A Personal Dedication

- You instilled discipline and loyalty in me
- You showed me how to live and love
- You enhanced the quality of my life
- You were my friend, trusted confidant, and child
- I will miss you very much

- Bo Swaminathan, 1990 – March 25, 2002

PulseNet and Beyond

Bala Swaminathan, Ph.D.

Foodborne and Diarrheal Diseases Branch

Centers for Disease Control and Prevention,

Atlanta, GA

DEPARTMENT OF HEALTH & HUMAN SERVICES

PulseNet

The National Molecular Subtyping Network
for Foodborne Disease Surveillance

PHL CSTE FDA USDA

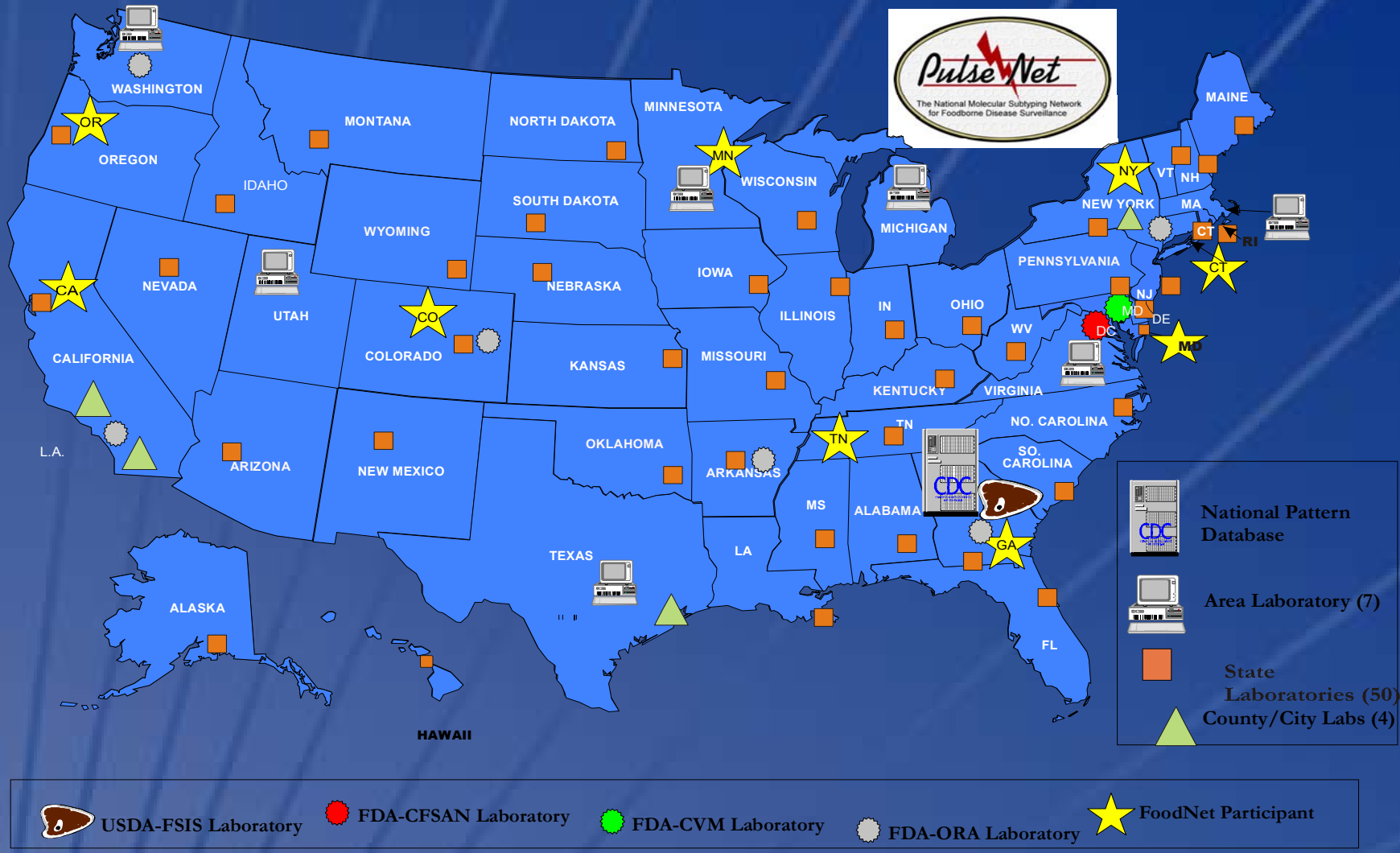
CDC

SAFER • HEALTHIER • PEOPLE™

What is PulseNet?

- PulseNet is the National molecular subtyping network for foodborne pathogens
- Pulsed-field Gel Electrophoresis (PFGE) is used to subtype pathogens
- PFGE images normalized using customized software
- PFGE images are electronically submitted to National database located at CDC in Atlanta, GA

The National Molecular Subtyping Network for Foodborne Disease Surveillance



The National Molecular Subtyping Network for Foodborne Disease Surveillance

Area Lab Service and Support Zones

PFGE Patterns Received - 2001

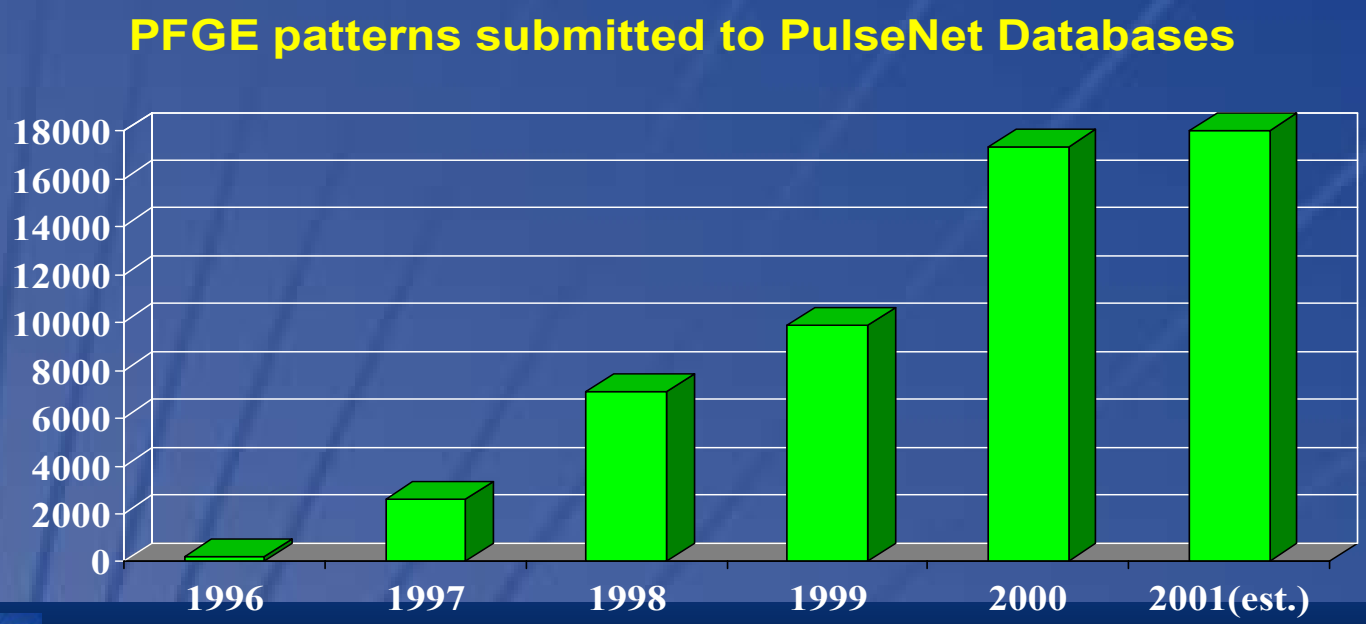
E. Coli O157:H7	3,788
Salmonella serotypes	10,426
Listeria monocytogenes	1,242
Shigella spp.	2,128

PulseNet Activity, 1996-2001

	1996	2000	2001
No. of pathogens	1	4	6
No. of U.S. participating laboratories	10	37	64

E. Coli O157:H7, Salmonella, Listeria, Shigella

Campylobacter, Clostridium perfringens



Expanding the Net: Beyond Foodborne Pathogens

- 2000
  - Division of Bacterial and Mycotic Diseases / MSPB
    - *N. meningtidis* and *B. pertussis*
  - Division of Health Quality Promotion
    - MRSA
  - Division of Viral and Rickettsial Diseases
    - Calicinet

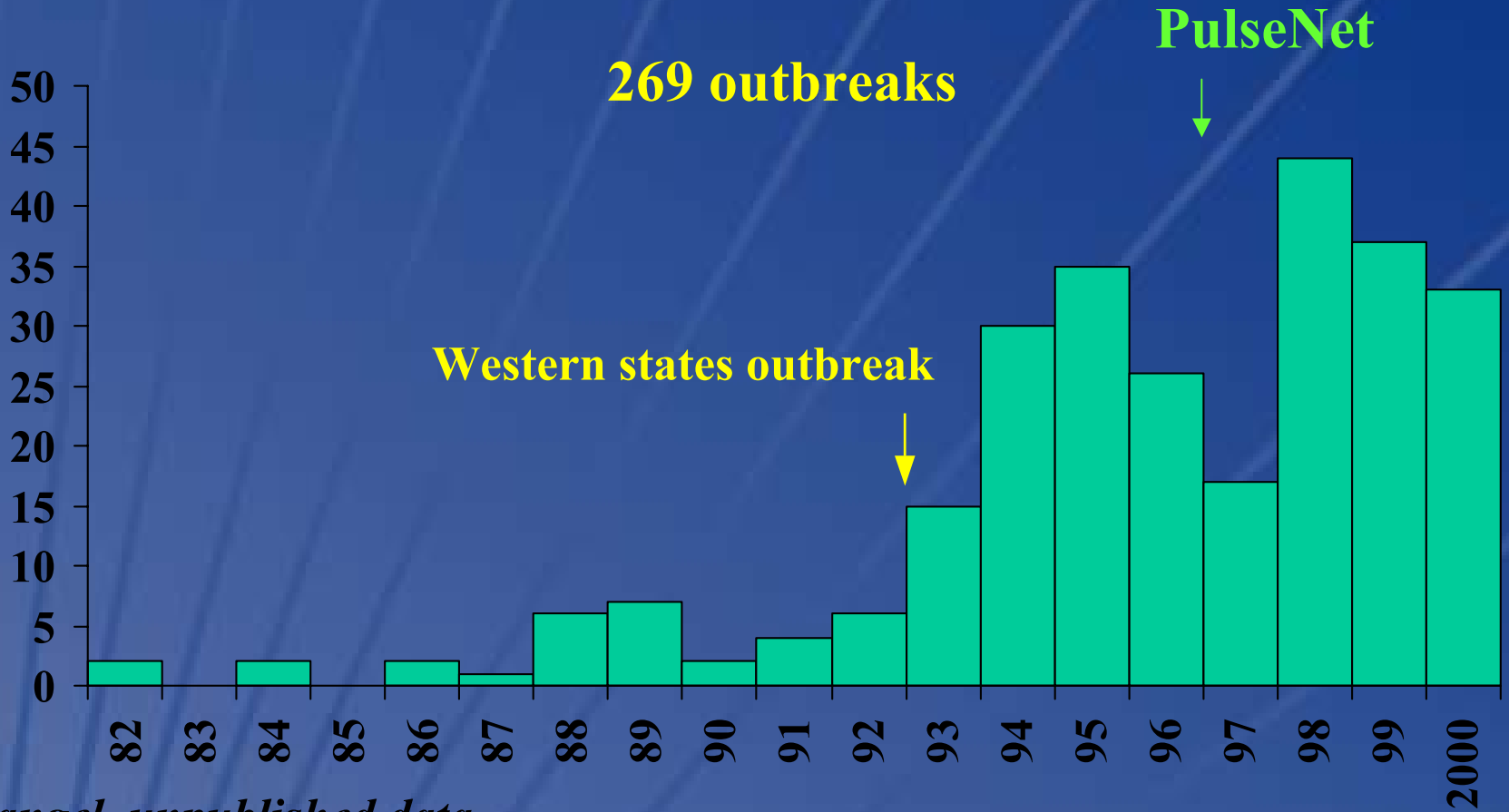
2001

  - Division of Bacterial and Mycotic Diseases / RDB
    - S. *pneumoniae*
    - *Legionella sp.*

PulseNet has revolutionized foodborne disease surveillance

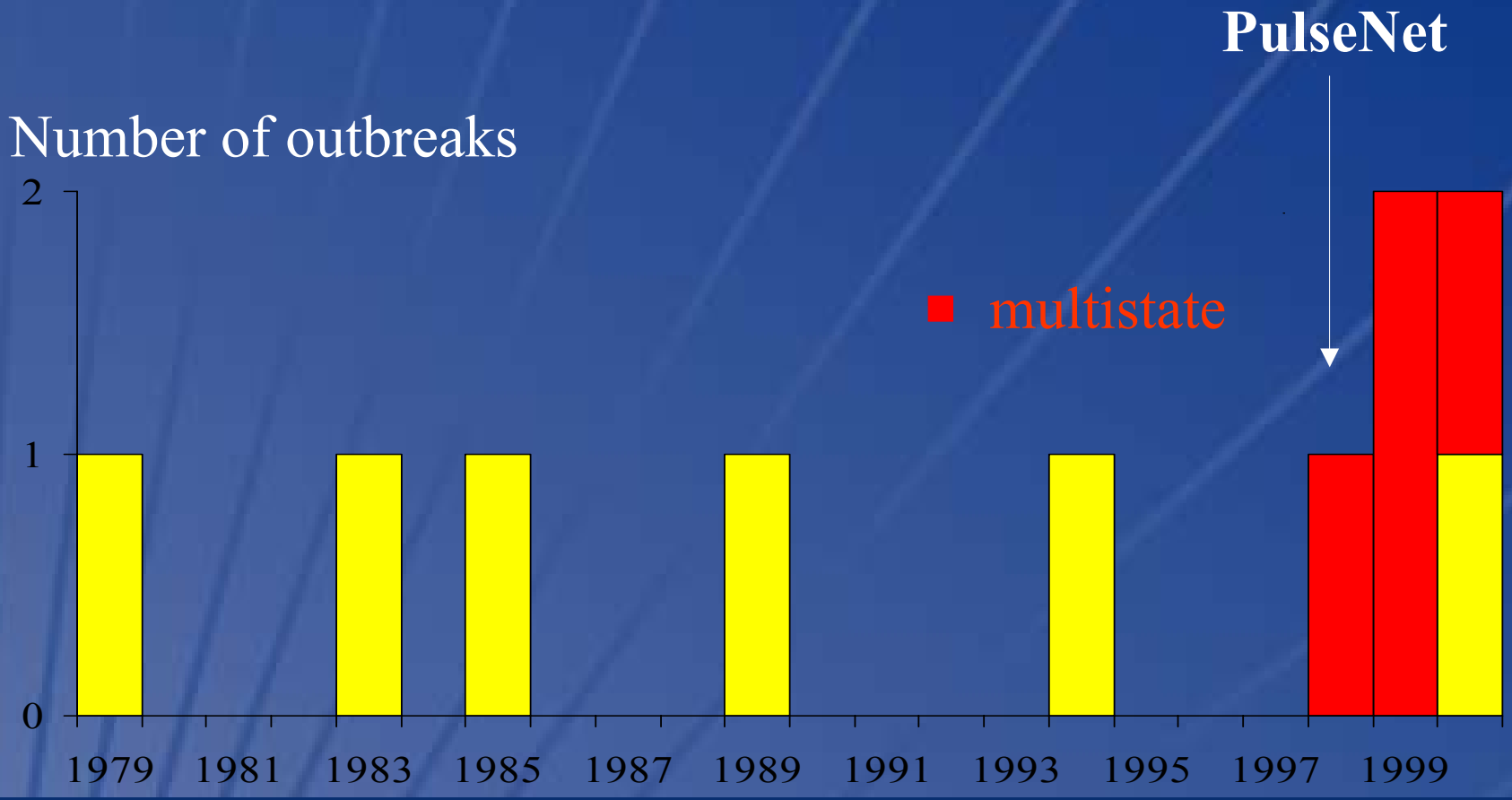
- Real-time laboratory data available to epidemiologists
  - Cluster detection
  - Outbreak investigation
  - Scope of outbreak
  - Identification of source of outbreak
  - Effectiveness of prevention measures

Outbreaks of *E. coli* O157 infections, United States



Rangel, unpublished data

Outbreaks of listeriosis, 1979-2000



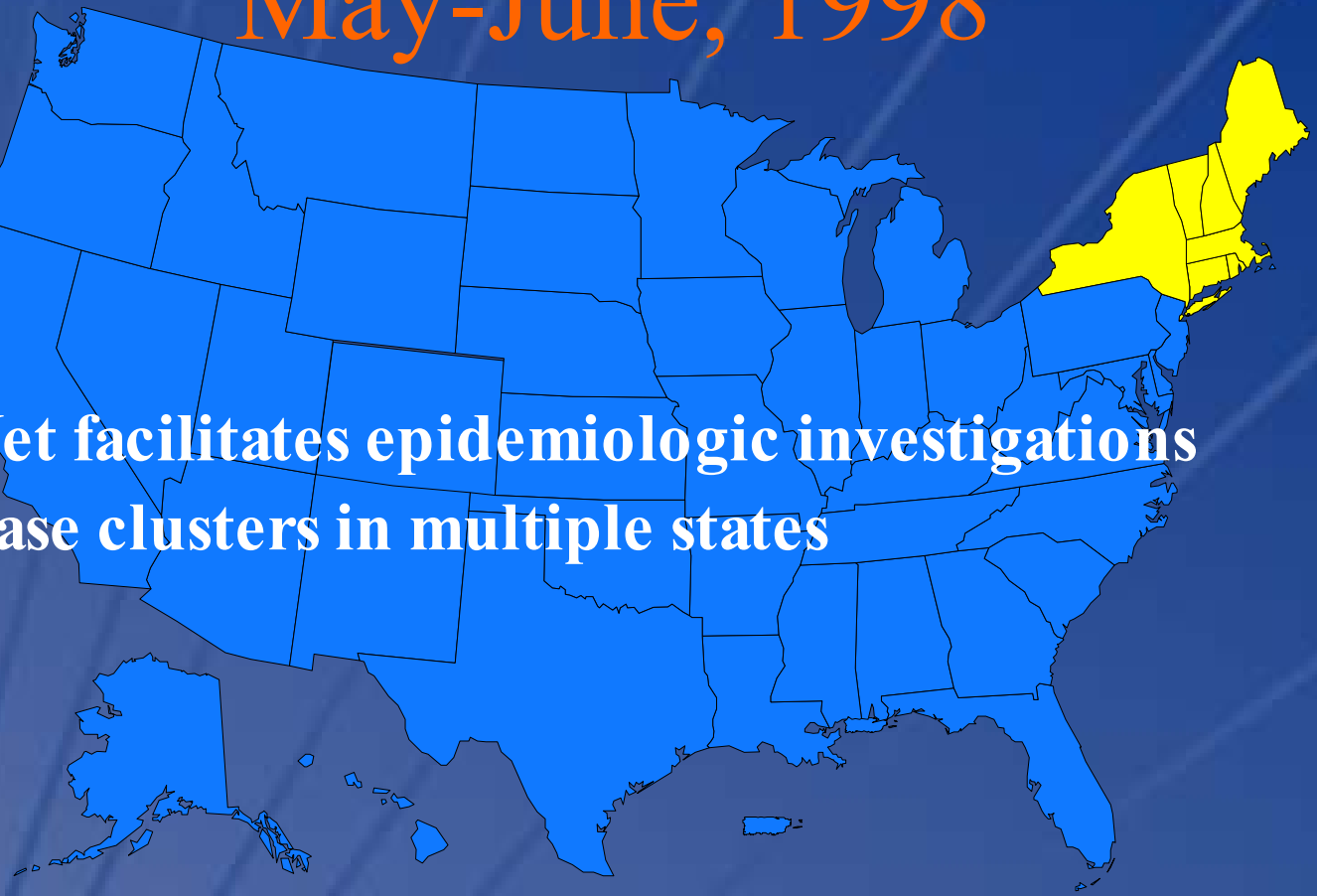
First Demonstration of PulseNet at Work

- 1997: 16 *E. coli* O157:H7 infections linked by PFGE in two states, 25 million pounds of ground beef recalled
- Network laboratories informed CDC within 48 hours that they had not encountered the outbreak pattern – helped CDC determine that the scope of the outbreak was limited

PulseNet's Role in Multistate Outbreak of Shigellosis

- 1998: 486 *Shigella* infections in 3 states and Canada traced to parsley imported from Mexico.
- Food source suspected after same PFGE pattern was seen in seemingly unrelated restaurant outbreaks in Minnesota and California
- Source traced to a single farm in Mexico

Cluster of *E. coli* O157:H7 Infections in northeastern USA, May-June, 1998



PulseNet facilitates epidemiologic investigations of disease clusters in multiple states

shaw's Media Release

For Immediate Release

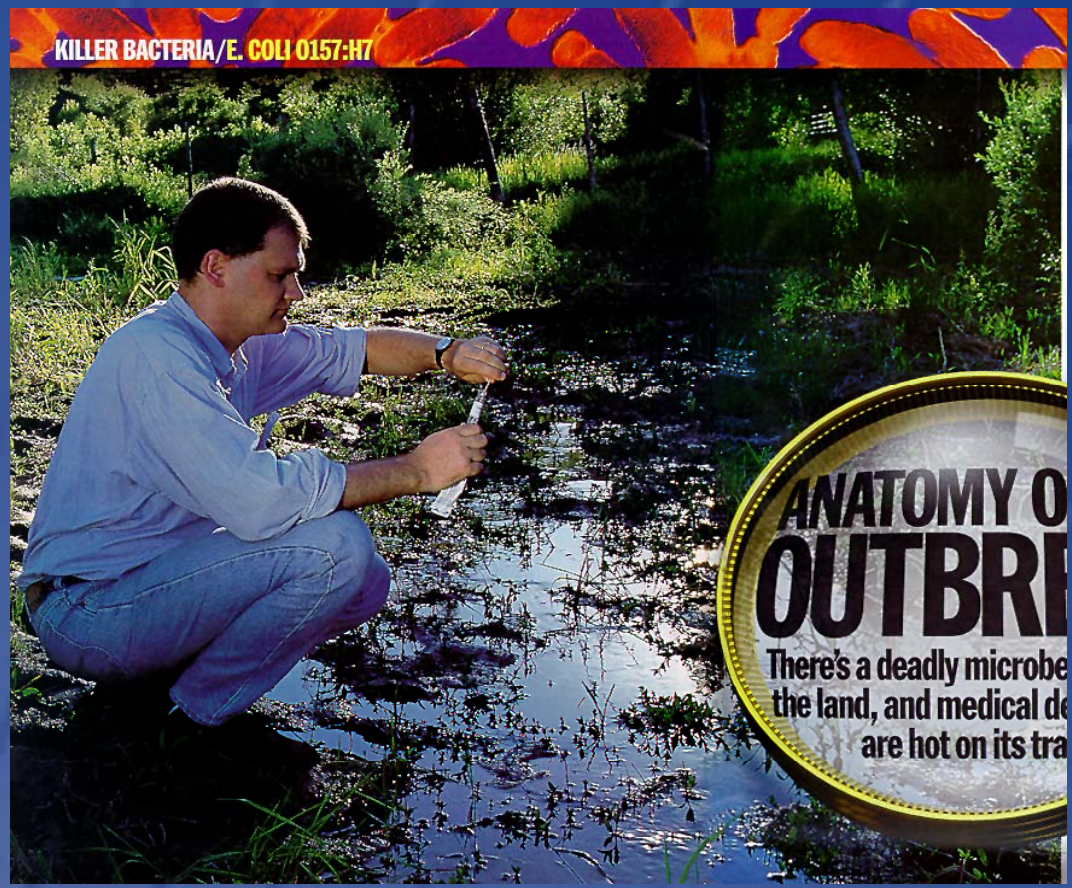
Contact: Bernard Rogan
(508) 350-3316
Pager Service: 1-800-LESHAWS

SHAW'S SUPERMARKETS VOLUNTARILLY RECALLS AND REMOVES FROM SALE SHAW'S FROZEN GROUND BEEF

East Bridgewater, MA, June 12, 1998 – Shaw's Supermarkets, Inc. is voluntarily removing from sale all store produced frozen ground beef from all stores. The customer recall affects fresh ground beef with sell-by-dates between May 9th and June 6th. It also

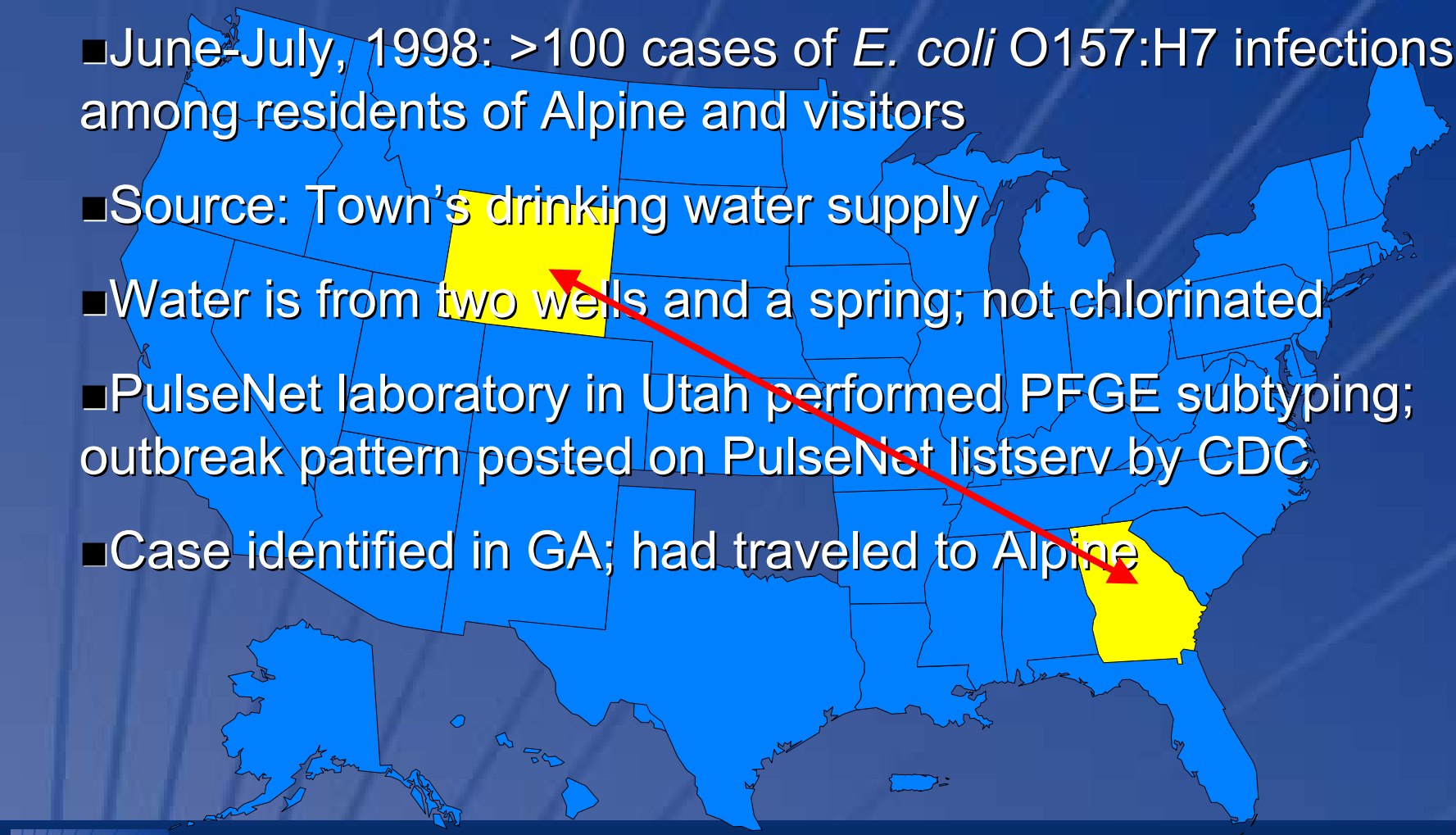
CDC SAFER • HEALTHIER • PEOPLE™

PulseNet helps identify cases occurring at places far away from the epicenter of investigation



Outbreak linked to drinking water, Alpine, Wyoming

- June-July, 1998: >100 cases of *E. coli* O157:H7 infections among residents of Alpine and visitors
- Source: Town's drinking water supply
- Water is from two wells and a spring; not chlorinated
- PulseNet laboratory in Utah performed PFGE subtyping; outbreak pattern posted on PulseNet listserv by CDC
- Case identified in GA; had traveled to Alpine



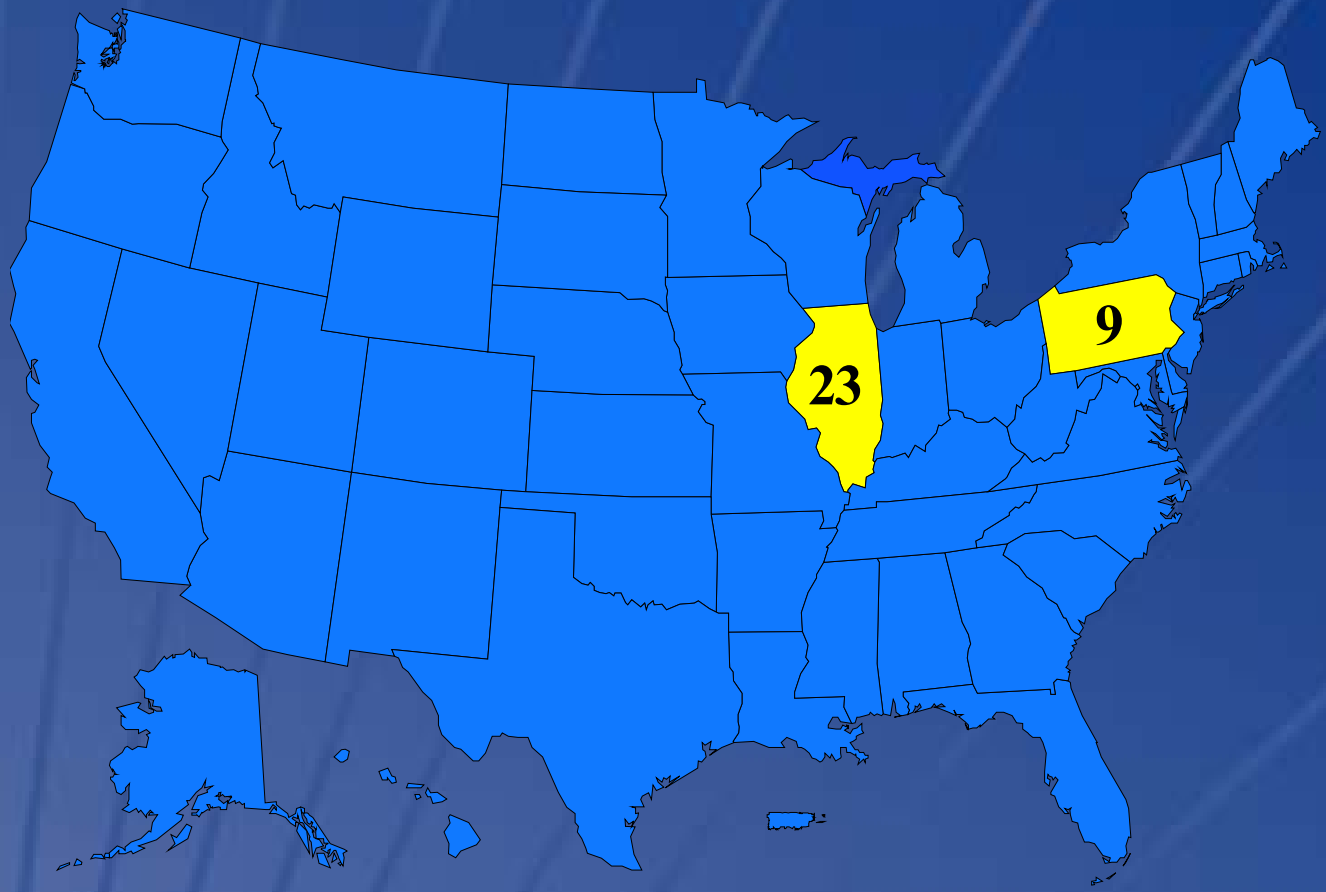
"*Salmonella* Outbreak Tied to Cereal"

"*Salmonella* Contaminated Breakfast Cereal"

"*Salmonella* Found in Sealed Cereal Boxes"

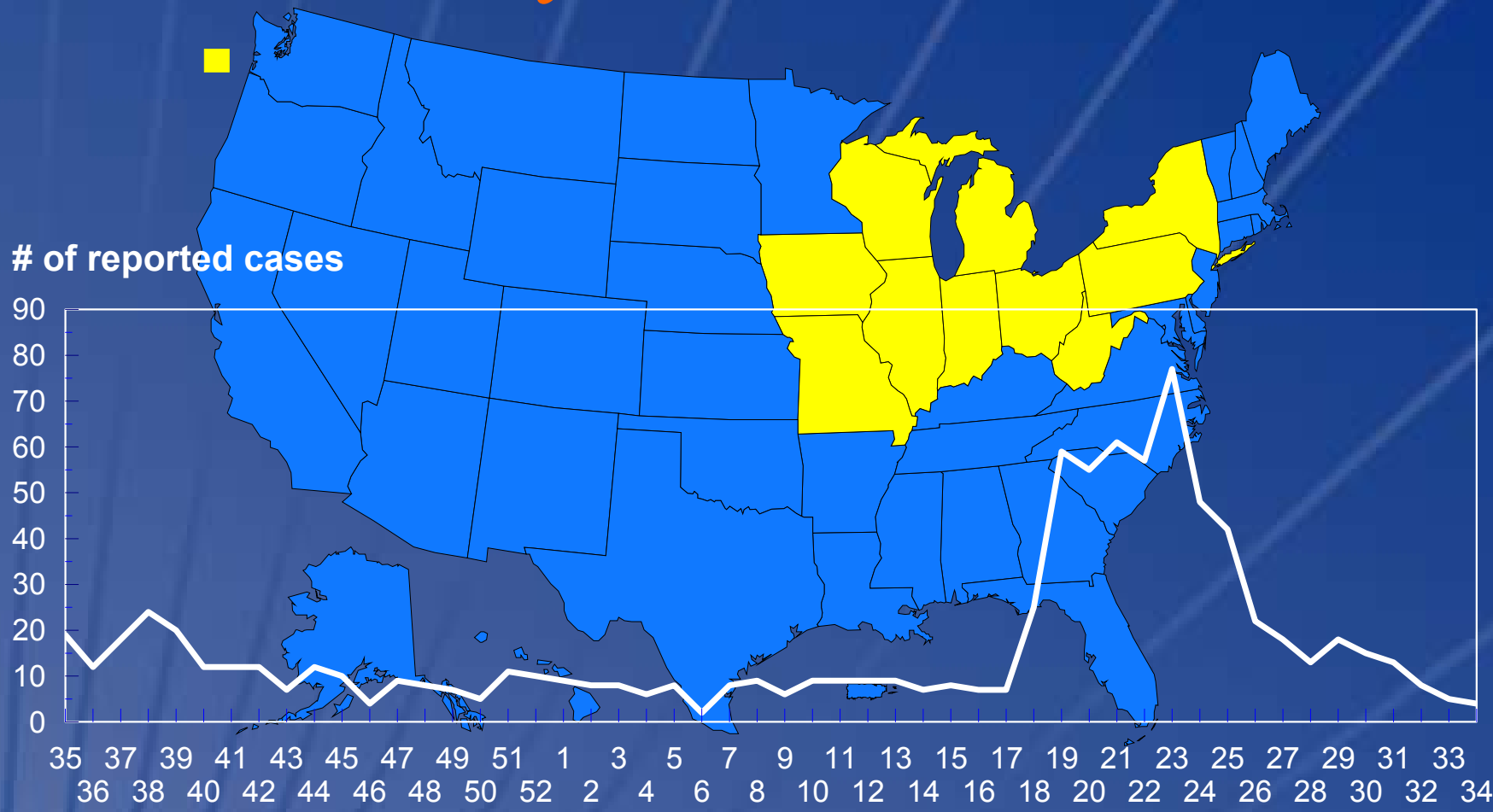
Real-time subtyping facilitates epidemiologic investigation of large multistate outbreaks

May 28, 1998

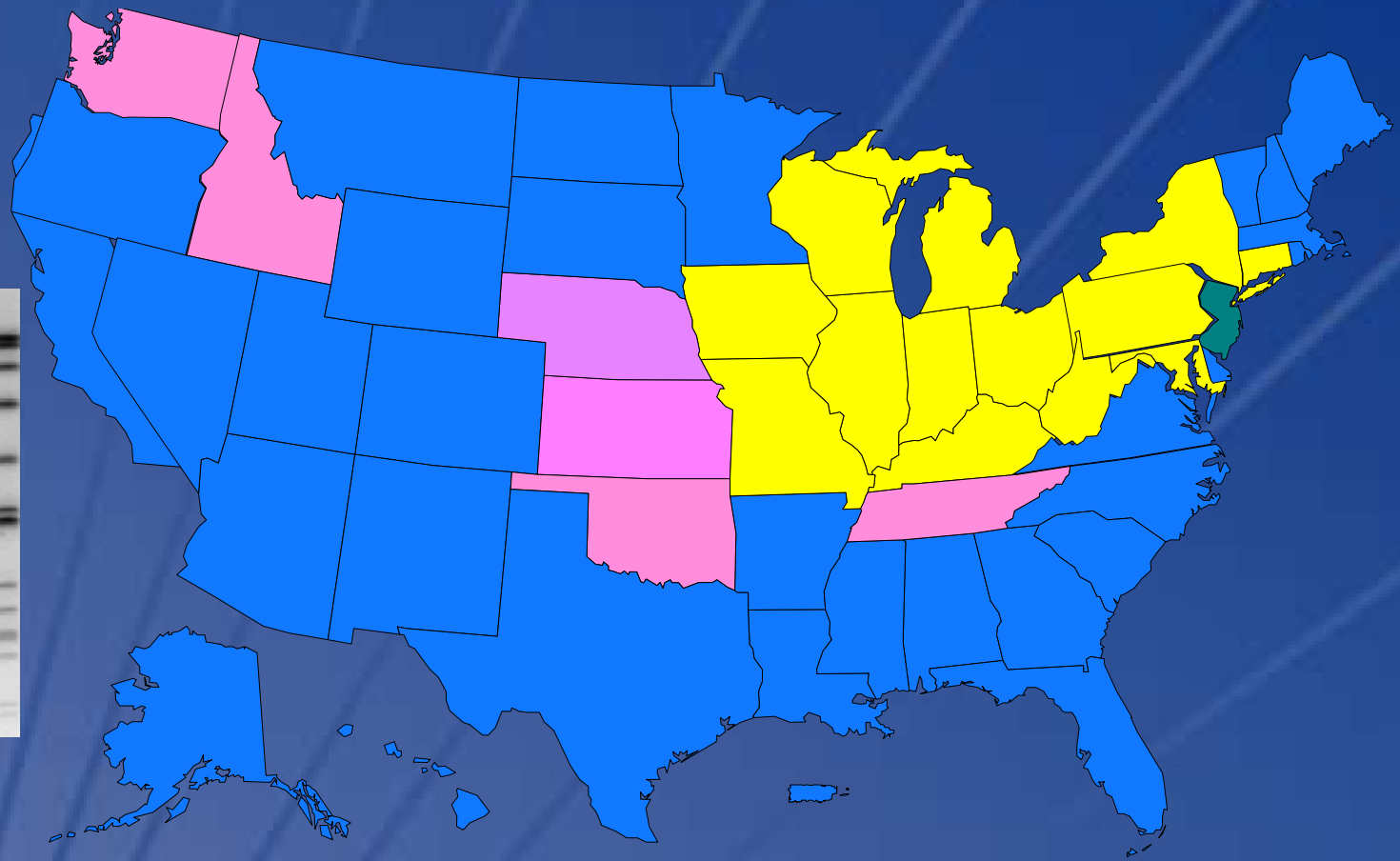


Illinois and Pennsylvania reported increases in *S.* Agona

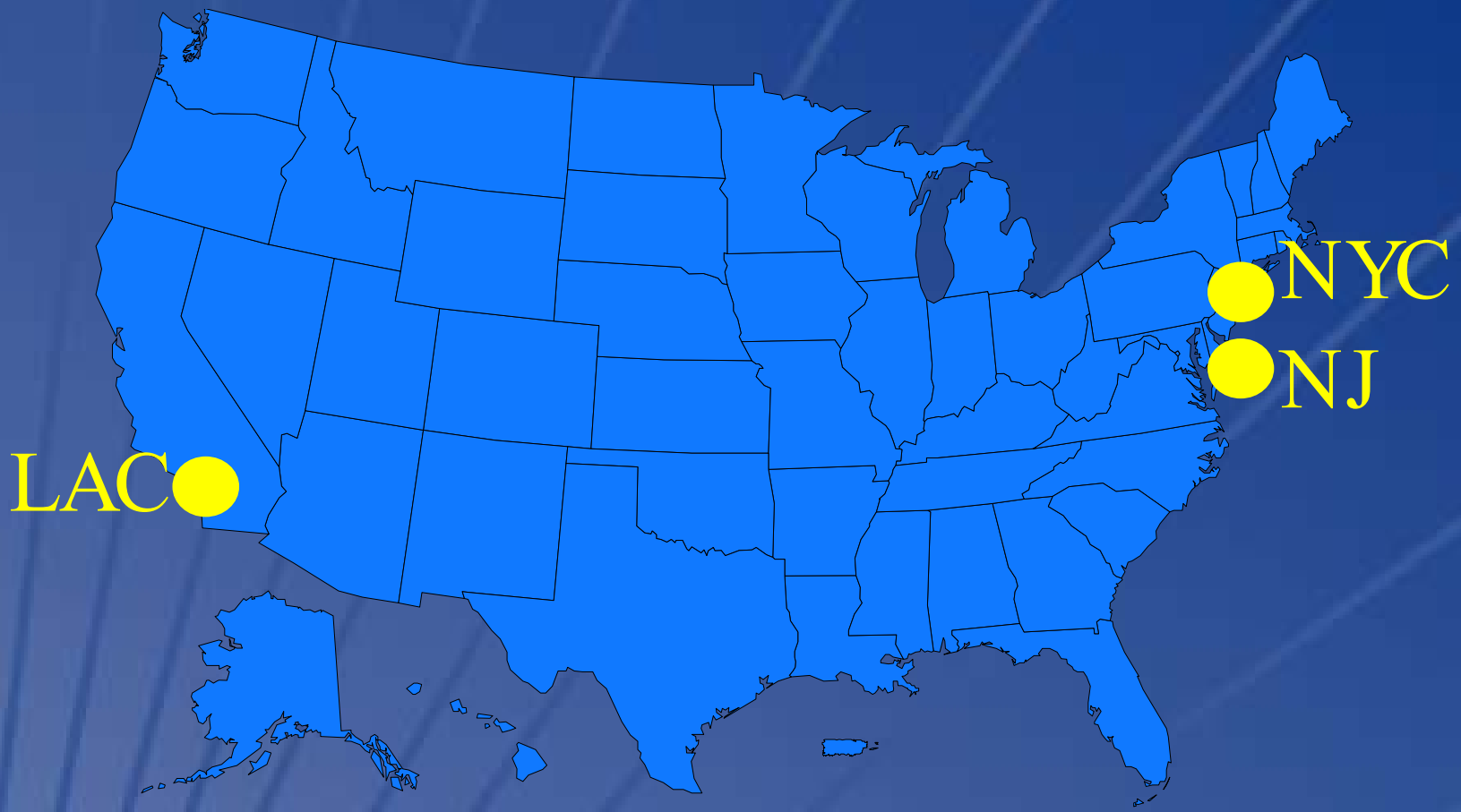
May 28 afternoon



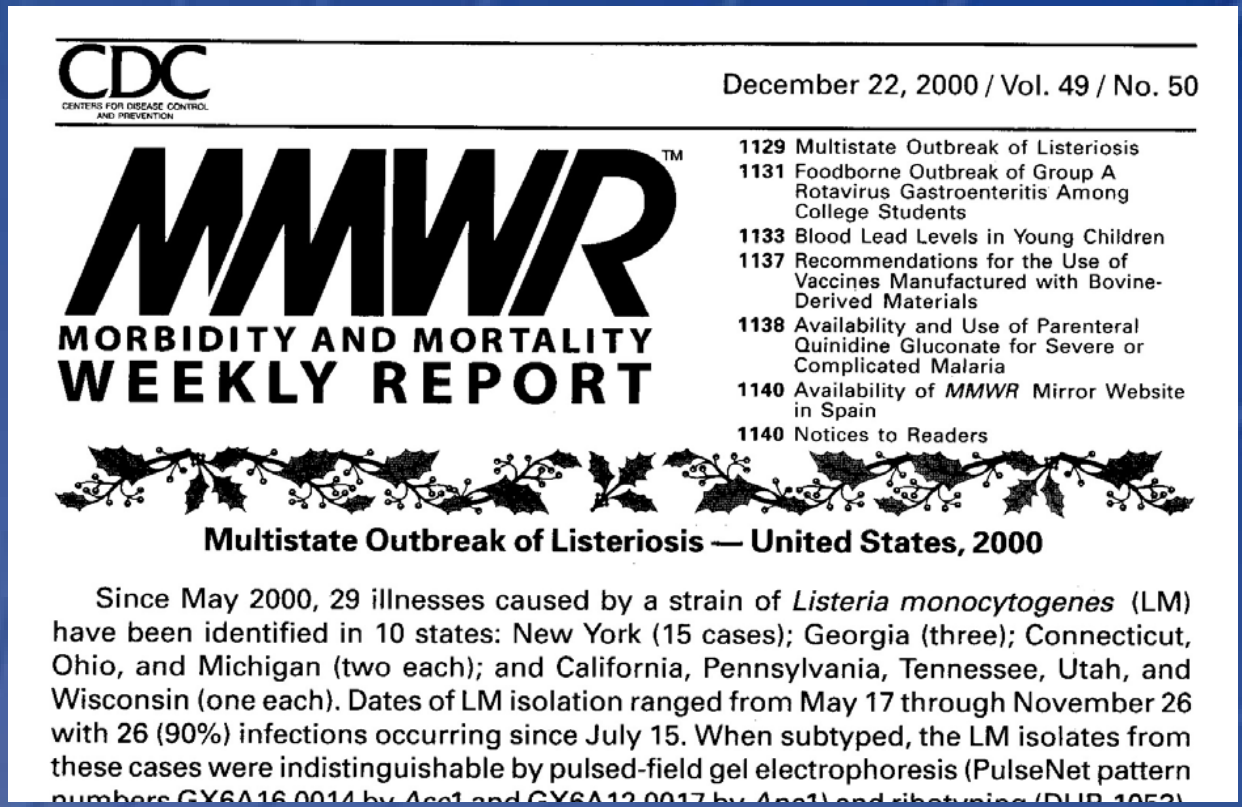
Rapid subtyping and data sharing help identify additional states with outbreak cases



Real-time Subtyping Helps Exclude Cases Unrelated to Outbreak



Multistate Listeriosis Outbreak-2000



CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

December 22, 2000 / Vol. 49 / No. 50

MMWR™
MORBIDITY AND MORTALITY
WEEKLY REPORT

1129 Multistate Outbreak of Listeriosis
1131 Foodborne Outbreak of Group A Rotavirus Gastroenteritis Among College Students
1133 Blood Lead Levels in Young Children
1137 Recommendations for the Use of Vaccines Manufactured with Bovine-Derived Materials
1138 Availability and Use of Parenteral Quinidine Gluconate for Severe or Complicated Malaria
1140 Availability of *MMWR* Mirror Website in Spain
1140 Notices to Readers

Multistate Outbreak of Listeriosis — United States, 2000

Since May 2000, 29 illnesses caused by a strain of *Listeria monocytogenes* (LM) have been identified in 10 states: New York (15 cases); Georgia (three); Connecticut, Ohio, and Michigan (two each); and California, Pennsylvania, Tennessee, Utah, and Wisconsin (one each). Dates of LM isolation ranged from May 17 through November 26 with 26 (90%) infections occurring since July 15. When subtyped, the LM isolates from these cases were indistinguishable by pulsed-field gel electrophoresis (PulseNet pattern numbers GX6A16.0014 by Ace1 and GX6A12.0017 by Ape1) and ribotyping (DUP-1053)

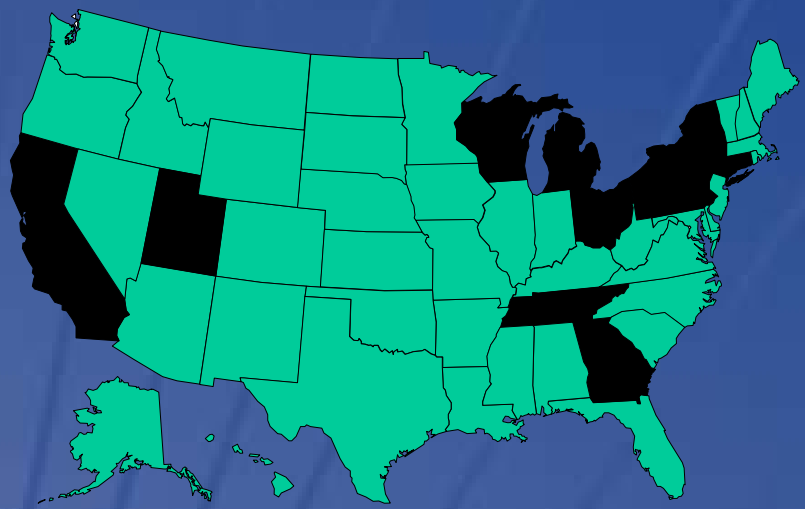
2000 multistate outbreak

September

- New York identifies small cluster of cases
- Other states alerted, PFGE pattern posted to PulseNet
- **Case-control study using patients with outbreak strain vs. other strains**

2000 multistate outbreak

Results of active case finding



- 29 cases
  - 72% non-perinatal
  - median age 64
- 4 adult deaths
- 3 miscarriages

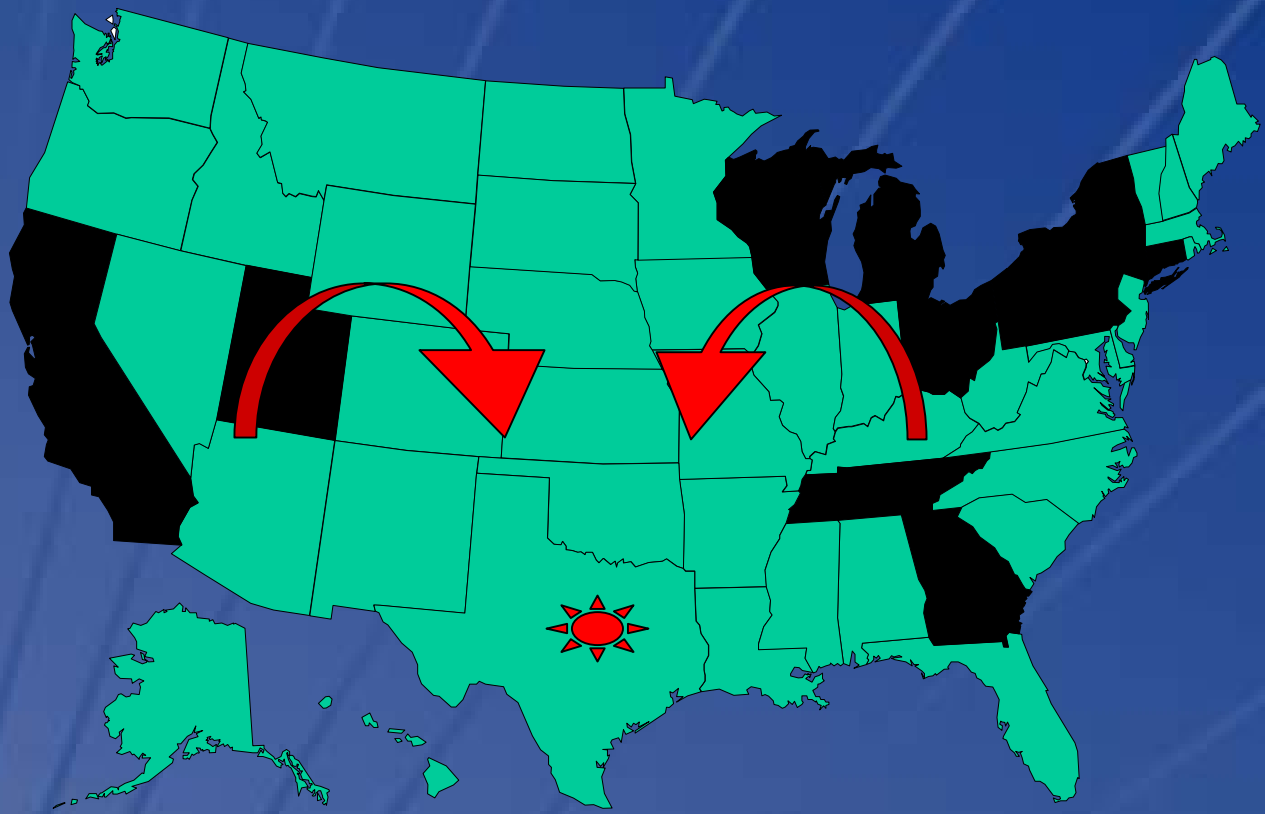
2000 multistate outbreak

Epidemiological Investigation

- 76% cases vs 21% controls ate sliced turkey purchased from a deli
  Odds ratio 8.0; $p<0.01$

- 13 delis visited
  27 different turkey meat suppliers
  Only 2 suppliers in common to all 13 delis
  1 of 2 suppliers produced meat for the other

2000 multistate outbreak



Cost effectiveness of PulseNet

- Elbasha et al. (Emerging Infectious Diseases 6:293-297, 2000) assessed the societal costs and benefits of PulseNet in Colorado
- If only 5 cases of *E. coli* O157:H7 infections were averted by the recall of ground beef in the Colorado outbreak, the PulseNet system would have recovered all costs for start up and operation for 5 years.

Future plans for PulseNet

- Include all significant foodborne disease-causing bacteria and all state public health laboratories by 2002
- Output PFGE pattern information to Public Health Surveillance Systems
- Explore ways to partner with the food industry
- Continue building international consensus
- Develop next generation typing method

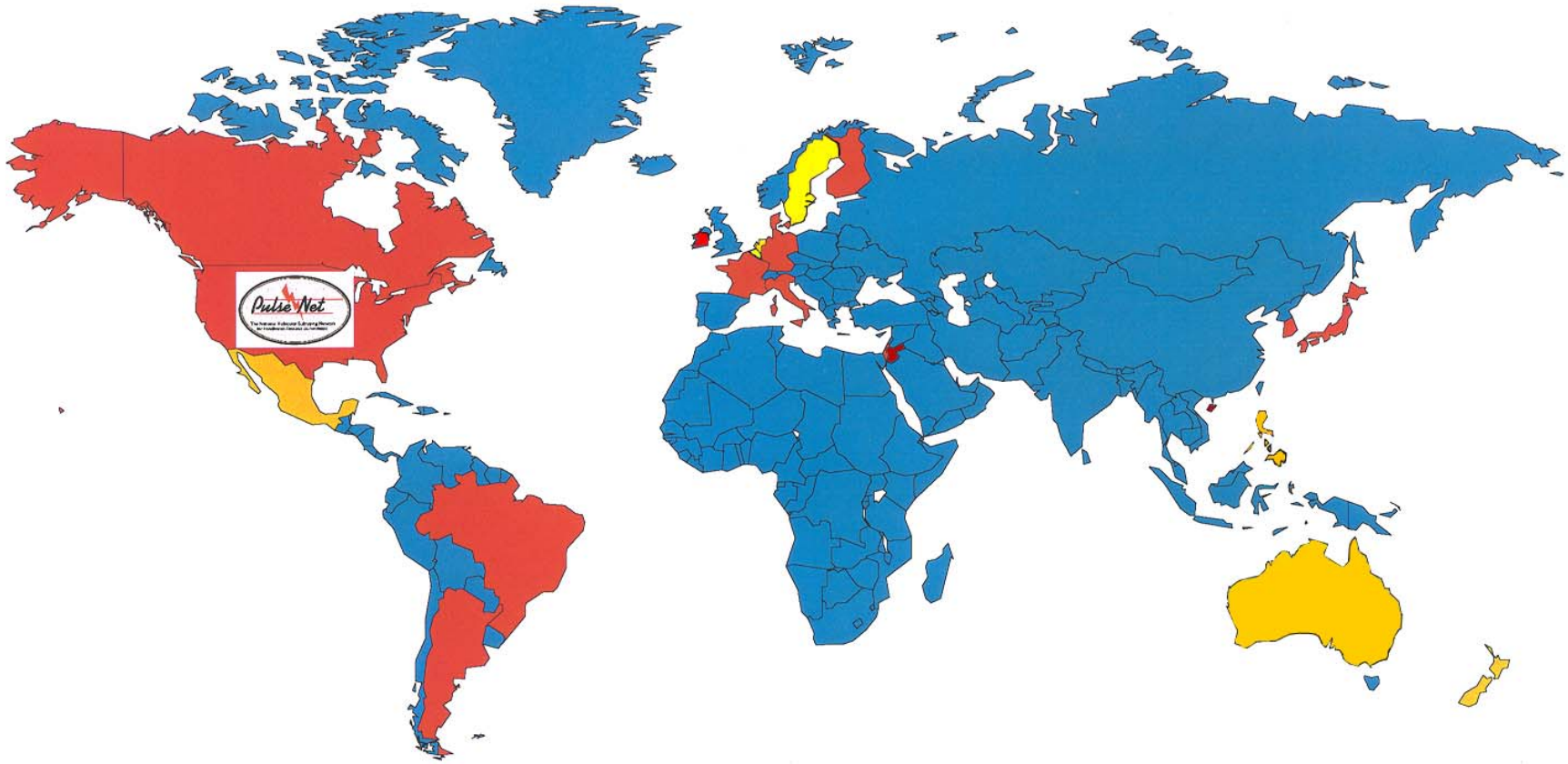
Future plans for PulseNet

- Include all significant foodborne disease-causing bacteria and all state public health laboratories by 2002
- Output PFGE pattern information to Public Health Surveillance Systems
- Explore ways to partner with the food industry
- **Continue building international consensus**
- Develop next generation typing method

PulseNet International

PulseNet International

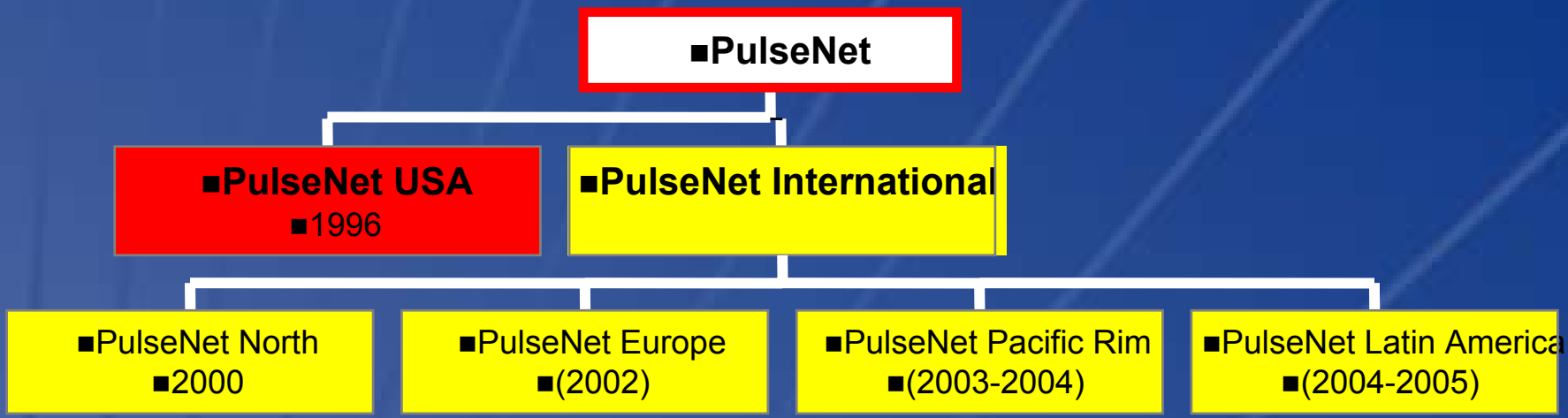
Training and Protocol Distribution



Attended PulseNet workshop at CDC

Received PulseNet protocols from CDC

Possible Organization

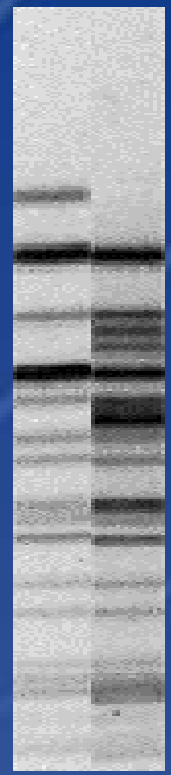


Future plans for PulseNet

- Include all significant foodborne disease-causing bacteria and all state public health laboratories by 2002
- Output PFGE pattern information to Public Health Surveillance Systems
- Explore ways to partner with the food industry
- Continue building international consensus
- **Develop next generation typing method**

The next generation subtyping method for PulseNet

- Criteria
  - Better discrimination than PFGE
  - Quantitative relatedness between strains
  - Sequence multiple targets on the genome
  - Target conserved and variable genes to get an accurate snapshot of the genome
  - Ensure backward compatibility with PFGE data



.....GATTCGTGGTCTCTGGGTAC...Isolate1
.....GATCCGTGGTCTGTGGGTAC..Isolate 2

Methodologic Approaches

- Multi-locus Variable-Number Tandem Repeat Analysis (MLVA)
- Multi-locus sequence typing (MLST)
- Explore other variable genes

Who will develop the new methods?

- Three state public health laboratories (MA, MN and CT) provided grants in 2001 through APHL
- Each laboratory responsible for one pathogen
- First meeting held at CDC to help identify the most productive approaches – mentors
- CDC will play a coordinating role

Driving Forces for the Next Decade

- Move towards non-culture diagnostic tests and antimicrobial susceptibility testing
  - Isolates not readily available to the public health laboratory
- Demand for real-time data from the public health laboratory for Intervention and Prevention
- Rapid response is essential for investigating intentional acts of food contamination

Move towards non-culture diagnostic tests

- *E. coli* O157:H7 diagnostics: Shiga-toxin testing by PCR or ELISA
- DNA Probe Array for *Mycobacterium* species identification and rifampin resistance testing

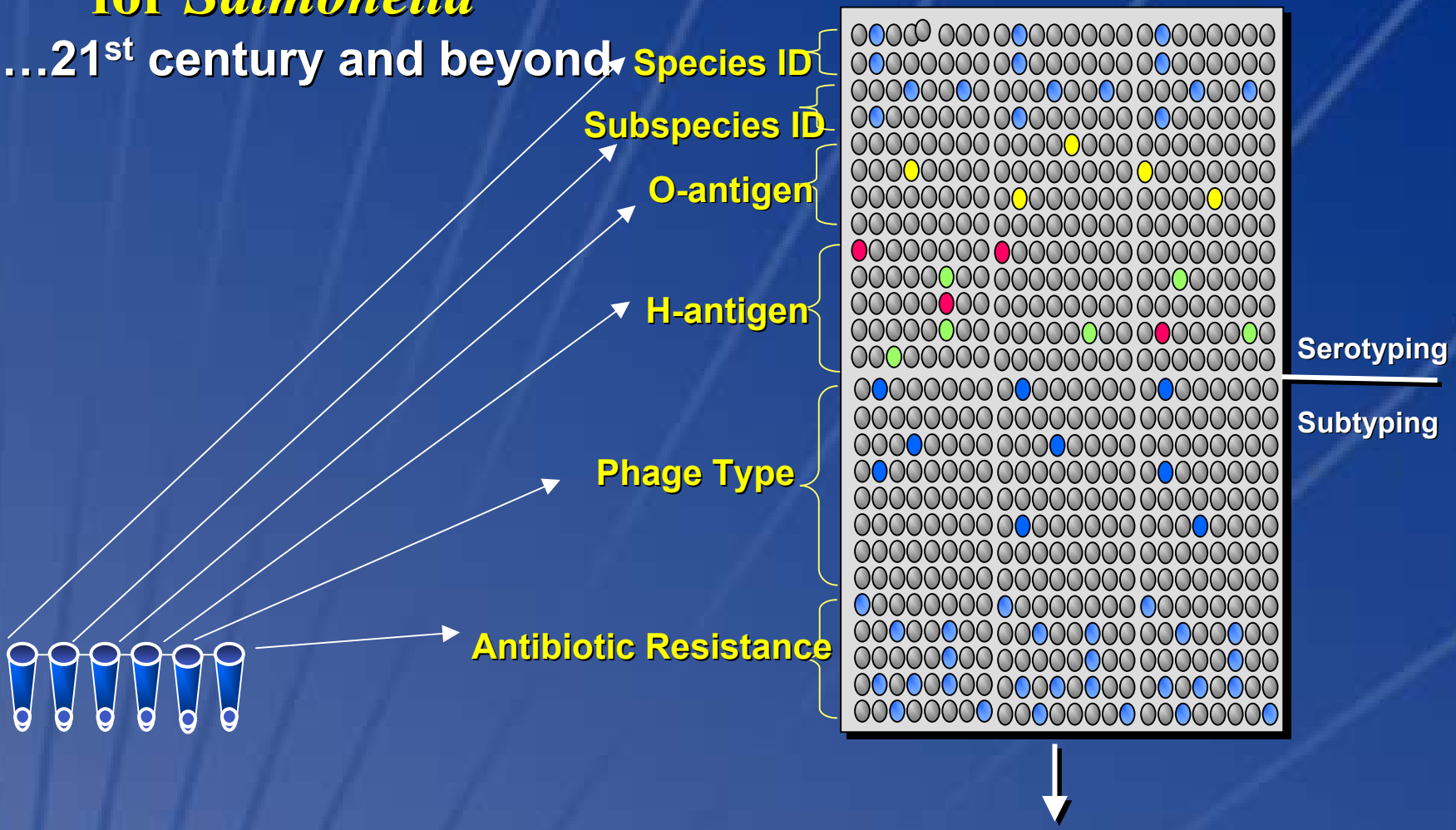
Isolates not readily available to the public health laboratory

- Species ID
- Serotyping, phage typing
- Virulence characterization
- Antimicrobial resistance
- DNA “fingerprinting”

Today’s public health needs isolates of bacteria

Proposed molecular assay for *Salmonella*

……21st century and beyond



Salmonella **ser. Typhimurium**

I : 1,4,5,12 : i :1,2, DT104, ACSSuT

Acknowledgements

- John Besser
- Collette Fitzgerald, Ph.D
- Patricia Griffin, M.D.
- James Hughes, M.D.
- Susan Hunter
- Paul Mead, M.D.
- John McQuiston
- Josefa Rangel, M.D.
- Lindsay Sails
- Robert Tauxe, M.D., M.P.H.