median intervals (and ranges) from onset to outbreak recognition:
  - 21 (2-24) days for complaint
  - 10 (5-12) days for case report and follow-up
  - 22 (7-48) days for PFGE subtype

Preliminary Assessment: Outbreak Recognition to Intervention Multistate Outbreaks, 1998-2003



NATIONAL CENTER FOR
FOOD PROTECTION AND DEFENSE
A HOMELAND SECURITY CENTER OF EXCELLENCE

Preliminary Assessment: Onset of Symptoms to Outbreak Complaint or Recognition, Multistate Outbreaks, 1998-2003

- Median intervals (and ranges) from outbreak recognition to intervention:
  - 7 (1->72) days for outbreaks investigated by a single state
  - 18 (6-62) days for multistate outbreak investigations
- Interventions were made within 8 days in 8/21 multistate outbreaks reviewed. Investigations were conducted primarily by single states in 6 (75%) of these.

Preliminary Conclusions: Onset of Symptoms to Outbreak Complaint or Recognition, Multistate Outbreaks, 1998-2003

- Consistent with EDITS results,
  - Multistate outbreaks of *E. coli* O157:H7 detected sooner than outbreaks of *Salmonella*
  - Multistate outbreaks detected by case reports and follow-up recognized sooner than outbreaks identified by PFGE-cluster evaluation
- Public health interventions made more quickly in multistate outbreaks investigated primarily by individual states.

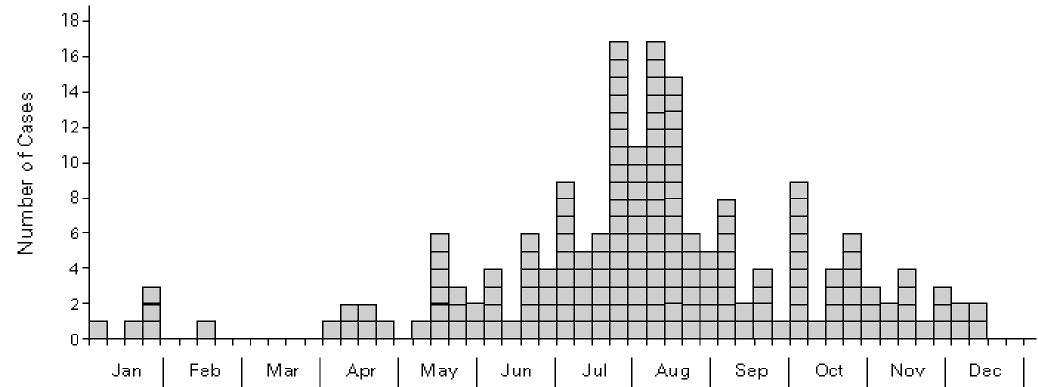
Preliminary Implications: Onset of Symptoms to Outbreak Complaint or Recognition, Multistate Outbreaks, 1998-2003

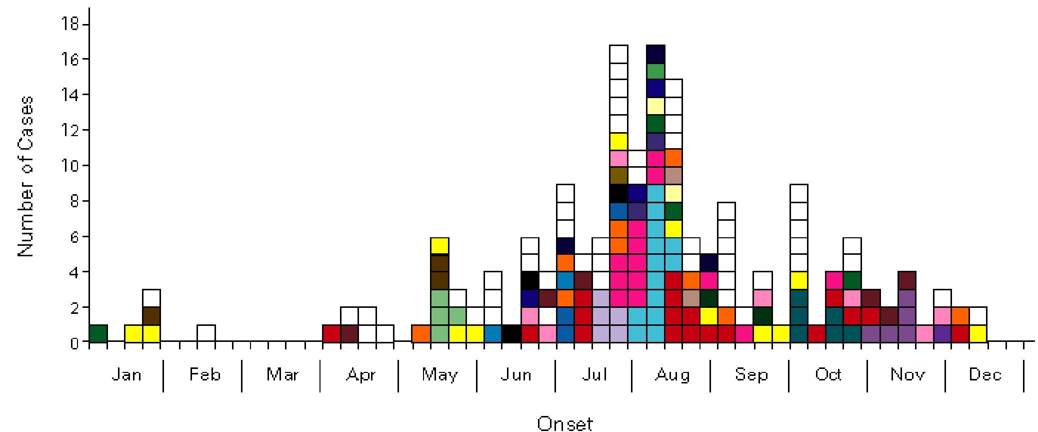
- Strong state and local foodborne disease surveillance programs are necessary for effective national responses.
- Rapid and thorough investigation of outbreaks and clusters by individual state and local health departments should be encouraged, even if a multistate outbreak is suspected.
- Supported by CDC's findings with regard to "successful" cluster investigations:
  - Varied in number of cases and states involved
  - Favored by "unusual exposure suspected or subset of cases linked" Lynch M, et al, 1st National Foodborne Disease Epidemiology Meeting.

Surveillance and Cluster Analysis for *E. coli* O157:H7 MN, 1994-1995

- 10 outbreaks and 35 PFGE clusters
- Common source identified:
  - 6/9 (67%) clusters with ≥ 5 cases
  - 4/36 (11%) clusters with 2-4 cases

Bender, et al NEJM 1997;377:388-94.





Public Health Response and Epidemiology

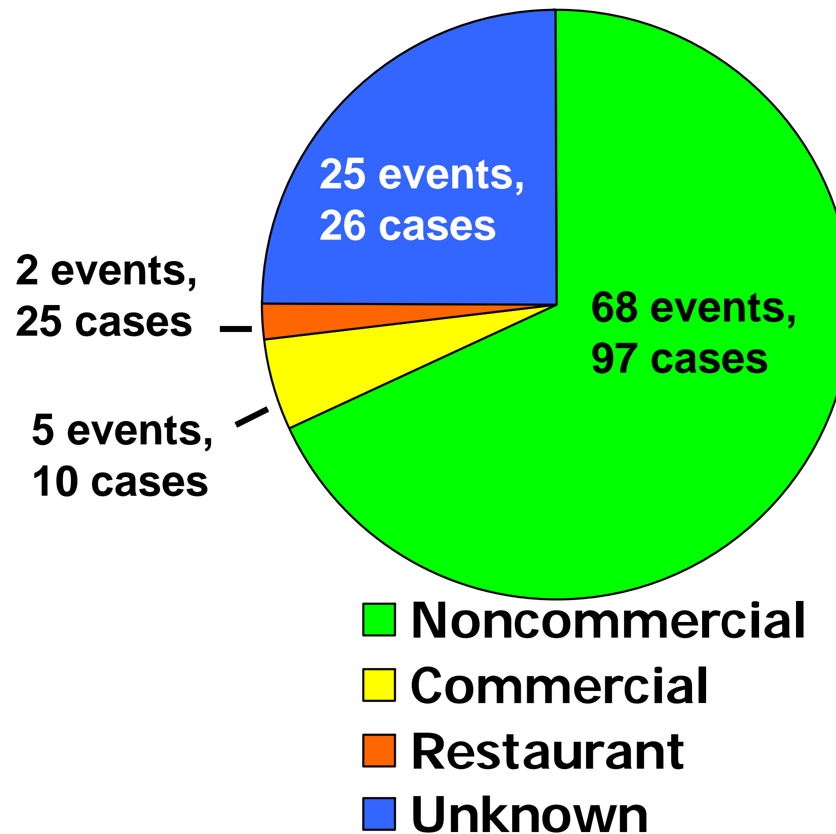
- Predictive Modeling and Decision Making Tool To Limit the Impact of Attacks on the Food System
- Modeling Public Health Response and Remediation Strategies
  - Processes and Decision Making Structures in Multi-State Outbreak Investigations
  - Diagnosis, Reporting & Investigating Botulism Outbreaks
- Public Health Core

Preliminary Assessment:
Diagnosis, Reporting & Investigating Botulism Outbreaks

- Foodborne botulism in the US, 1990-2000
  - Sobel J, et al. EID 2004;10:1606-11

Preliminary Assessment: Diagnosis, Reporting & Investigating Botulism Outbreaks

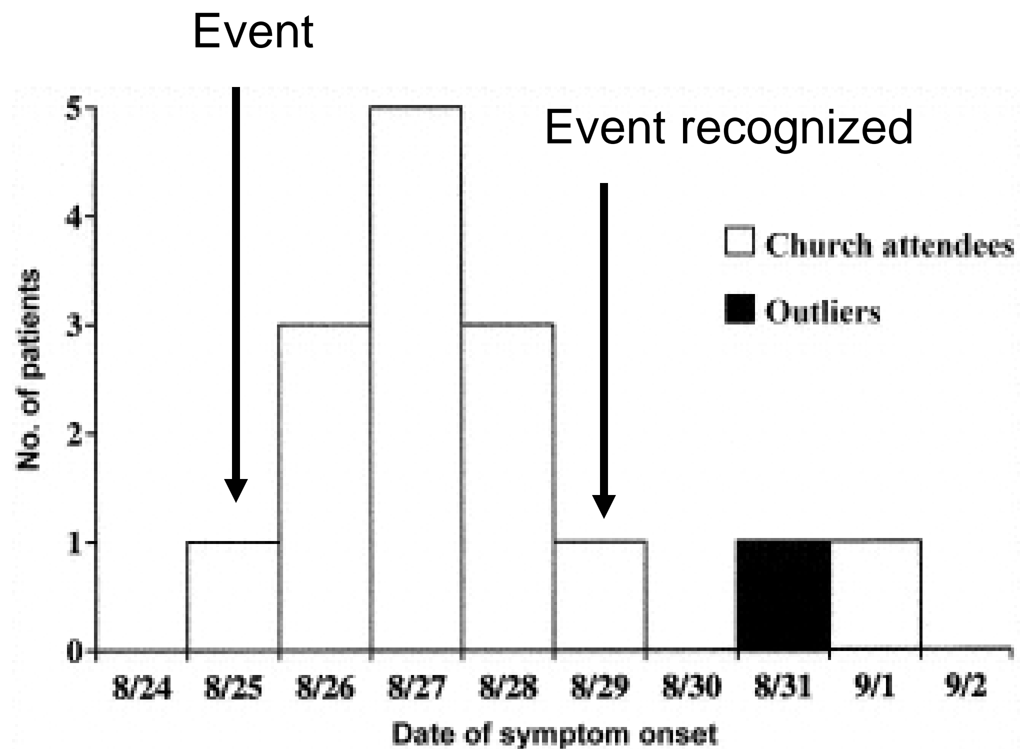
- Foodborne botulism in the US, 1990-2000
  - Sobel J, et al. EID 2004;10:1606-11
- 102 events, 160 cases in lower 48 states



A Tale of Two Outbreaks: Part 1

- August 25, Church supper
  - 15 (40%)/38 ill
- August 29, 4 men admitted to hospital
- Diagnosis delayed by 1-7 d in 4 persons
- Outlier sought treatment 4x over 3 days before diagnosis

  - Kalluri P, et al. CID 2003;37:1490-1495



A Tale of Two Outbreaks: Part 2

- July 12, whale found
- July 13-15, 14 persons ate
- Median incubation period 24 h (range 12-72h)
- July 17, Physician reported 3 suspect cases
  - 8 cases identified
  - 5 hospitalized
  - 4 received antitoxin within 30h following onset

FIGURE. A juvenile beluga whale beached on the Alaska shoreline

Photo/Natural Resources Canada

A Tale of Two Outbreaks

- Response to outbreaks based on level of awareness, previous experience and outbreak setting.
- Survey of physicians to determine preparedness to diagnose and treat potential cases of bioterrorism:
  - Anthrax: 71% correct diagnosis, 17% proper management
  - Smallpox: 51% correct diagnosis, 15% proper management
  - Botulism: 50% correct diagnosis, 60% proper management
  - Plague: 16% correct diagnosis, 10% proper management

  Cosgrove , Arch. Int. Med. 2005;165:2002-6.
- Thus, any reasonably large botulism outbreak will be quickly identified.

NCFPD Teams

Critical Response Team

Public Health Workgroup

Industry Workgroup

Public Health Workgroup

Critical expertise, guidance and feedback on public health system capabilities, needs and applicability of results

Assess the implications of systems research to improve the performance of public health surveillance

E. coli O157:H7 Cases Associated with Dole Prepackaged Lettuce