CDC perspective on non-O157 Shiga toxin-producing *E. coli* (STEC) in the United States

Patricia M. Griffin, M.D.

Chief, Enteric Diseases Epidemiology Branch

October 17, 2007

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E. coli that cause human gastrointestinal illness

- Shiga toxin-producing (STEC), also called Enterohemorrhagic (EHEC)
- Enteropathogenic (EPEC)
- Enterotoxigenic (ETEC)
- Enteroinvasive (EIEC)
- Other types, less well characterized

E. coli that cause human gastrointestinal illness

- Shiga toxin-producing (STEC), also called Enterohemorrhagic (EHEC)
  - *E. coli* O157 serogroup
  - Non-O157 serogroups
- Enteropathogenic (EPEC)
- Enterotoxigenic (ETEC)
- Enteroinvasive (EIEC)
- Other types, less well characterized

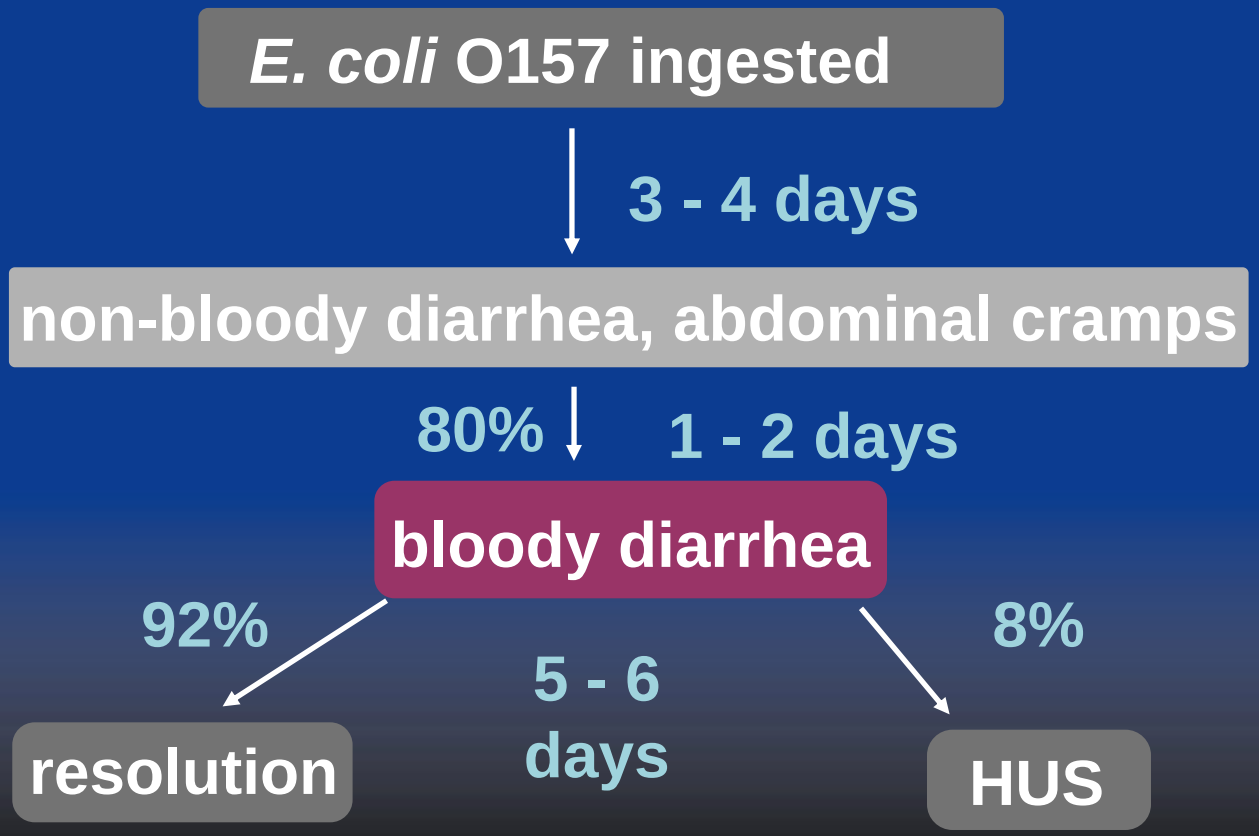
Animals are the reservoirs for STEC

- Cattle
- Other ruminants
- Other animals
  - especially those who have contact with cattle

Major modes of transmission of STEC to humans – how the fecal matter gets to the mouth

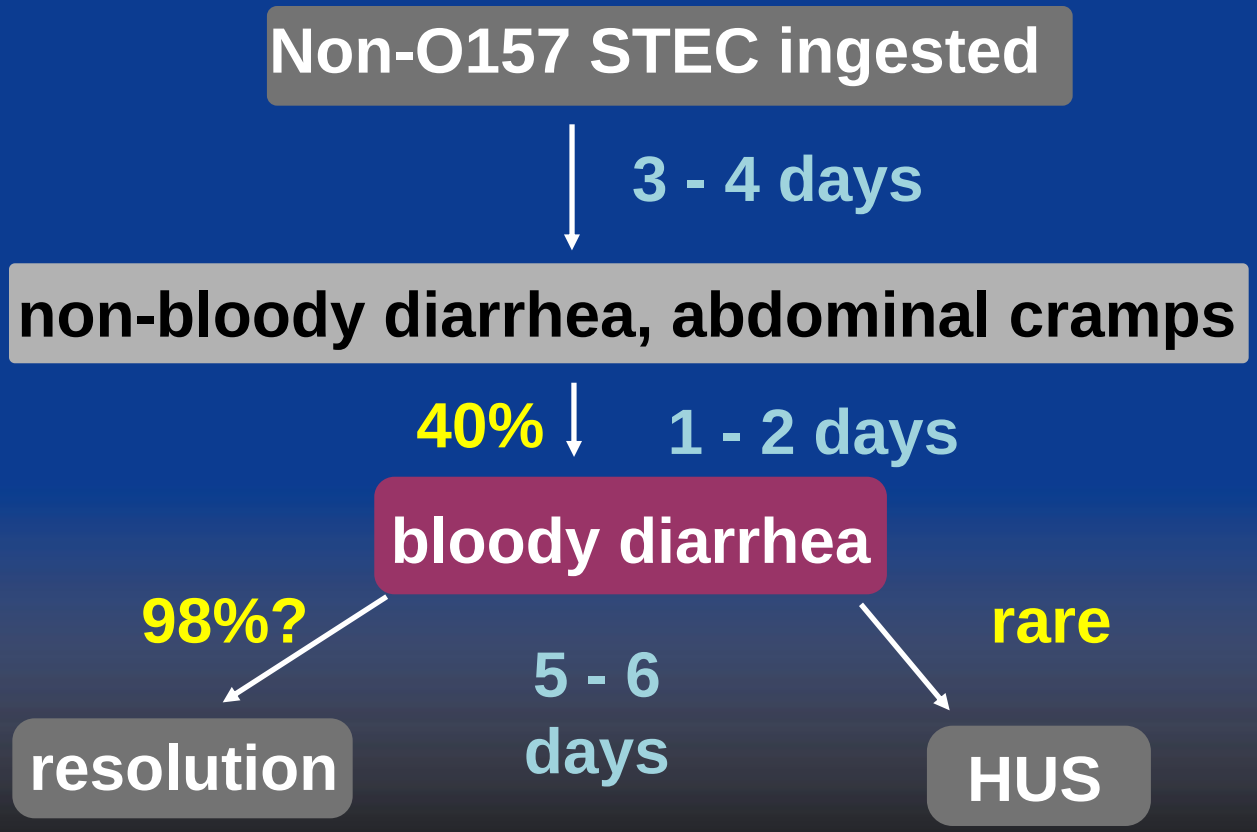
- Food
  - cattle products, e.g., beef, raw milk
  - food contaminated with cattle or human feces e.g., lettuce
- Water
  - Drinking water
  - Recreational water
- Animal contact
  - contact with farm animals, e.g. petting zoos
  - contact with farm animals' environment
- Person contact
  - With the feces of infected persons

Sequence of events in *E. coli* O157:H7 infection



Mead. Lancet 1998

Sequence of events in non-O157 STEC infection



Compared to persons with *E. coli* O157 infection,

- **persons with non-O157 STEC have less severe illness**
- **But non-O157 STEC include many serogroups, with varying virulence**
  - some typically cause only mild diarrhea
  - others can cause HUS and death

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Clinical lab testing for STEC

- *E. coli* O157
  - Unusual feature: does not ferment sorbitol
    - streak stool specimen onto plate containing Sorbitol-MacConkey (SMAC) medium
      - select clear colonies (others are pink)
        - O157 strains agglutinate when O157 antisera is added
- Non-O157 STEC
  - Lack unusual features, look like good *E. coli*

Timeline of public health recommendations for STEC

1994 ***E. coli* O157 infection made reportable**

1995 **Commercial Shiga toxin enzyme immunoassay (EIA) introduced**

2000 **Non-O157 STEC infections made nationally reportable**

Testing for non-O157 STEC using the Shiga toxin EIA

- Clinical lab cultures stool specimen in broth
  - tests broth for Shiga toxin using EIA
    - positive test could be O157 or non-O157 STEC
- Clinical lab can send Shiga toxin-positive broth to State Health lab
  - State Health lab isolates STEC
    - State Health Lab sends STEC to CDC
      - CDC determines serotype

Some challenges arising from use of the Shiga toxin EIA

- After adopting the EIA, some clinical labs stopped testing for *E. coli* O157 using selective media
  - *E. coli* O157 outbreaks could be missed
- Some clinical labs discard Shiga toxin-positive specimens without obtaining an isolate, so
  - simply report “Shiga toxin positive” to doctor
  - serogroup not determined
    - *E. coli* O157 strains not identified and sub-typed for outbreak detection
    - Non-O157 outbreaks less likely identified

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How do we learn about non-O157 STEC?

- FoodNet conducts active surveillance
- Some clinical labs isolate non-O157 STEC
  - strains are serotyped at CDC
- Some health departments are doing studies, e.g.,
  - Minnesota
  - Connecticut
- Outbreak investigations
- Studies of HUS

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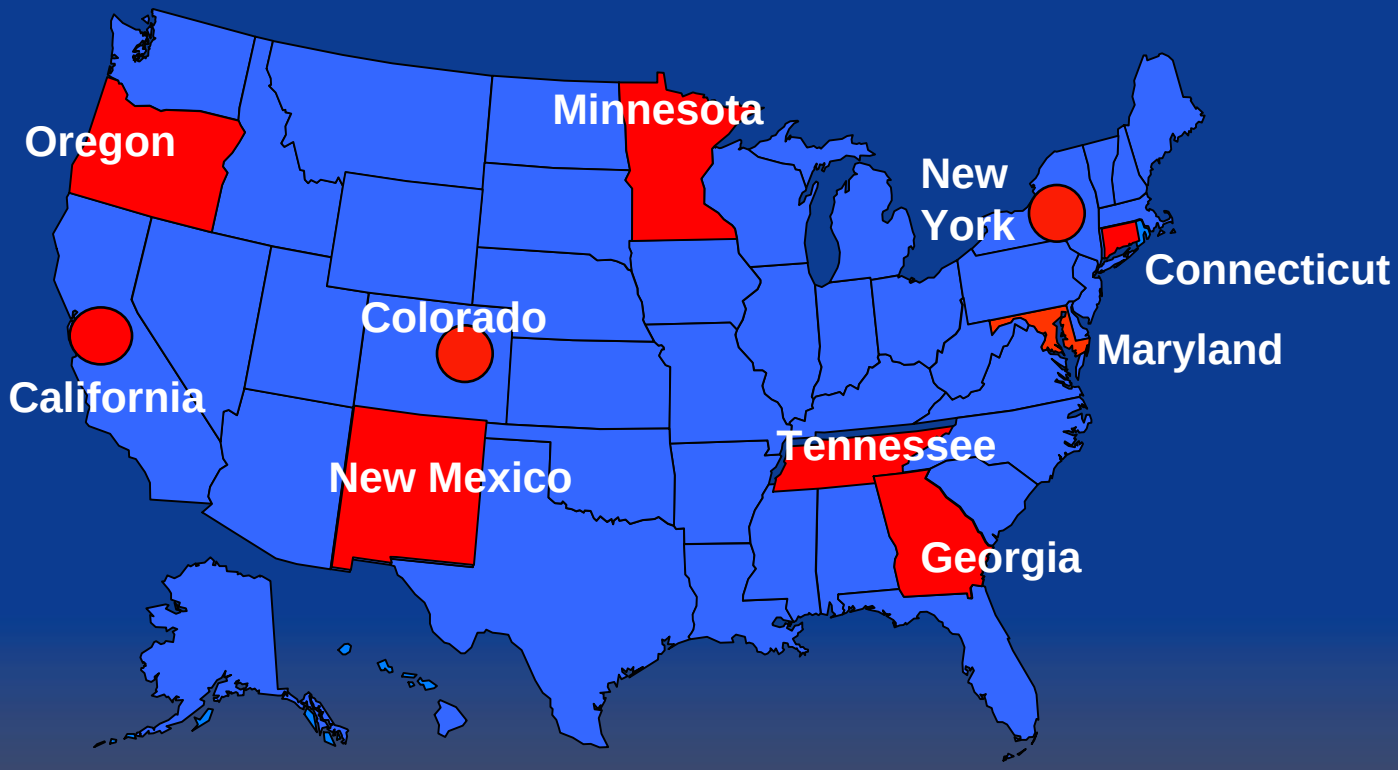
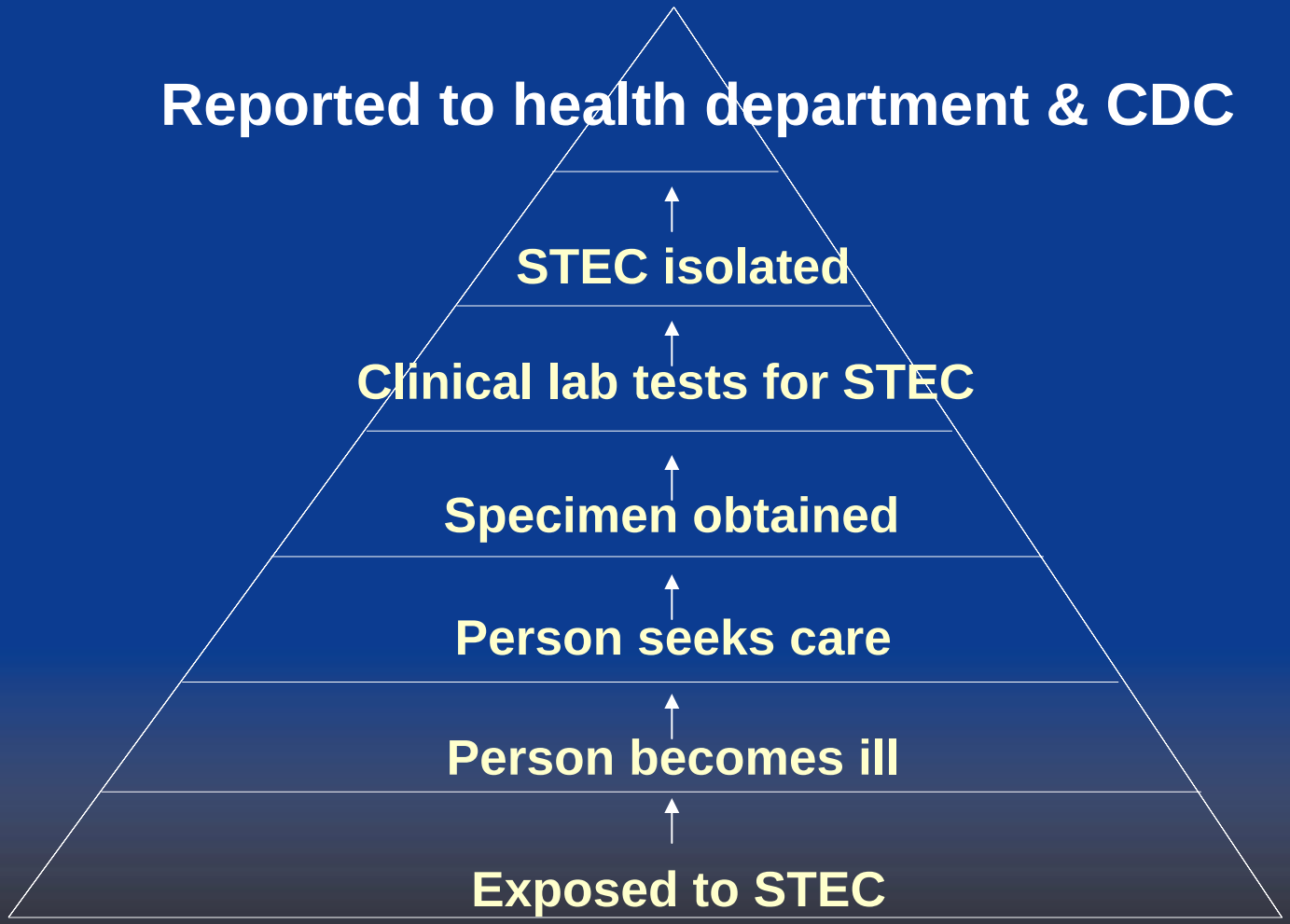
FoodNet Catchment Area, 2007



Catchment population 45 million persons
(15% of U.S. population)

Pyramid of Surveillance



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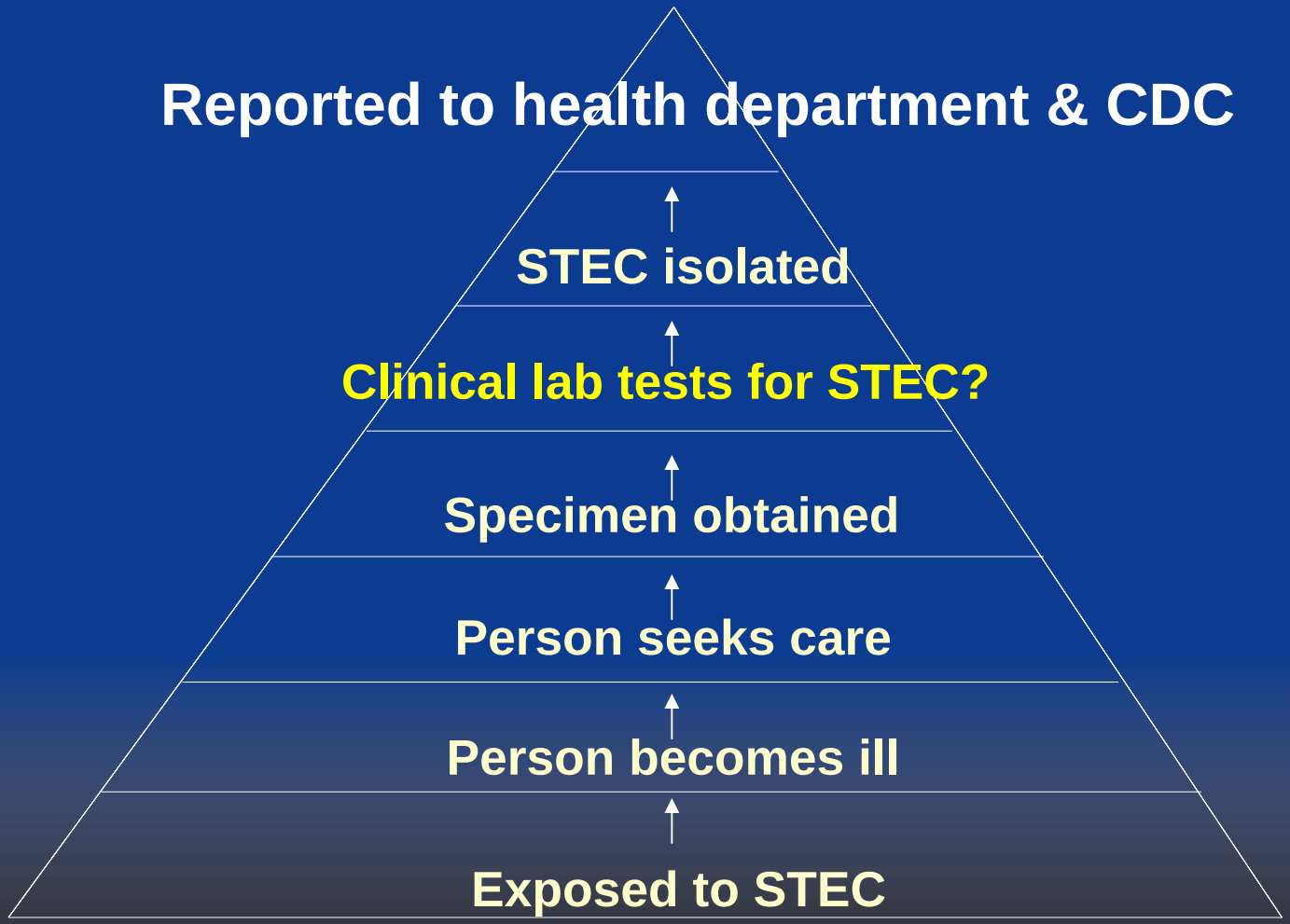
Pyramid of Surveillance



CDC
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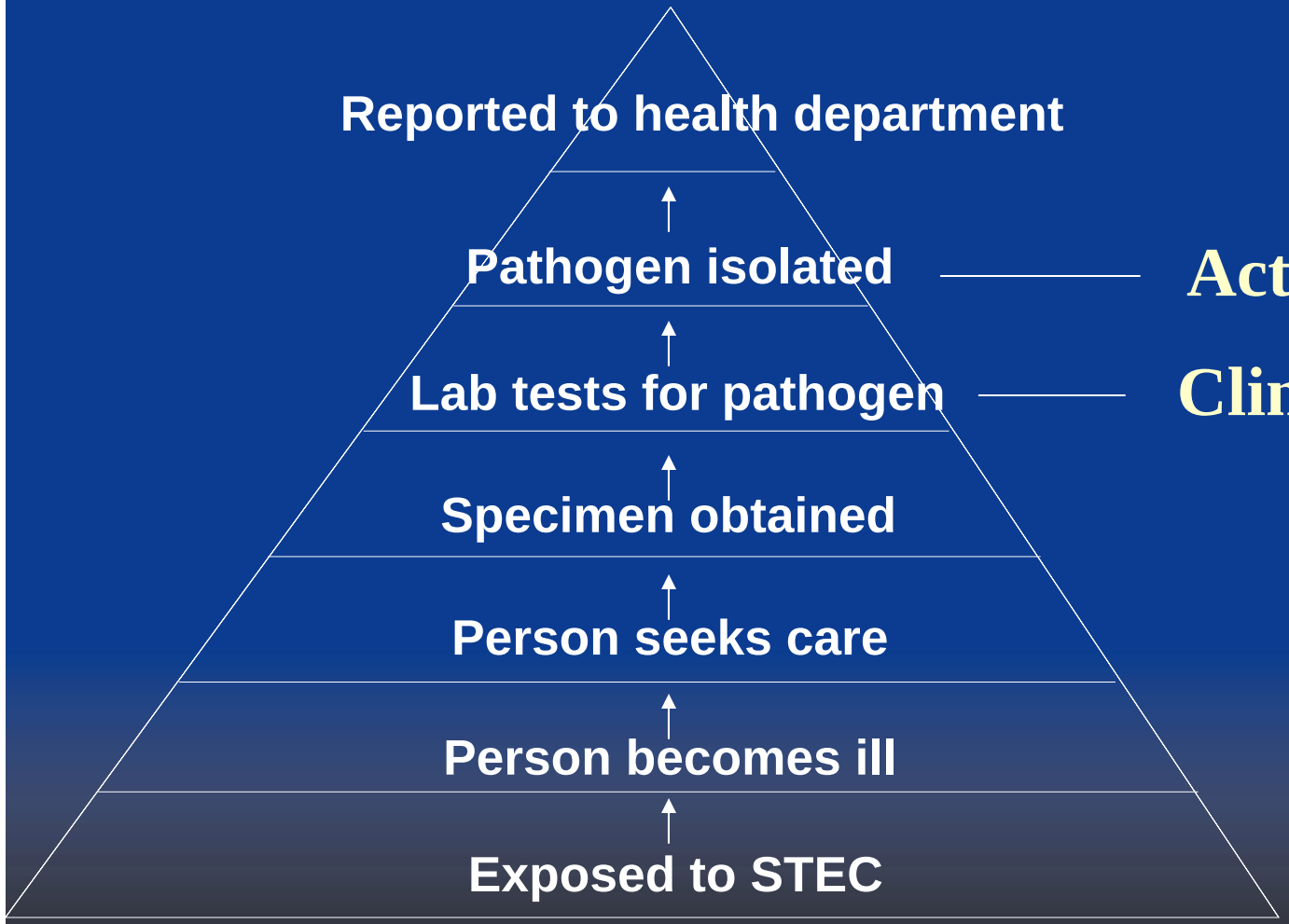

Active surveillance

Clinical lab survey

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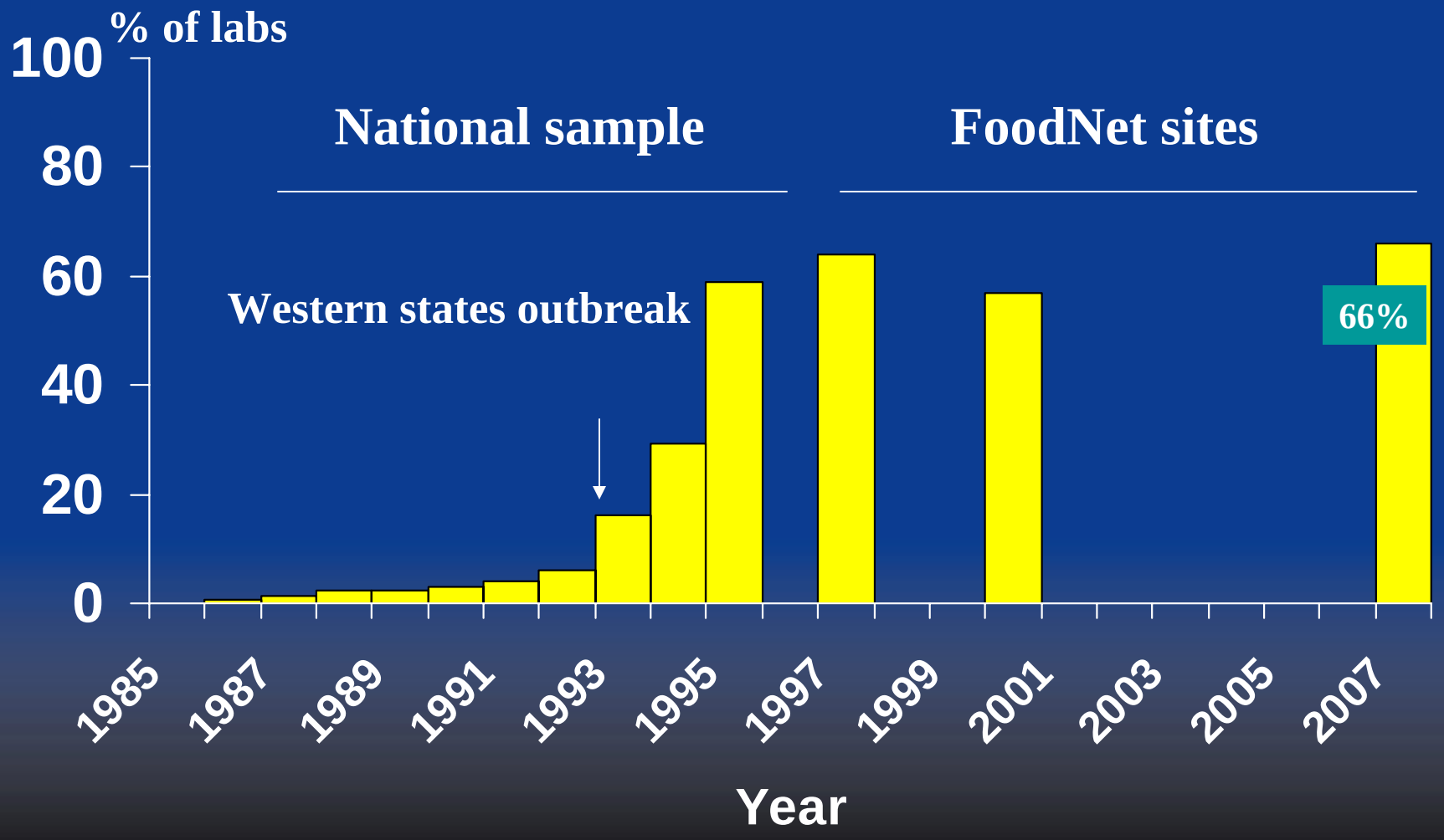
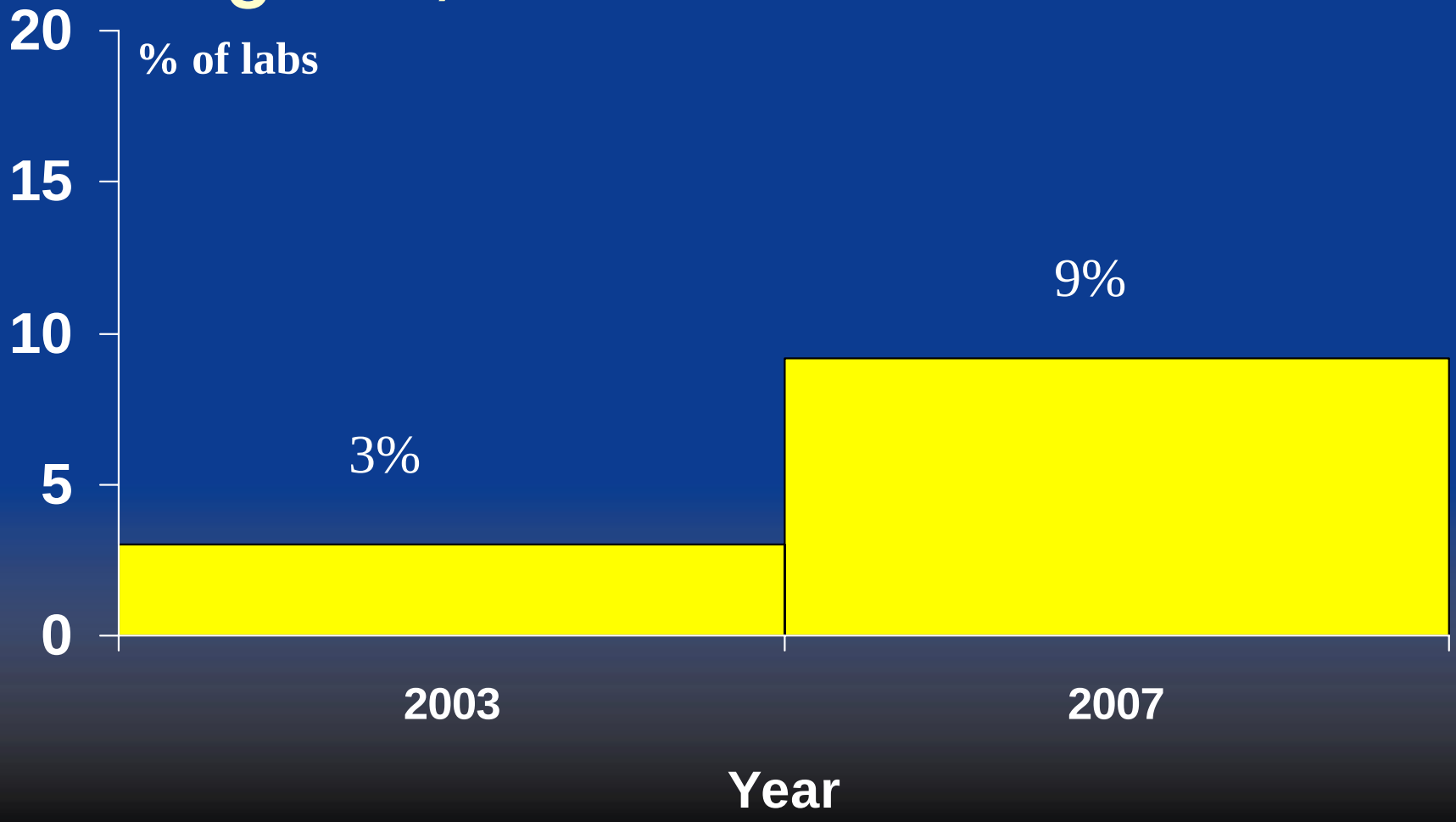
Percent of clinical labs screening <u>all</u> stools for *E. coli* O157



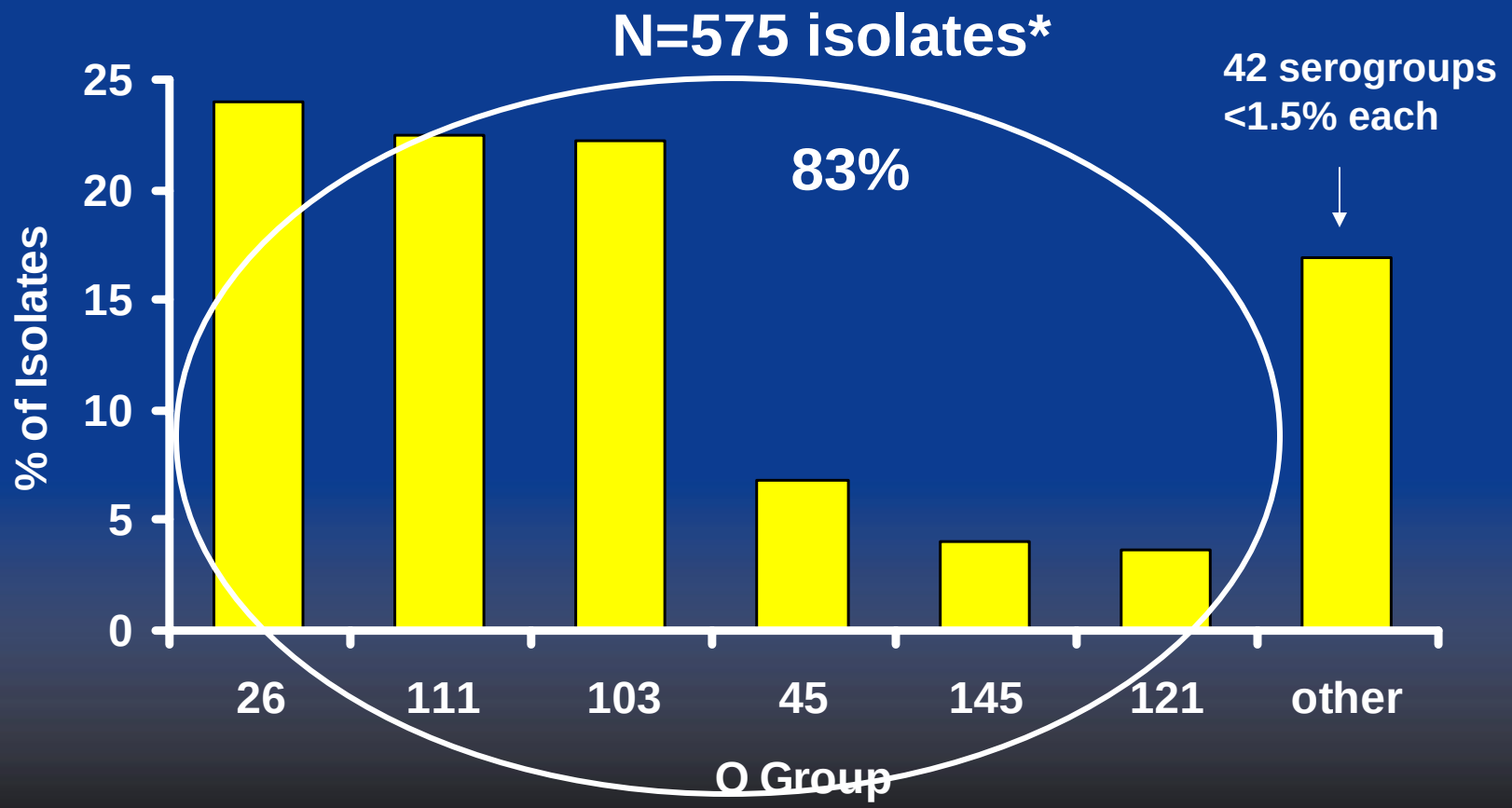
Boyce, J Clin Micro 1995; Voetsch CID 2004; and unpublished preliminary data

Percent of clinical labs that ever conduct on-site testing for STEC using EIA, FoodNet



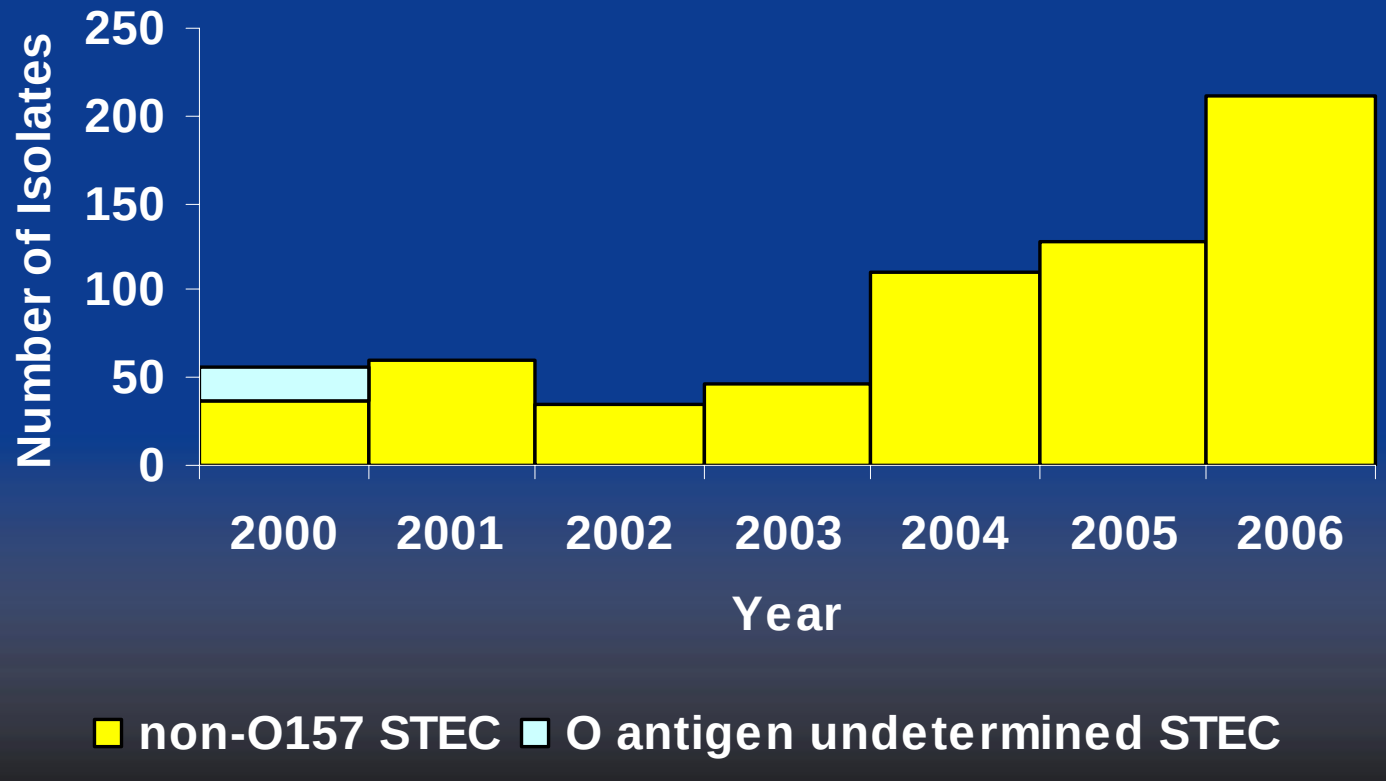
Preliminary data

Human isolates of non-O157 STEC, by serogroup, FoodNet sites, 2000-2006



**preliminary data; an additional 54 isolates had missing O group information*

Number of non-O157 STEC identified in FoodNet sites, 2000-2006



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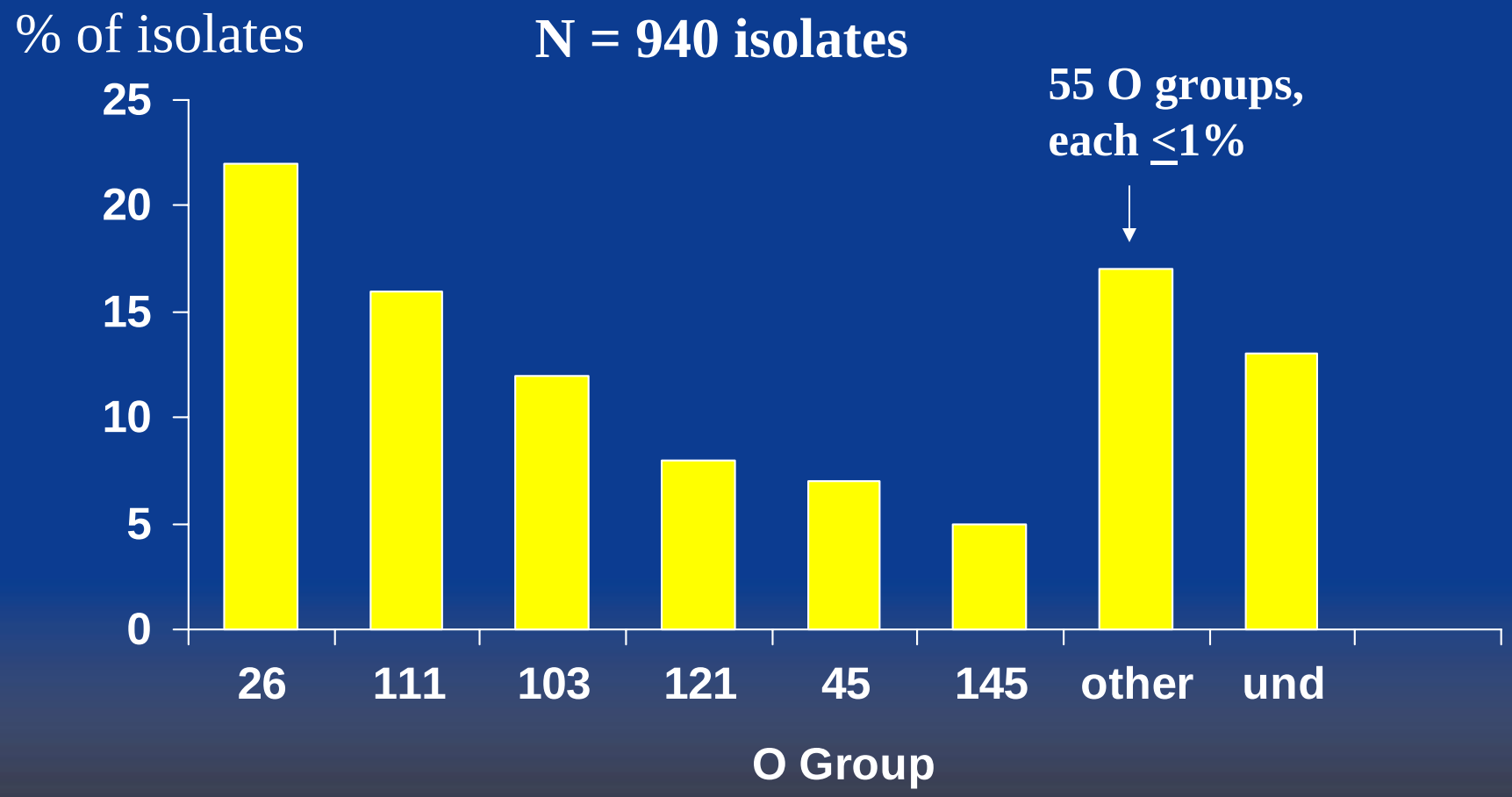
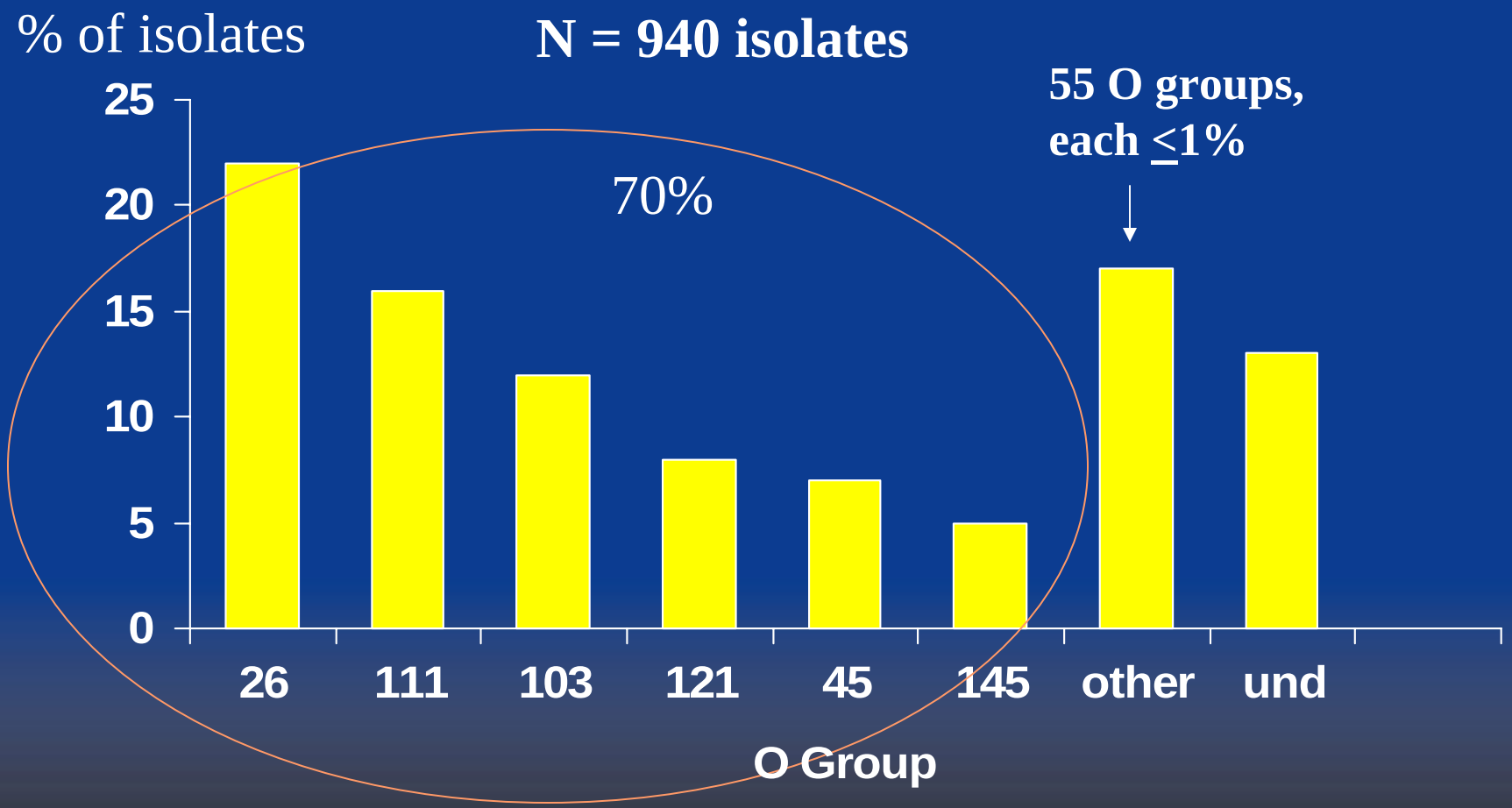
- Studies of HUS

Human isolates of non-O157 STEC serotyped by CDC, by serogroup, 1983-2002



Brooks, JID 2005;192:1422

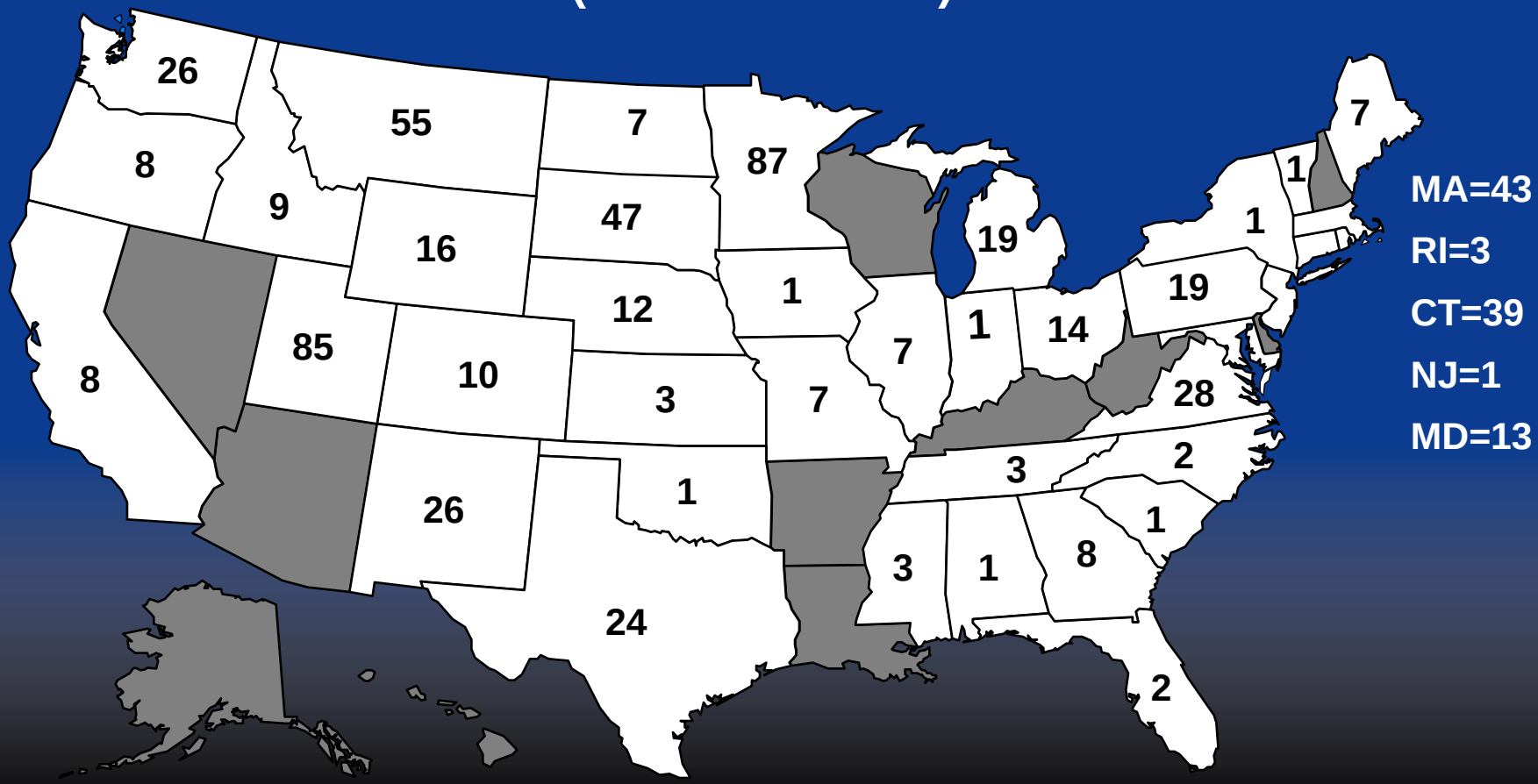
Human isolates of non-O157 STEC serotyped by CDC, by serogroup, 1983-2002



Brooks, JID 2005;192:1422

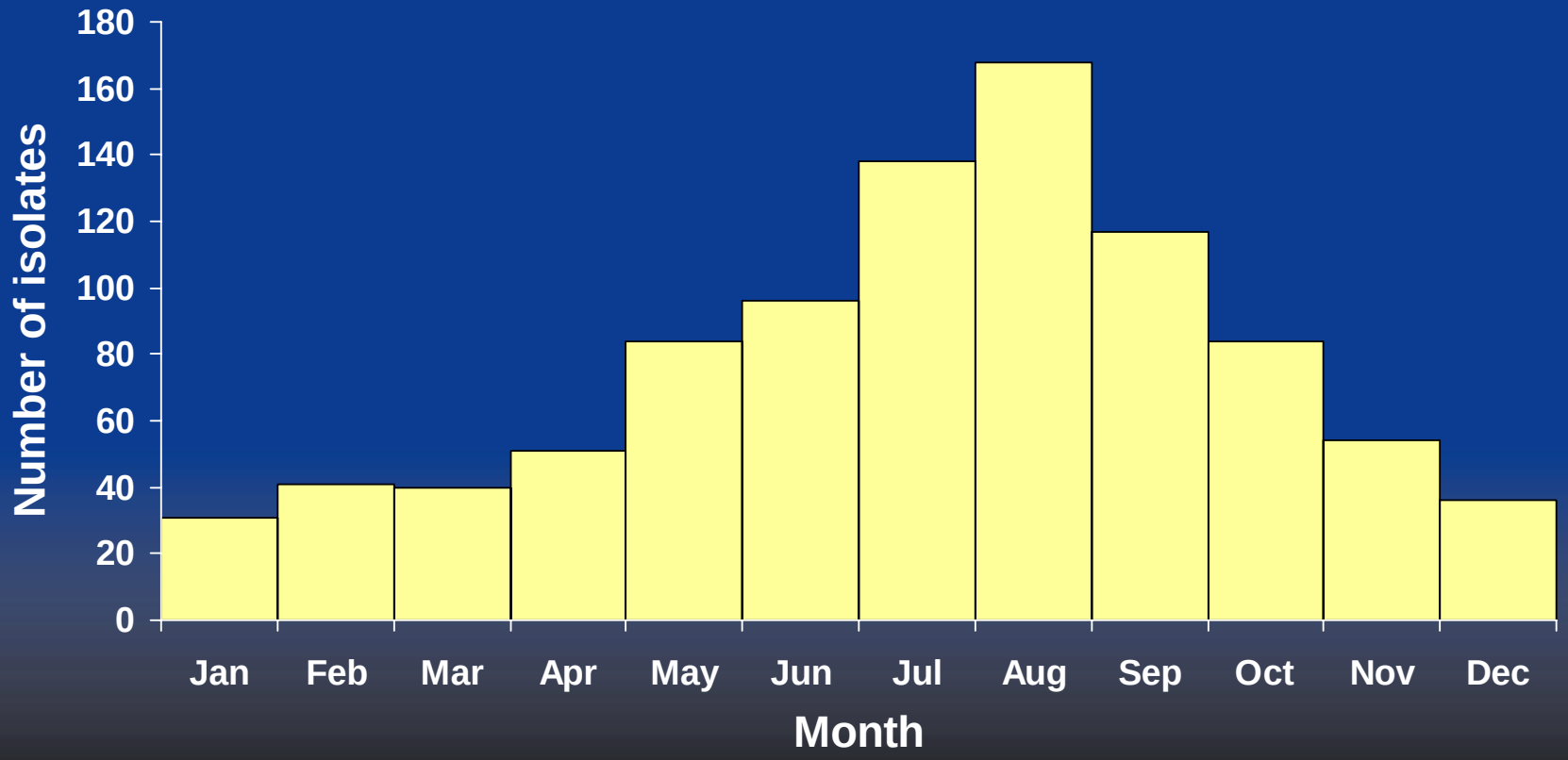
Human non-O157 STEC isolates submitted to CDC by states, 1983-2001

(N = 653 isolates)



Seasonality of human non-O157 STEC isolates submitted to CDC, 1983-2002

(N=940 isolates)



Brooks, JID 2005

Persons with HUS rarely had non-O157 STEC strains that produced only Shiga toxin 1

Isolates with clinical information submitted to CDC, 1983-2002

STEC toxin profile	HUS (n= 21)	No HUS (n=271)
Only Shiga toxin 1	5%	68%
Shiga toxin 2 (+/- Shiga toxin 1)	95%	32%
Total	100%	100%

Overall, 61% of human non-O157 STEC produced only Shiga toxin 1

Brooks, JID 2005

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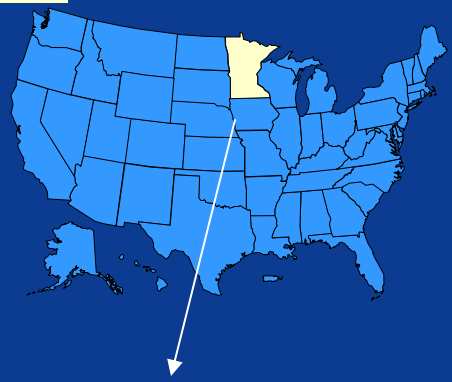
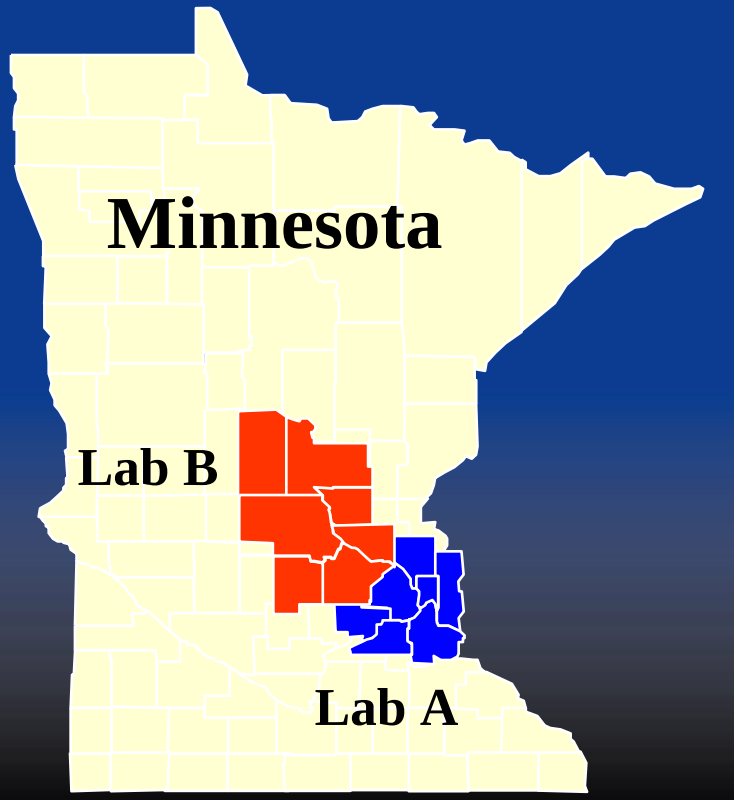
Surveillance for STEC in all diarrheal stools



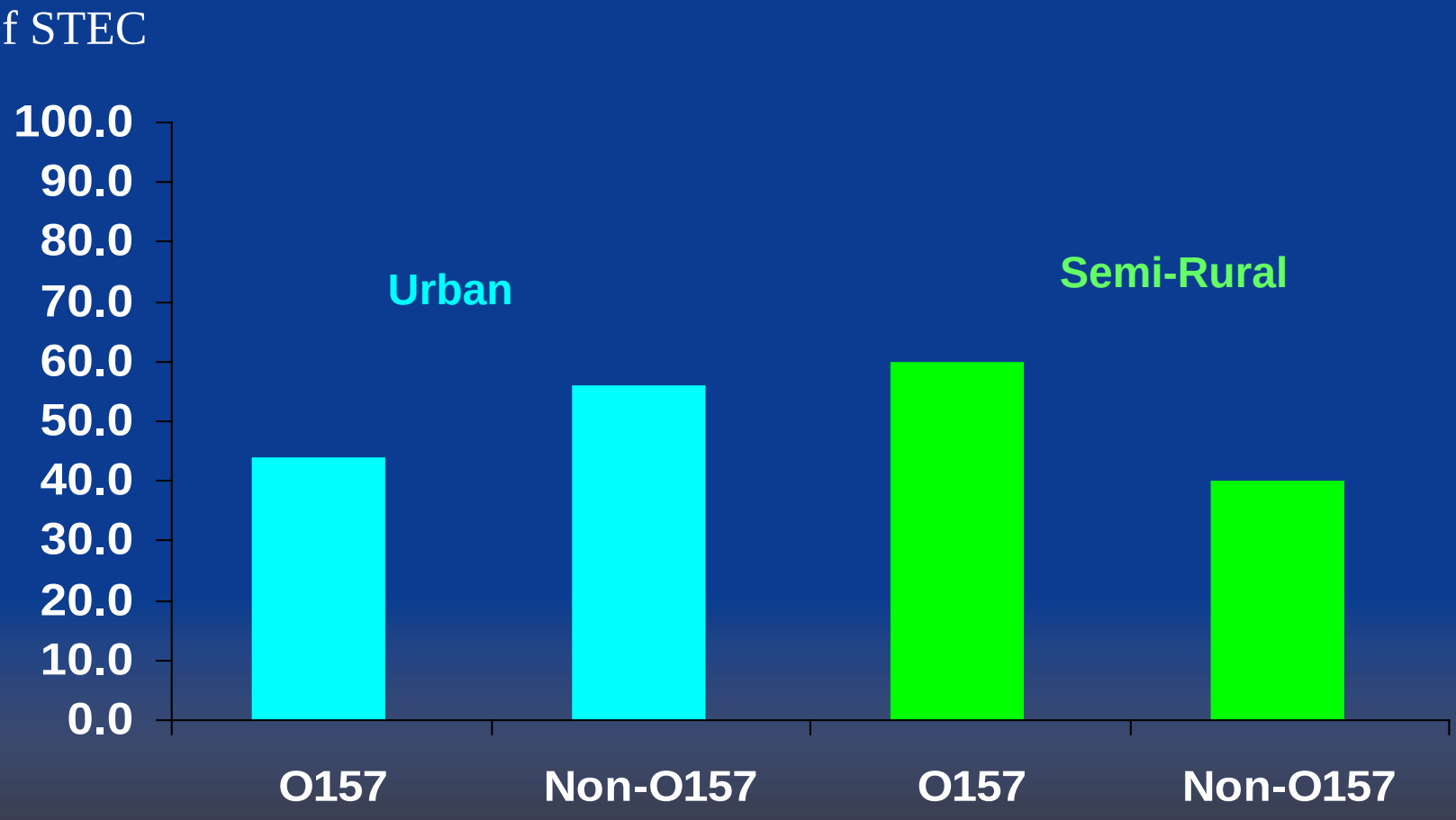
- Lab A: urban

- Lab B: serves a semi-rural area with agriculture and dairy farms



Medus, Besser, Hedberg, Bartkus, Juni, Smith, EID Conference 2003

Proportion of STEC that were O157 or non-O157, human diarrheal stools, Minnesota, 2000-2002



Juni, Besser, Hunt, Smith, Hedberg, Medus,Sullivan, Bartkus, unpublished

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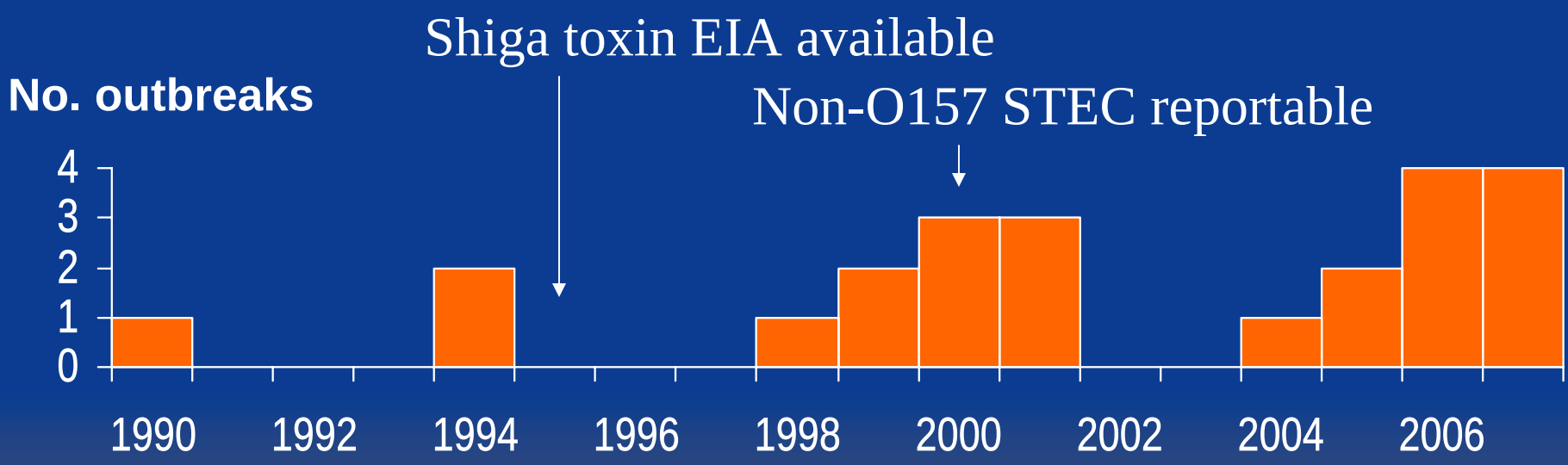
Outbreaks of non-O157 STEC infections, U.S., 1990-2007

N = 23 outbreaks



Data from 2007 are preliminary

Serogroups of non-O157 STEC outbreaks, U.S., 1990-2007

N = 23 outbreaks

Serogroup	No. outbreaks
O111 (one outbreak also had O157)	**10**
O121	**3**
O26	**3**
O45	**2**
O27, O103, O104, O153	**1 each**
O26 and O121 together	**1**

Data from 2007 is preliminary

Serogroups of 23 non-O157 STEC outbreaks, U.S., 1990-2007

Green shows most common serogroups of sporadic cases

Serogroup	No. outbreaks
O111 (one outbreak also had O157)	**10**
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O45	**2**
O27, O103, O104, O153	**1 each**
O26 and O121	**1**

Data from 2007 is preliminary

Modes of transmission in non-O157 STEC outbreaks, U.S.,1990-2007

(N = 23)

Mode	No. outbreaks
Food	11
Person-to-person	6
Lake water	3
Animal contact	2
Undetermined	1

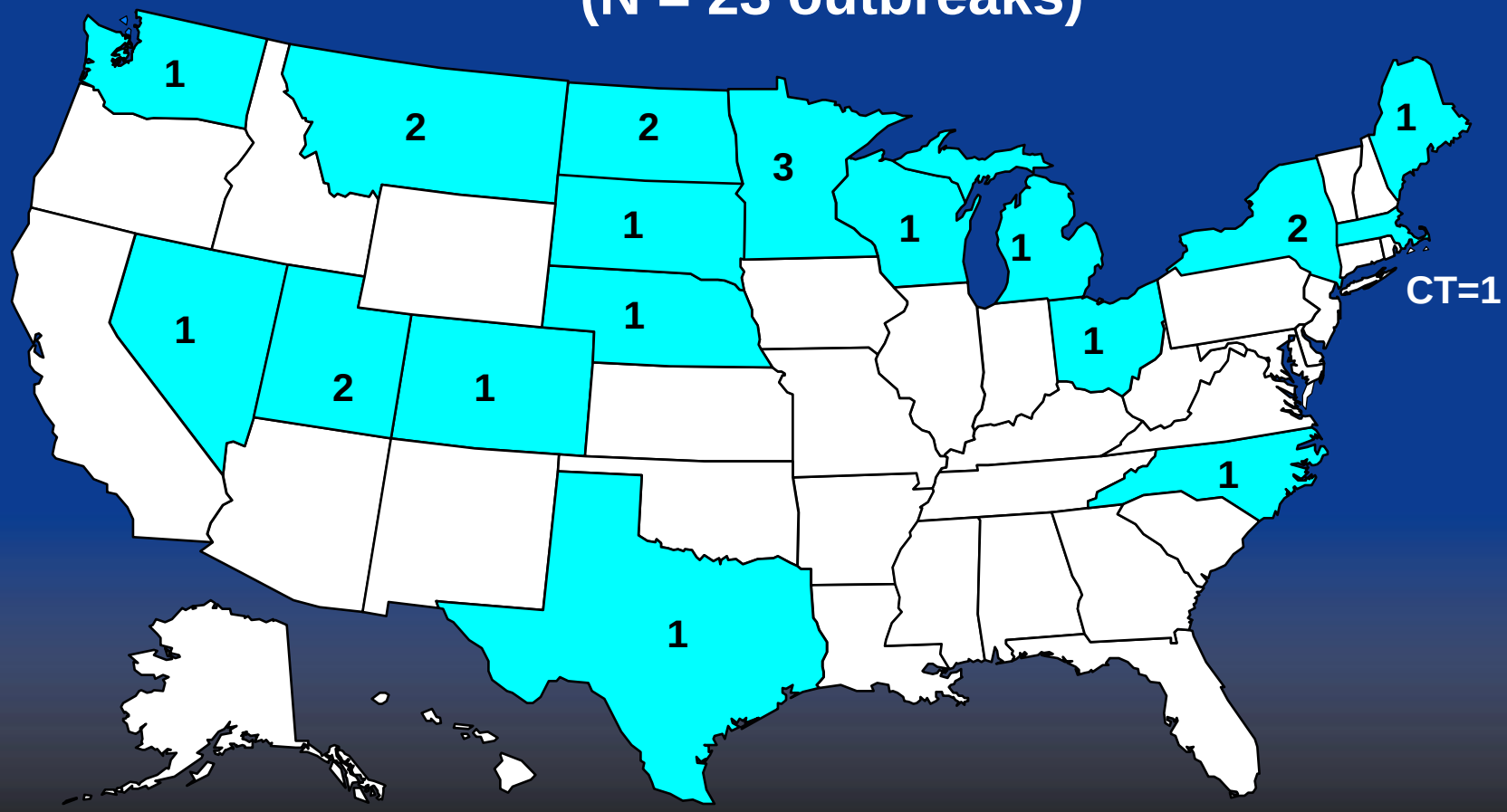
Food vehicles in non-O157 STEC outbreaks, U.S., 1990-2007

N = 11

Food Vehicle	No. outbreaks
Salad bar	1
Salad and ice	1
Berries	1
Milk	1
Cider	1
Punch	1
Unknown	5

Human non-O157 STEC outbreaks reported to CDC, 1990-2007

(N = 23 outbreaks)



Data from 2007 is preliminary

Outbreak of STEC O111 infections, cheerleading camp, Texas, 1999

- 55 persons with diarrhea
  - most were teenage girls
  - 18 had bloody stools
  - 2 develped hemolytic uremic syndrome (HUS)
- Transmitted by salad bar and ice

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National prospective diarrhea-associated (D^+) HUS study, 1987-1991

- Enrolled adults and children with D^+HUS
- Requested
  - stool sample
  - serum to measure antibodies to O157 lipopolysaccharide (LPS)

Banatvala, JID 2001

U.S. National HUS Study, 1987-1991

Patients with both stool culture and serology results (N=55)

- 18% had no evidence of STEC infection
- 82% had evidence of STEC infection
  - 98% of these had evidence of *E. coli* O157 infection
    - 3 of 4 with non-O157 STEC isolated from stool also had antibodies to O157 LPS
      - suggests that *E. coli* O157 may have caused their HUS

Banatvala, JID 2001

The results of the national study suggest that the proportion of HUS cases in the United States caused by non-O157 STEC was small

Other studies of HUS with stool cultures

- Among HUS cases tested within 6 days of onset of diarrhea, proportion with *E. coli* O157:H7 isolated
  - United States (25 cases) 96%
    (Tarr, J Infect Dis 1990)
  - Canada (30 cases) 87%
    (Rowe, Epidemiol Infect 1993)

Other studies of HUS with serology

- Proportion of D^+HUS cases with O157 LPS antibodies
  - England: 73% *(Chart, Lancet 1991)*
  - Central Europe: 73% *(Bitzan, Epidemiol Infect 1993)*
  - France: 67% *(Decludt, Epidemiol Infect 2000)*

Other studies
in the United States and other countries
have also reported that
E. coli *O157 is the major cause of HUS*

CDC work to improve diagnosis of STEC infections

- Began a clinical diagnostics working group
  - includes CDC, clinical labs, others
  - Meetings
    - May 2006
    - January 2007
- Published MMWR with guidelines, September 2006

MMWR
Weekly
September 29, 2006 / 55(38);1042-1045

Importance of Culture Confirmation of Shiga Toxin-producing *Escherichia coli* Infection as Illustrated by Outbreaks of Gastroenteritis --- New York and North Carolina, 2005

Escherichia coli O157:H7 and other strains of *E. coli* that produce Shiga toxin are collectively known as Shiga toxin-producing *E. coli* (STEC). The current outbreak of STEC O157 infections associated with eating fresh spinach illustrates the importance of obtaining isolates to identify the source of the infections (*1*). Laboratory methods that do not require bacterial culture of stool specimens to identify STEC are being used increasingly by clinical diagnostic laboratories, sometimes without subsequent confirmation of a strain by isolating it in culture. This report describes findings from outbreaks of gastroenteritis in 2005 in New York and North Carolina in which clinical diagnostic laboratories initially used only non-culture methods to detect Shiga toxin (Stx). The findings highlight the importance of confirmation of Stx-positive stool specimens by bacterial culture for timely and reliable identification of STEC infections, including *E. coli* O157 and non-O157 STEC, to enable implementation of appropriate public health actions. An important part of that identification is determining the serotype of all STEC isolates and the subtype of STEC O157 strains so that outbreaks can be detected and traced back to sources.

New York

During August 28--September 13, 2005, a total of 52 (2.4%) of 2,160 inmates at a state correctional facility reported diarrhea, including 17 (33%) with bloody diarrhea. Nineteen inmates were treated at the prison infirmary; three were hospitalized for an average of 1.8 days. Stool specimens from these three inmates tested positive for Stx by enzyme immunoassay (EIA) at a clinical diagnostic laboratory. Subsequently, stool specimens collected from 21 ill inmates were submitted to the New York State Department of Health (NYSDOH)-Wadsworth Center. Stool specimens were inoculated to *E. coli* enrichment broth and sorbitol MacConkey

MMWR
Weekly
September 29, 2006 / 55(38);1042-1045

Importance of Culture Confirmation of Shiga Toxin-producing *Es*...teritis

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- **Clinical laboratories should strongly consider including STEC O157 in their routine bacterial enteric panel**
- **The best way to identify all STEC infections is to screen all stool samples…..for Shiga toxins**
- **Laboratories that use a Shiga toxin EIA….should culture all positive broths….**
- **When a Shiga toxin-positive broth does not yield STEC O157, the broth...should be quickly forwarded to the state…laboratory for identification of non-O157 STEC.**
- **All non-O157 STEC…should be sent…to CDC.**

Summary: non-O157 STEC in the United States

- Non-O157 STEC are a diverse group
  - but ~75% of human infections are due to 6 serogroups
- Clinical illness due to non-O157 STEC
  - includes diarrhea, bloody diarrhea, HUS
  - less likely severe than *E. coli* O157

Summary (continued)

- Most non-O157 STEC infections are not diagnosed
  - few clinical labs test stools for Shiga toxin
  - but use of the EIA has increased
    - more non-O157 STEC illnesses and outbreaks detected
- Challenges in testing for STEC by EIA
  - “Shiga toxin positive” is not sufficient
    - Serogrouping is important
  - Rapid identification of *E. coli* O157 is important for outbreak detection

Summary (continued)

- STEC Diarrhea
  - O157 and non-O157 STEC isolated with similar frequency
- STEC-associated HUS
  - estimate <10% caused by non-O157 STEC
    - strains that produce only Shiga toxin 1 much less likely to cause HUS than strains that produce Shiga toxin 2
      - 61% of human non-O157 STEC strains produced only Shiga toxin 1

Contributors

- State and local health departments
- Enteric Diseases Epidemiology Laboratory
- Many other collaborators

Enteric Diseases Epidemiology Branch

Thank you

Conclusions and opinions expressed herein are those of the presenter and do not necessarily represent the views and policies of CDC and DHHS.