The Role of the Clinical Laboratory and the Public Health Laboratory in Foodborne Diseases Surveillance, Outbreak Investigations and Prevention:

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Why do we conduct surveillance?

Surveillance is monitoring linked to action

- **Define the current magnitude and burden of a disease we can do something about**
- **Identify outbreaks, so control actions can be taken, and new problems identified**
- **Measure the impact of control and prevention efforts**

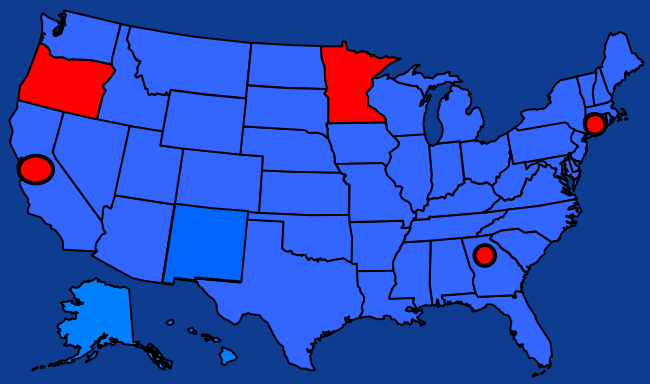
Since 1996, public health surveillance for foodborne diseases has been strengthened

- **Standard notifiable disease reporting: All 50 states.**
  - **Added *Listeria*, non-O157 Shiga toxin prod. *E. coli***
  - **Serotyping of *Salmonella*, *Shigella* strengthened**
- **NARMS: antibiotic resistance monitoring**
- **FoodNet: Active sentinel 10-site surveillance collects data about sporadic cases. Burden and trend monitoring.**
- **PulseNet: The national subtyping network for bacterial foodborne pathogens: All 50 states. Improved outbreak detection and investigation.**
- **Electronic Foodborne Outbreak Reporting (eFORS): Reporting foodborne outbreaks to CDC via the web**

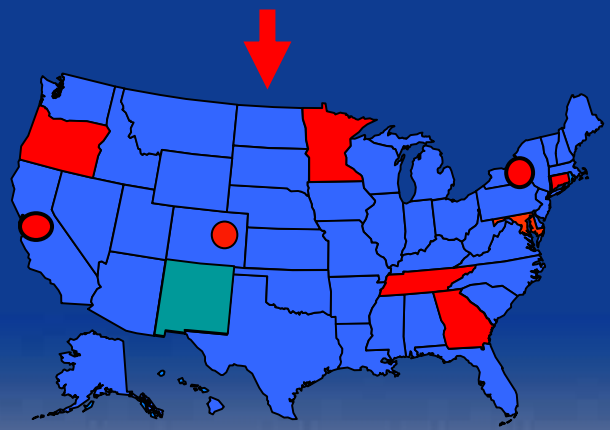
FoodNet Objectives

1. To determine the burden of foodborne diseases (Burden)
2. To determine the change in the burden of foodborne diseases over time (Trend)
3. To determine the proportion of domestically-acquired sporadic infections attributed to different food sources (Attribution)

FoodNet sentinel sites



1996 – 5% of U.S. population



2003 - 14% of U.S. population

Year	Population in millions
1996	14.3
1997	16.1
1998	20.7
1999	25.9
2000	30.5
2001	34.1
2002	38.0
2003	41.5

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Diagnosed infections are a small fraction of total foodborne disease burden

FoodNet

- Active surveillance
- Laboratory surveys
- (Physician surveys)
- Population surveys

Estimating the burden of non-typhoidal salmonellosis

	Syndrome specific multiplier	
Surveillance step	**Bloody diarrhea**	**Non-bloody diarrhea**
Lab identifies Salmonella	**1.4**	**1.4**
Laboratory tests for Salmonella	**1.0**	**1.0**
Stool specimen obtained for culture	**1.0**	**5.5**
Patient seeks medical care	**6.8**	**8.6**
Overall	**9.8**	**67.7**

General multiplier: 39 cases per diagnosed case

1996-9: 36,000 diagnosed cases/year = 1.4 million cases total (520/100,000)

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Voetsch et al. CID 38 (Suppl 3) S129-134, 2004

Top 20 *Salmonella* Serotypes from Human Sources reported to CDC, 2003 (n=33,589)

- *S.* Typhimurium
- *S.* Enteritidis
- *S.* Newport
- *S.* Heidelberg
- *S.* Javiana
- *S.* Montevideo
- *S.* Saintpaul
- *S.* Muenchen
- *S.* Oranienburg
- *S.* Infantis
- *S.* Braenderup
- *S.* Agona
- *S.* Thompson
- *S.* I 4,[5],12:i:-
- *S.* Mississippi
- *S.* Typhi
- *S.* Paratyphi B var.
- *S.* Hadar
- *S.* Bareilly
- *S.* Stanley

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How Does Subtyping Help in Epidemiologic Investigations?

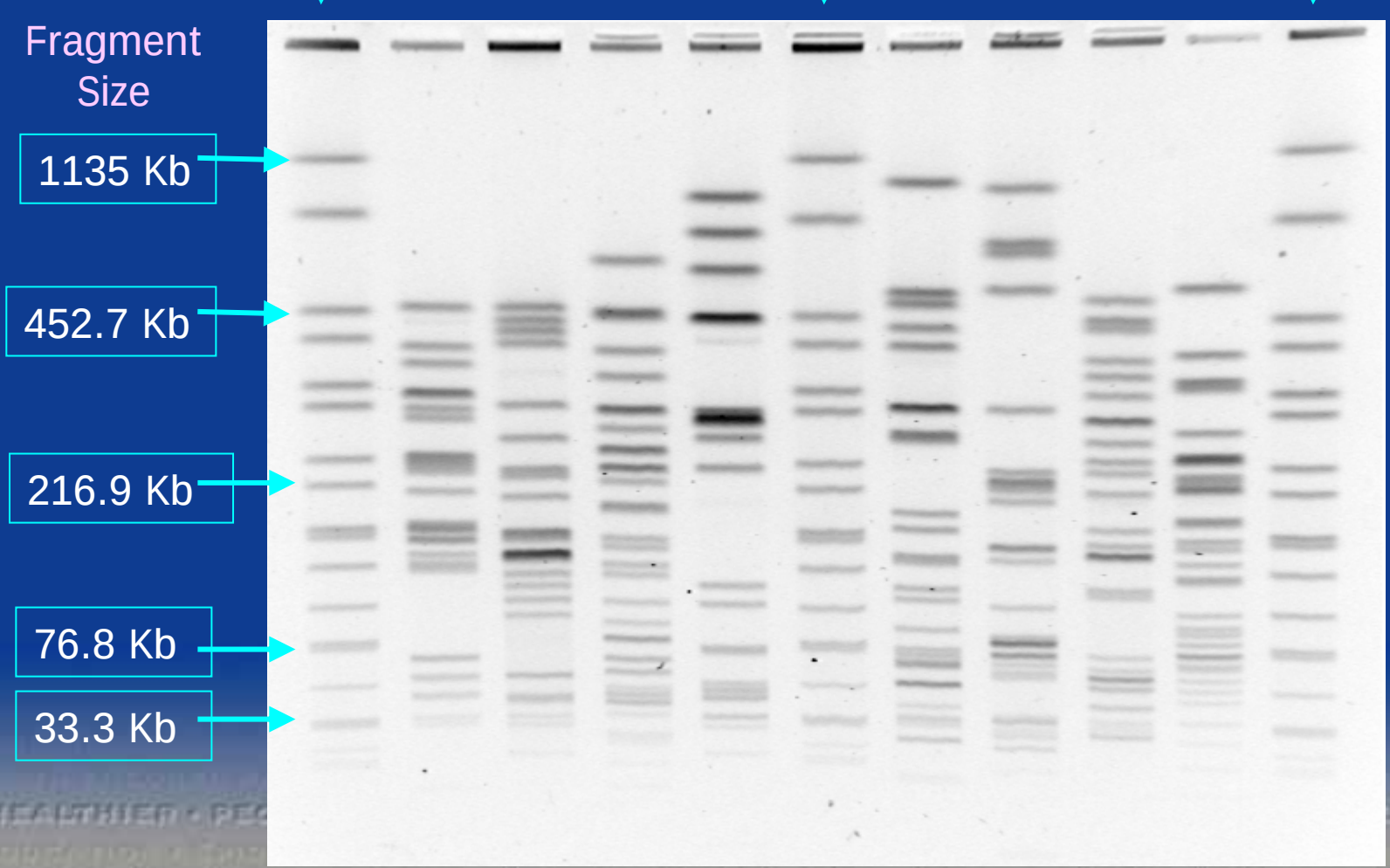
- Identifying who is part of outbreak
  - Distinguish from concurrent sporadic cases
  - Reduce misclassification
- Detecting outbreaks through surveillance
  - Linking apparently sporadic cases
    - Too widely dispersed to detect
    - Organism too common to notice small increase
    - Identifying related cases and separate them from unrelated ones ones
  - DNA “fingerprinting” methods have greatly increased sensitivity of subtyping

PFGE: the current "gold standard" for bacterial DNA fingerprinting

- Early 1990s: Evaluation of PFGE as a molecular tool to aid in epidemiologic investigations
- Sensitivity, specificity, reproducibility all high (but not 100%!)
- 1993: Outbreak investigation of *E. coli* O157:H7 in the western United States demonstrated usefulness of PFGE in outbreak investigations
- 1994: Published results of the investigation
  - **Barrett, T. J., et al.,** 1994. Laboratory investigation of a multi-state food-borne outbreak of *Escherichia coli* O157:H7 by using pulsed-field gel electrophoresis and phage typing. J. Clin Microbiol. **32**(12)**:**3013-7.

A typical *E. coli* O157:H7 PFGE Gel

PulseNet Universal Reference Standard



In an attempt to better control foodborne disease outbreaks, federal and state health agencies created the PulseNet system

Centers for Disease Control and Prevention: National Center for Infectious Diseases

CDC
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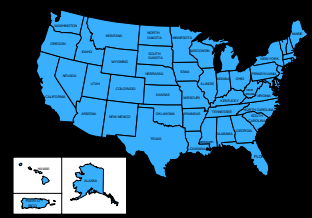
+

Association of Public Health Labs

PHL

+

All 50 States + Growing Internationally



"PulseNet is an early warning system for outbreaks of foodborne disease. It is a national network of public health laboratories that performs DNA "fingerprinting" on bacteria that may be foodborne."

Prevention and Control

Applied Research

Surveillance and Response

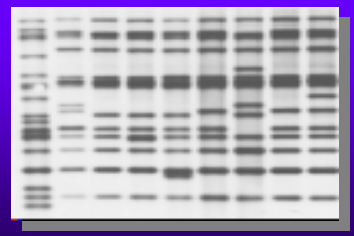
Infrastructure

PulseNet USA
The National Molecular Subtyping Network for Foodborne Disease Surveillance
CDC

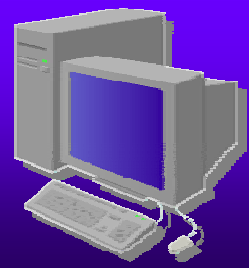
Sources: IBM Institute for Business Value

Culture growth

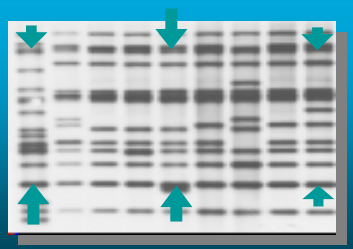
Electrophoresis



Digitization

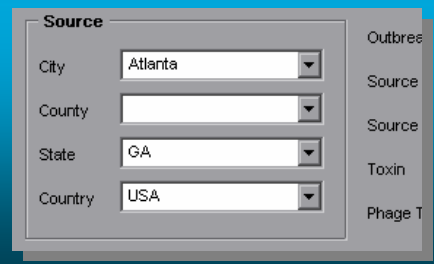


Normalization



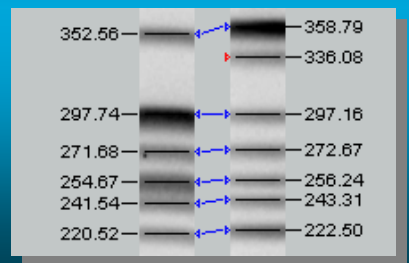
Band assignment

Information entry



Server upload

Match with server



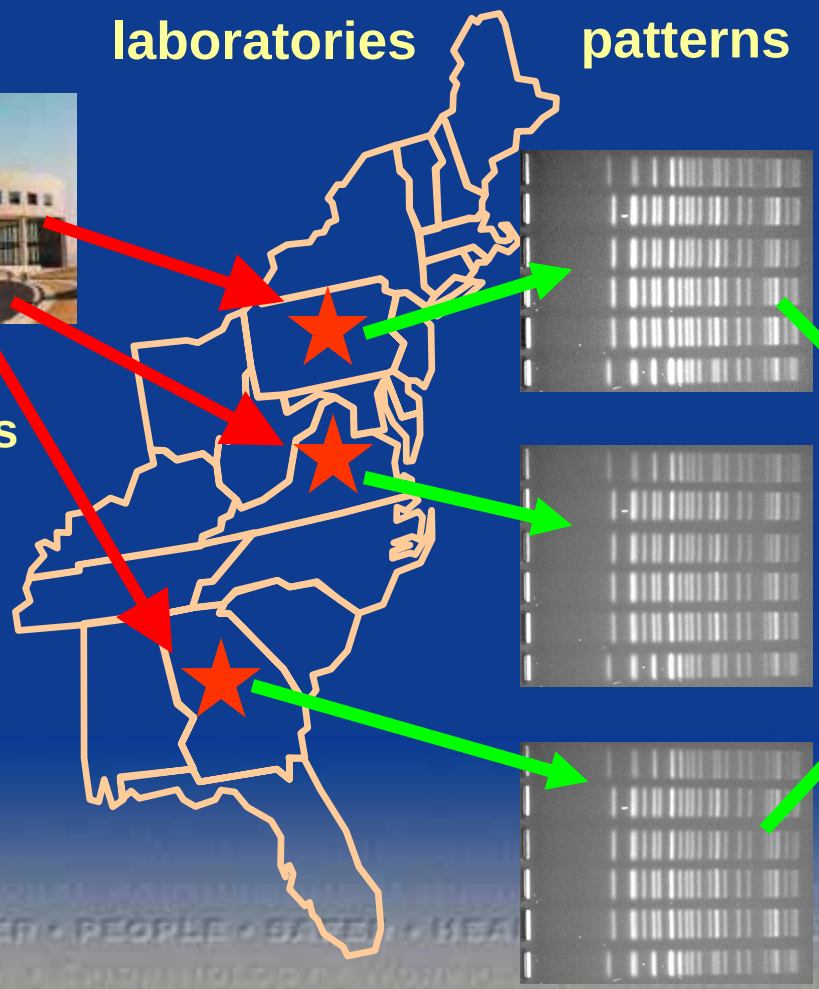
Report

Laboratory coordination in PulseNet

Public health laboratories

PFGE patterns

Clinical laboratories



PulseNet

The National Molecular Subtyping Network for Foodborne Disease Surveillance

National database

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The National Molecular Subtyping Network for Foodborne Disease Surveillance

August 2002

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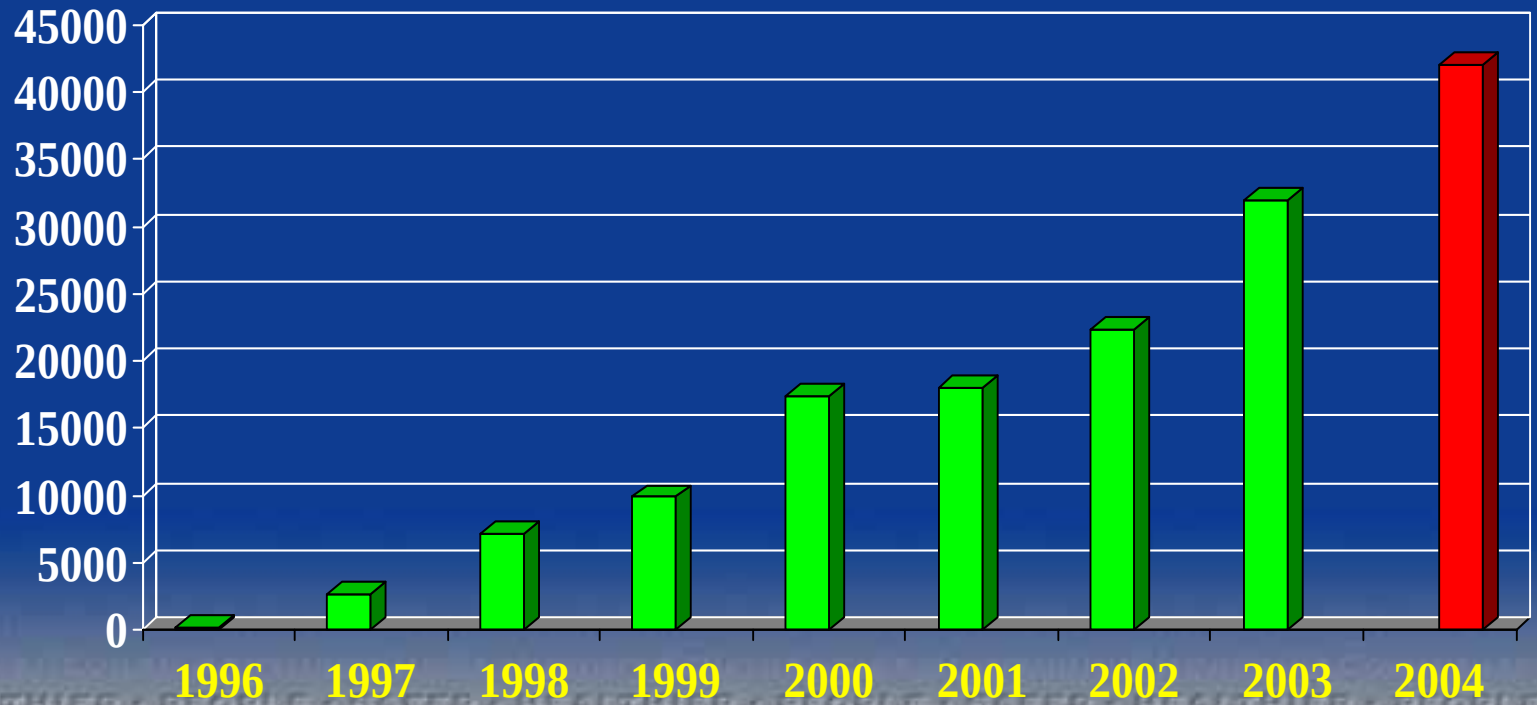
Rapid Standardized PFGE Protocols for Subtyping Foodborne Pathogenic Bacteria

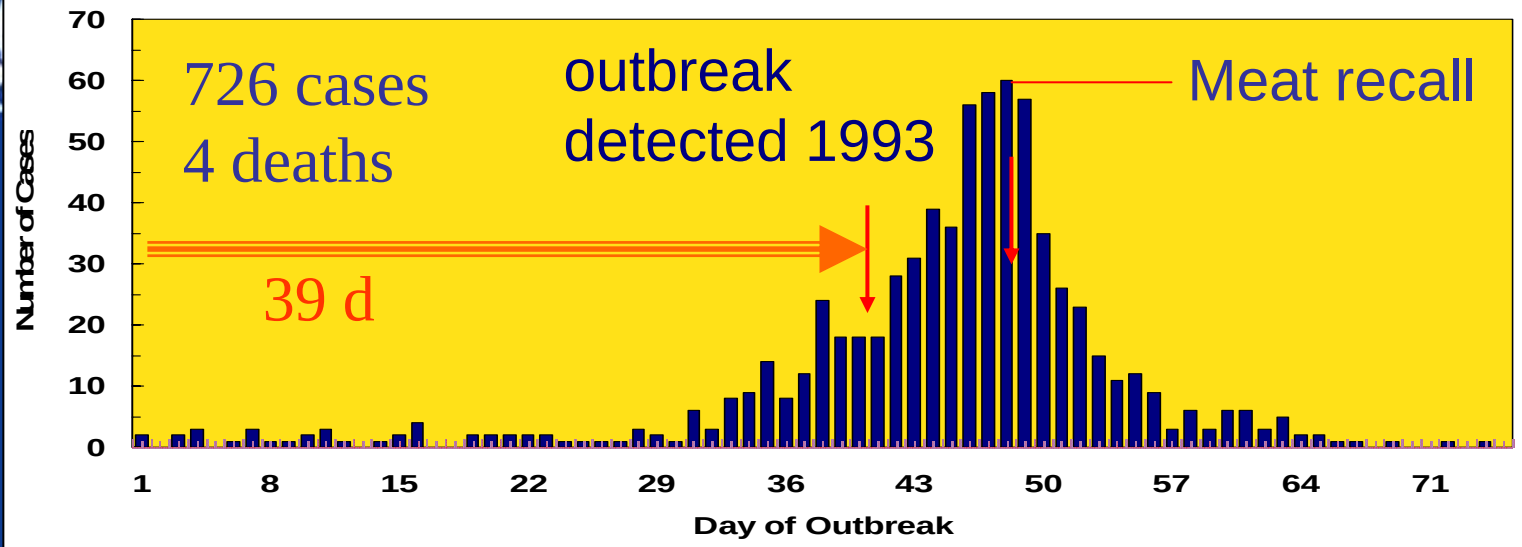
- *E. coli* O157:H7
- *Salmonella*
- *Listeria monocytogenes*
- *Shigella sonnei*
- *Campylobacter jejuni*
- *Clostridium perfringens*
- *Vibrio cholerae* (2003/04)
- *Vibrio parahaemolyticus* (2004)
- *Yersinia enterocolitica* (2004)
- Non-O157 STEC (2004)

PulseNet Activity, 1996-2004

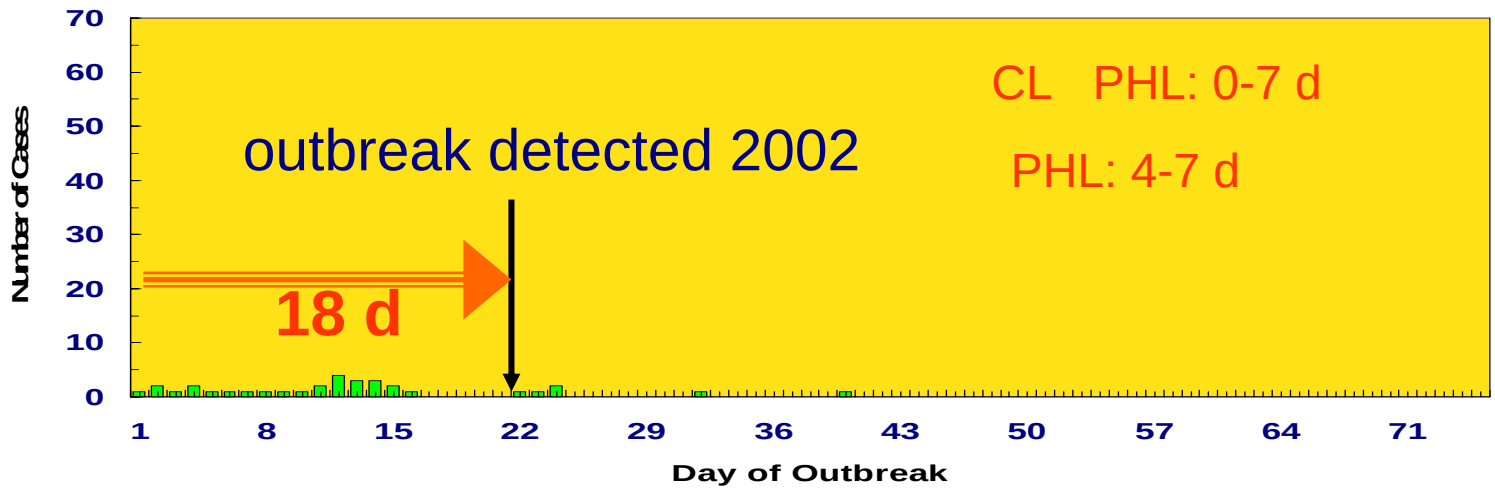
PFGE patterns submitted to PulseNet Databases



1993 Western States *E. coli* O157 Outbreak



2002 Colorado *E. coli* O157 Outbreak



Common features between FoodNet, NARMS, PulseNet, *Salmonella* surveillance

- All are critically important for foodborne disease surveillance, recognition of emerging/reemerging problems/pathogens, outbreak detection and investigation, prevention measures
- Entirely dependant on timely reporting of notifiable cases
- Absolute need for timely submission of pathogen isolates to appropriate state/local public health laboratory

An Emerging Problem

- Large clinical diagnostic laboratories are moving away from culture for *E. coli* O157:H7
- Using Premier EHEC test for Shiga toxins and reporting Stx + or –. No culture of positive broths/stools
  - Advantage: detects all Stx-producers
  - Disadvantage: No pathogen isolate available
- *E. coli* O157:H7 surveillance is compromised

Good things happen when EIA+ specimens are cultured

- Increased recognition of non-O157 STEC as a cause of diarrheal disease in the U.S.
- Information on the types of non-O157 STEC that are prevalent in the U.S.
- Recognition of new pathogens as the cause of diarrheal diseases

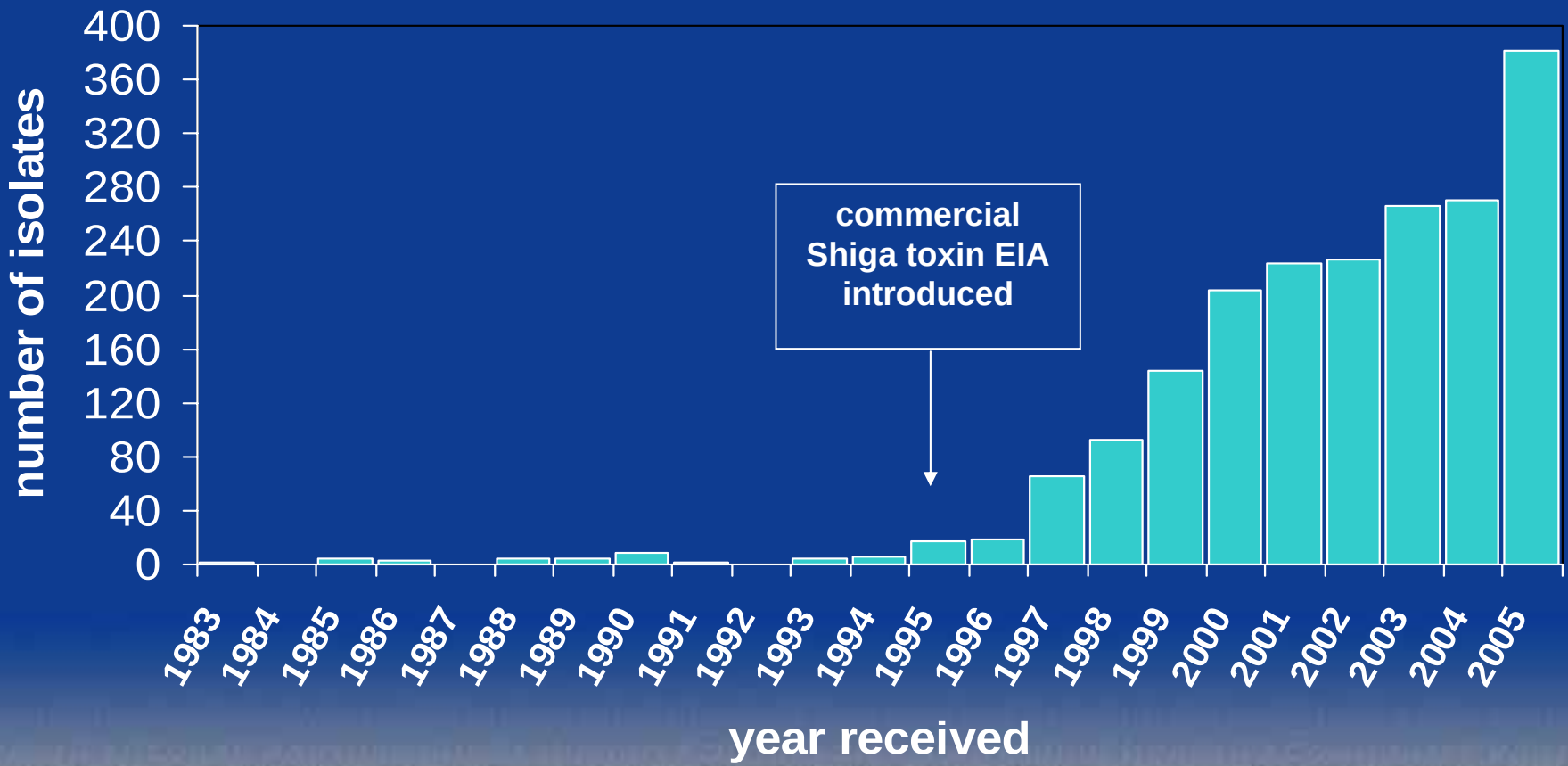
EIA + Culture assists in discovery of an emerging pathogen

- Three cases of Shiga toxin1-producing *Shigella dysenteriae* type 4 (SD4) among travelers to the island of Hispañola between 2002 and 2005
- Premeier EHEC for Stx and/or PCR for *stx* genes followed by culture led to the discovery
- SD1 is known to produce Stx1 but previous isolates of SD4 have been Stx-

Gupta, S.K, Strockbine, N.A, et al. (Manuscript in preparation)

Isolates of Non-O157 STEC Serotyped by CDC, 1983-2005

n=1,945



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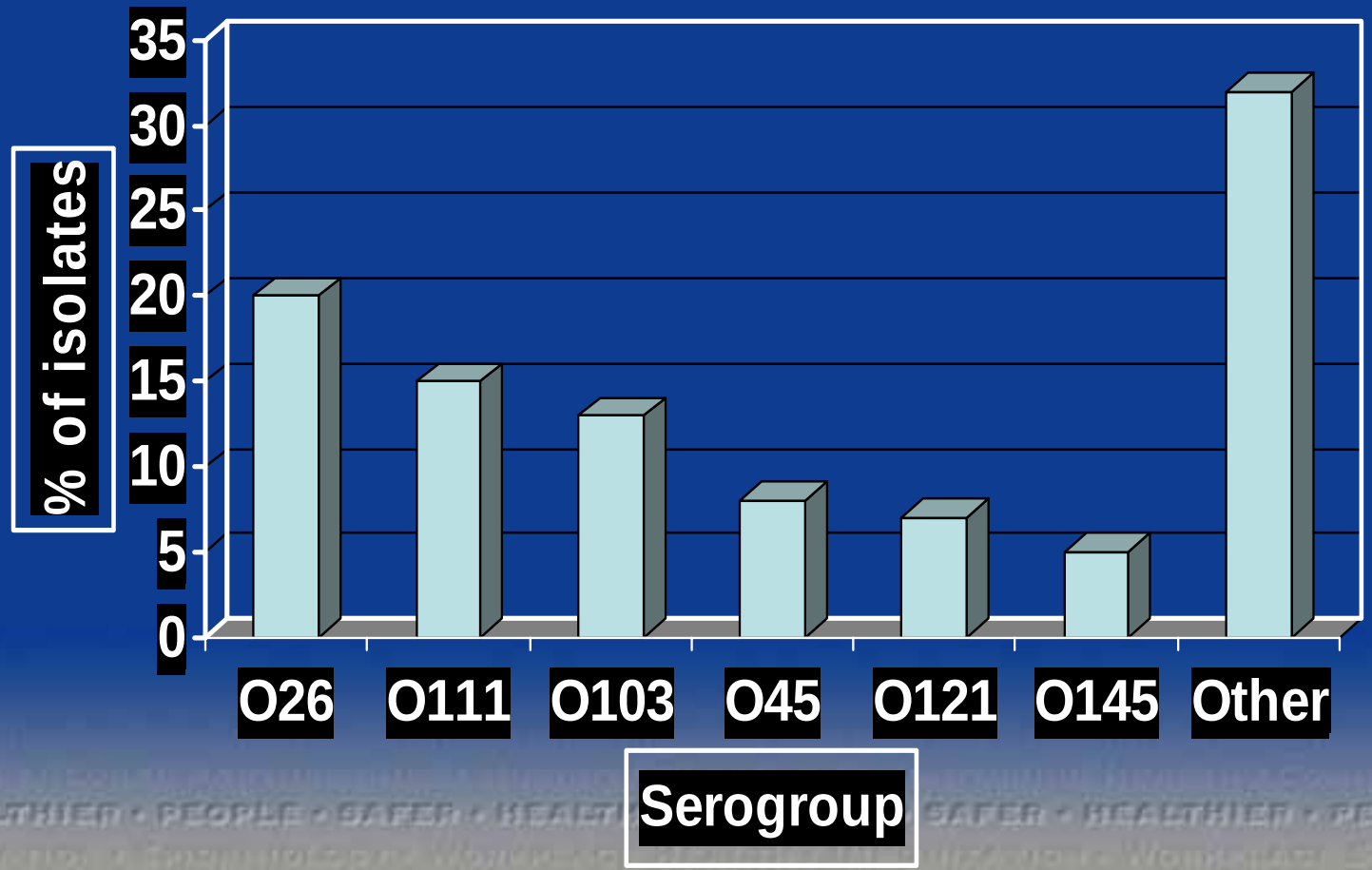
CDC, unpublished data

Human isolates of non - O157 STEC
Serotyped by CDC, 1998 – 2005 n = 1,623



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Non-culture test for *E.coli* O157:H7 and other STEC

- Positive predictive value of test may be low because few samples are positive
- In case of suspected outbreaks in daycare centers, possibility of unnecessary closure of daycare center on the basis of false-positive EIA test
- Diagnostic laboratory not willing to perform culture on positive broths but willing to send positive broths to public health laboratory
- Delays in recognition of public health problems

Added burden for Public Health Laboratory

- Diminishing resources – additional burden of culturing STEC from broths
- Frequently, broths received from clinical laboratory do not yield STEC (false-positive or pathogen viability lost during storage and transport?)
- Centralized clinical laboratory sending broths to in-state public health laboratory, overwhelming that public health laboratory's resources

Issues

- CDC supports the use of non-culture assays of high sensitivity and specificity for screening stool specimens for Shiga toxins
- Specimens positive by EIA or PCR tests must be cultured for *E. coli* O157:H7 and the isolate must be forwarded to the appropriate public health laboratory without delay.
- Specimens positive by EIA/PCR but negative for *E. coli* O157:H7 must be forwarded to the appropriate public health laboratory for further work-up

Issues (continued)

- Quality control of EIA testing of clinical specimens for Shiga toxins
  - Visual evaluation vs. spectrophotometric
- If reimbursement is a problem in culture of EIA+ specimens, can the CPT codes be changed to allow for culture of EIA+ specimens?