



Monitoring Emerging Resistance in *Neisseria gonorrhoeae* in the United States: A Call For Public Health Action

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Atlanta, GA (USA)

September 8, 2008

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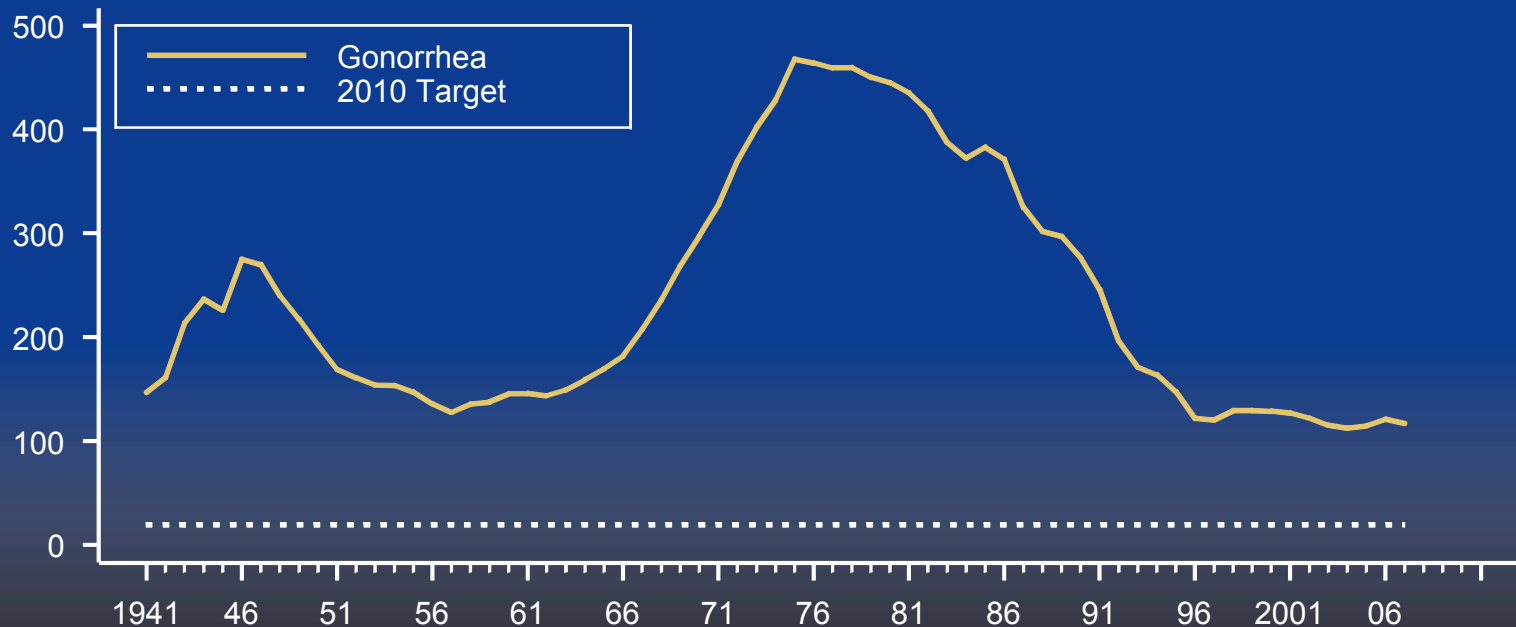
Overview

- Background
 - ◆ Antimicrobial resistance in *N. gonorrhoeae* in US
 - ◆ Gonococcal Isolate Surveillance Project (GISP)
- GISP antimicrobial susceptibility trends
- A Recent Call for Public Health Action
- Strengths
- Limitations
- Conclusions
- A Call for Global Public Health Action

Neisseria gonorrhoeae in the US

- In 2006, second most frequently reported notifiable disease in US
 - ◆ >350,000 cases reported in US
 - ◆ 120.9 cases/100,000 persons

Rate (per 100,000 population)



Why Monitor?

- High burden of disease
- Key to reducing burden is by effective prevention and control programs using prompt detection and effective treatment
- Public health importance & use of both epidemiological and laboratory data can translate into public health action

However, effective treatment is complicated by *N. gonorrhoeae*'s ability to develop resistance to effective antimicrobials

Brief History of AR GC in the US

Timeline

1930s

Sulfanilamides introduced to treat GC

1940s

Resistance to sulfanilamides develop;
Recommended drug: **Penicillin**

1970/1980s

Resistance to penicillin/tetracycline develop;
Recommended drug: **Ceftriaxone (cephalosporin)**
GISP started in 1986

1990s

Recommended drugs: **Ceftriaxone & Ciprofloxacin (fluoroquinolone);**
Resistance to fluoroquinolones (QRNG) identified first in Hawaii, then in West Coast, and then among MSM

2000s

Resistance to QRNG continues to increase and becomes widespread; FQs no longer recommended
Recommended drug: **Cephalosporins (Last class of drugs!)**

Gonococcal Isolate Surveillance Project (GISP)

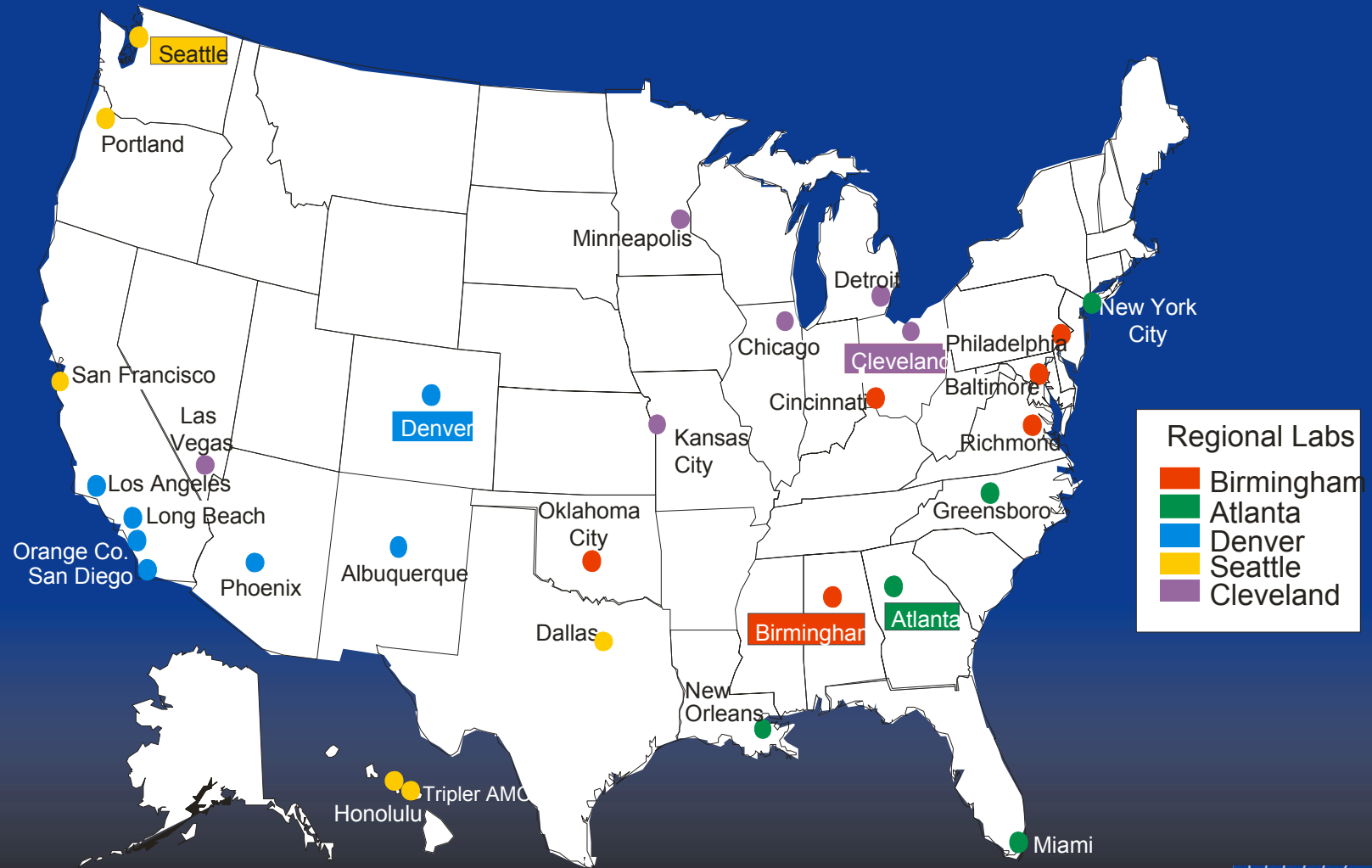
- Established in 1986
- Serves as national sentinel surveillance system:
 - ◆ To monitor trends in antimicrobial susceptibilities of *Neisseria gonorrhoeae*
 - ◆ To establish rational basis for the selection of antimicrobial treatment for gonococcal infections
- Collaborative effort: CDC, 25-30 publicly-funded STD clinics (GISP sentinel sites) and their respective local/state public health authorities, and 4-5 regional laboratories

GISP Sentinel Sites/Regional Labs

- Sentinel Sites
 - ◆ Submit first 25 male urethral gonococcal isolates to regional laboratory
 - ◆ Submit patient clinical/demographic data for all submitted isolates

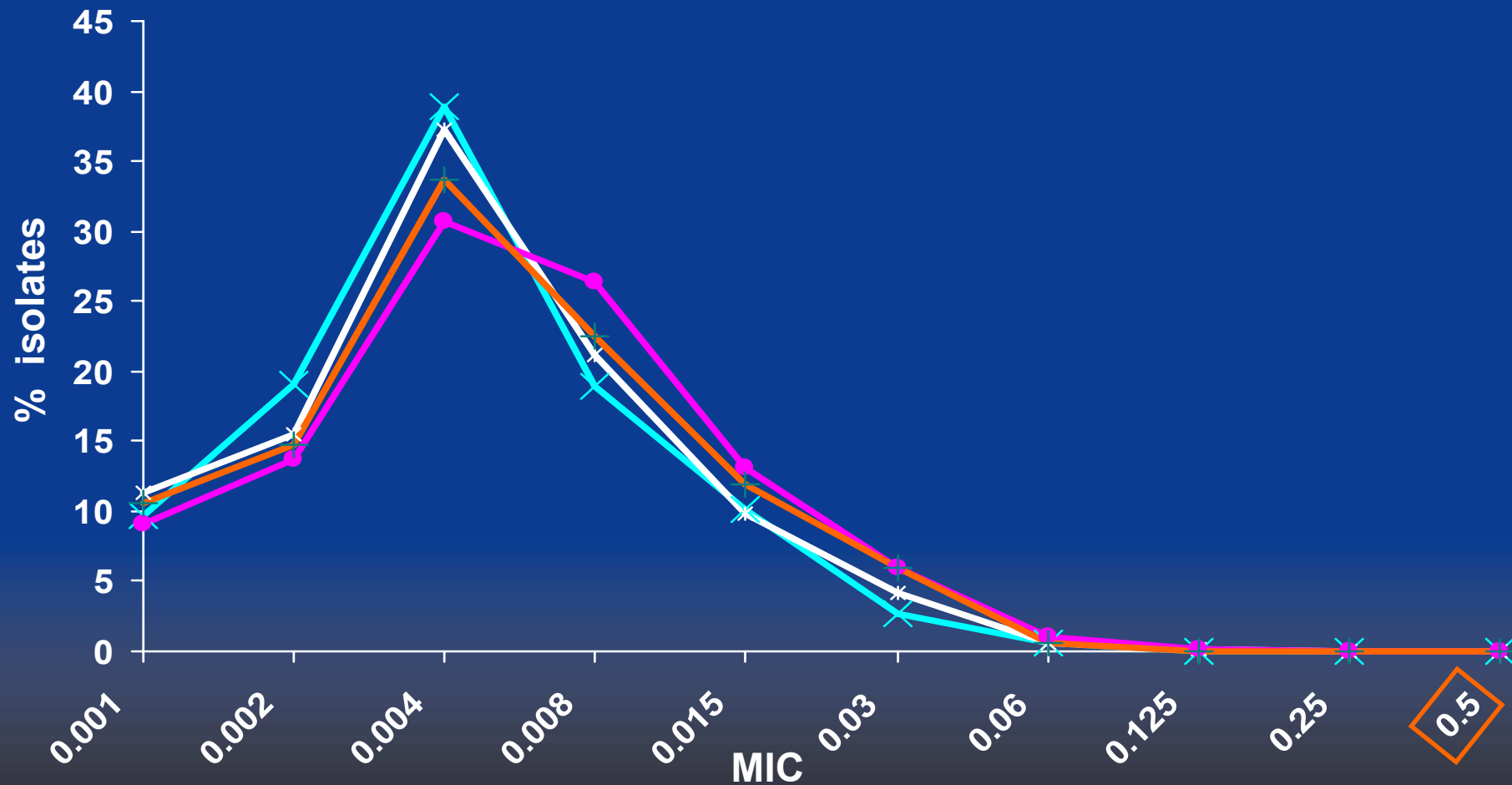
- Regional Labs
 - ◆ Perform antimicrobial susceptibility testing (AST) using agar dilution method
 - ◆ Antibiotics tested are:
 - ★ Penicillin, Tetracycline, Spectinomycin, Ceftriaxone, Ciprofloxacin, Azithromycin, & Cefixime (discontinued in 2007)

Locations of sites and regional laboratories: United States, 2007 (30 Sites)



GISP Antimicrobial Susceptibility Testing Trends

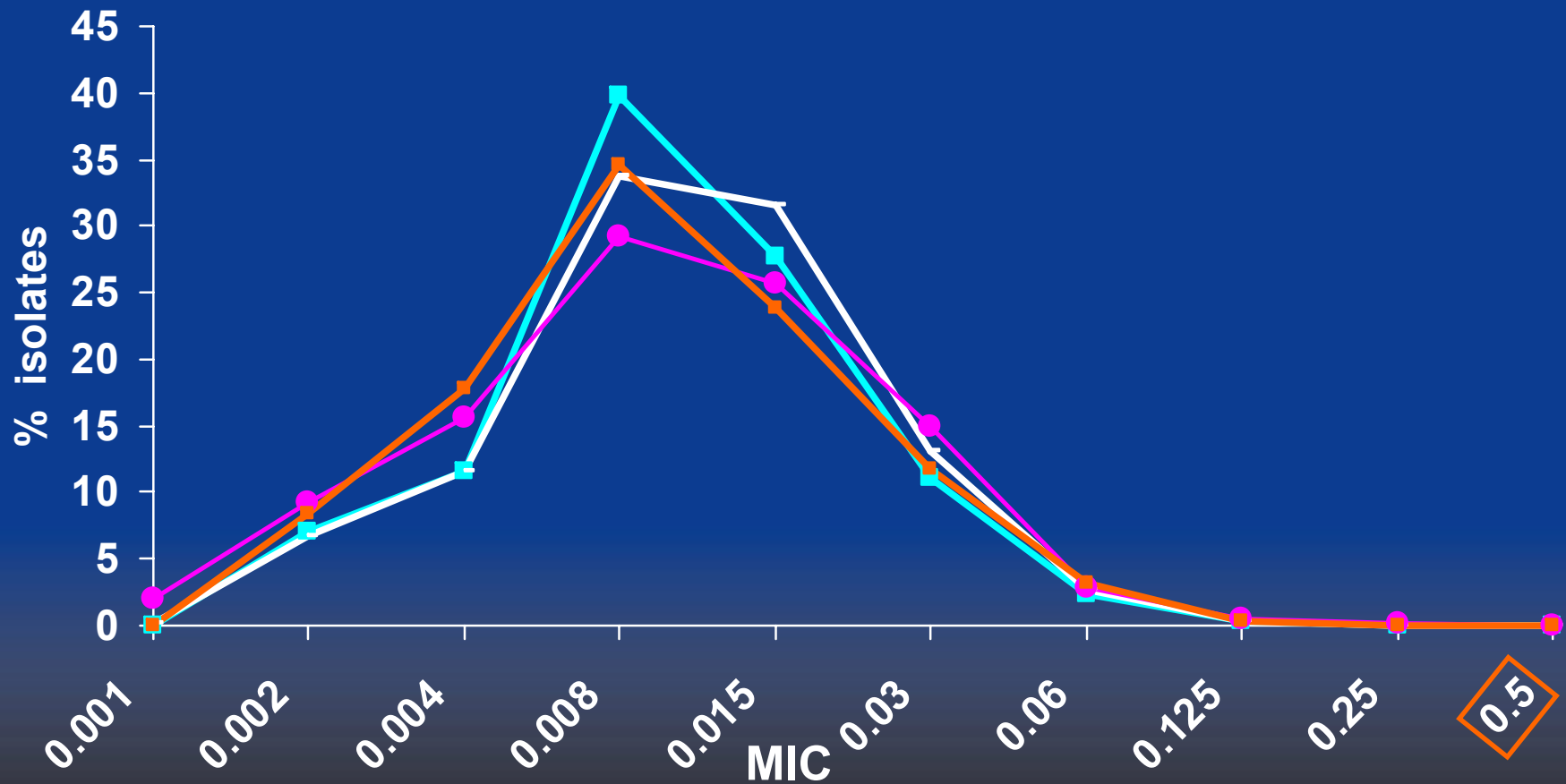
Distribution of MICs to Ceftriaxone, 2003-2006



—x— 2003 —*— 2004 —●— 2005 —+— 2006

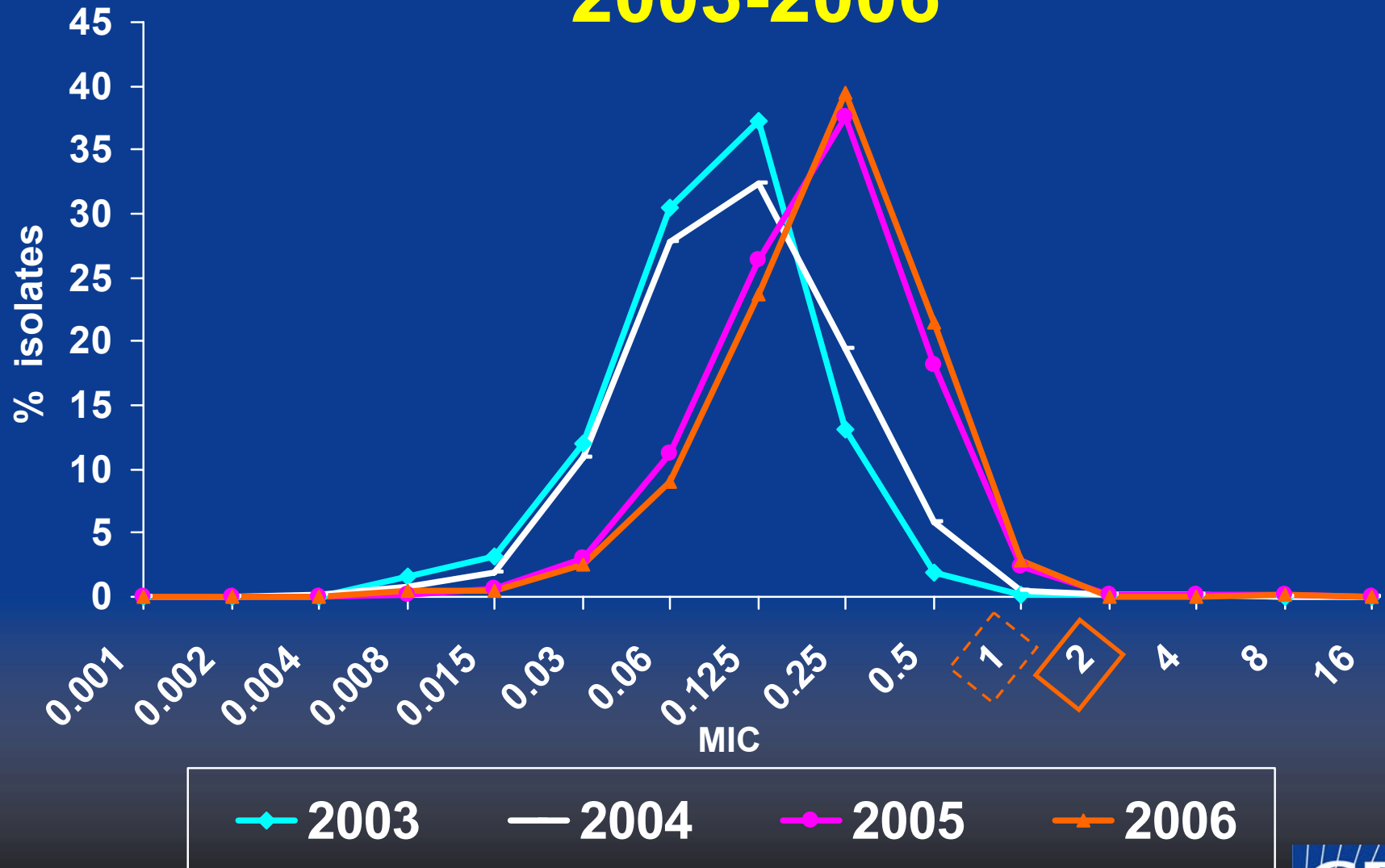


Distribution of MICs to Cefixime, 2003-2006



—■— 2003 — 2004 —●— 2005 —■— 2006

Distribution of MICs to Azithromycin, 2003-2006

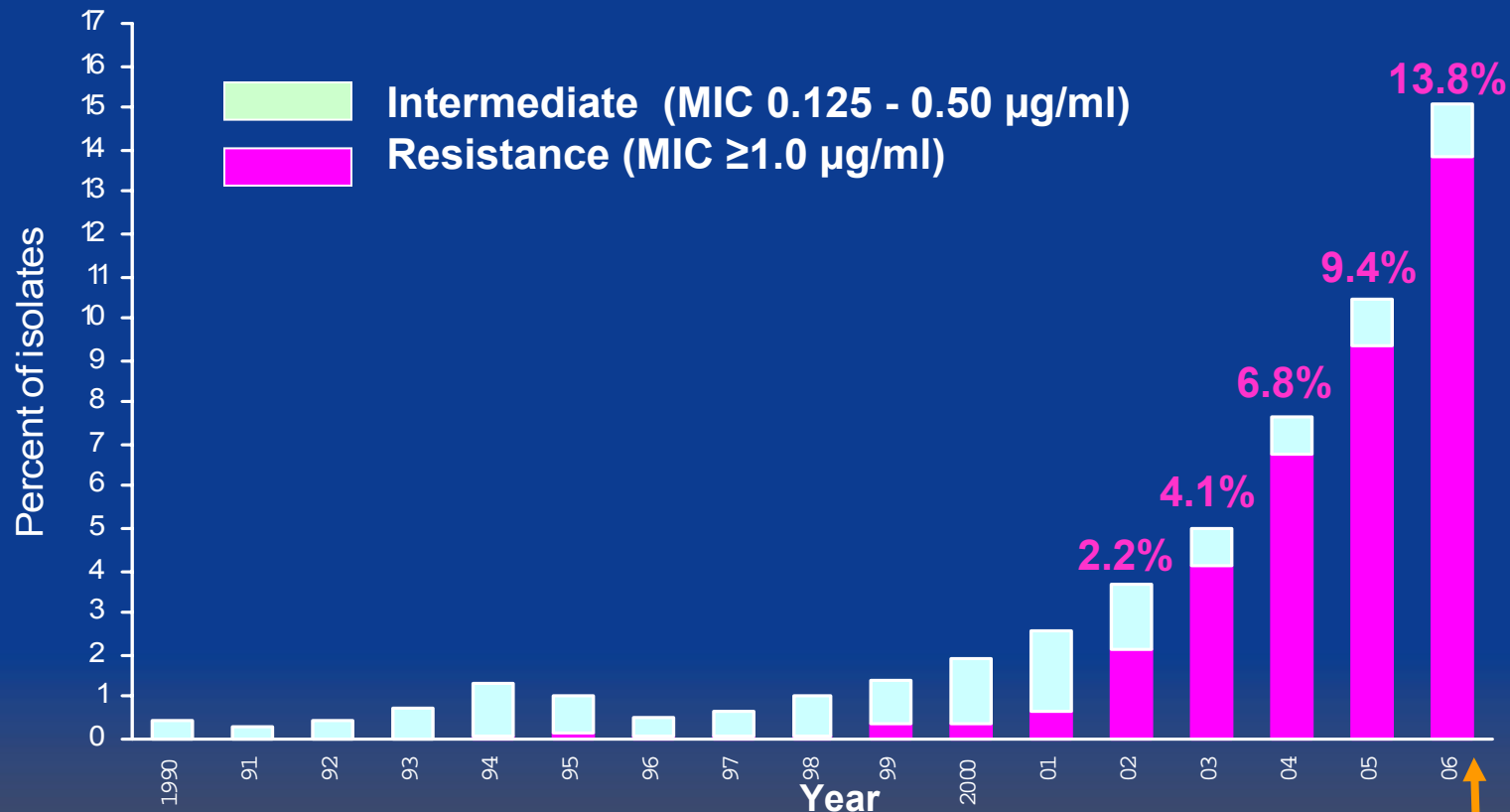


Antimicrobial Susceptibility Trend for Other Antibiotics 2006

- Penicillin/Tetracycline or both: >20%
- Spectinomycin: All susceptible
- Cefixime: 1 isolate (2006)
- Ceftriaxone: None
- Azithromycin:
 - ◆ (2006) 14 isolates (0.2%) with MIC \geq 2.0 μ g/ml

A Recent Call for Public Health Action

Percentage of isolates from GISP with intermediate resistance or resistance to ciprofloxacin, 1990-2006



April 13, 2007: Revised Guidelines—Fluoroquinolones No Longer Recommended for Treatment of Gonococcal Infections (MMWR (56), 14, pgs 332-336.)

GISP Strengths

- ◆ Usefulness: Over 20 years of trend data to guide national treatment recommendations
- ◆ Representativeness: Sentinel surveillance with sites in all regions of the country & over-sampling of Hawaii/West Coast to detect importation
- ◆ Acceptability: High retention of sites
- ◆ Timeliness/Simplicity: Data from sites/regional labs collected electronically on a monthly basis
- ◆ High data quality: AST uses agar-dilution method (“gold standard”), standardization of data collection tools, and laboratory proficiency testing done 2x/year

GISP Limitations

- ◆ No data on women & persons seen outside of STD clinics
- ◆ Limited data from military population
- ◆ GISP designed to monitor AR trends but may not readily detect a new case of emerging AR or a clinical treatment failure case

Additional CDC Activities to Prepare for Emergence of Cephalosporin Resistant GC

- Investigating other alternative antibiotic regimens through a clinical trial to assess clinical efficacy of using a combination drug therapy
- Maintaining and strengthening U.S. surveillance system in sentinel areas
- Developing national cephalosporin-resistant gonorrhea outbreak plan
- Implementing laboratory research to identify and understand mechanisms of cephalosporin resistance
- Providing funds to WHO WPRO/SEARO to increase surveillance and to enhance laboratory capacity for gonorrhea culture and antimicrobial susceptibility testing in the SE Asia, and Western Pacific regions

Conclusions

- GISP has been successful in monitoring antimicrobial resistant trends in *N. gonorrhoeae* in the United States
- Data from GISP has been critical in guiding treatment guidelines for gonococcal infections in the US
- Integration of both epidemiological and laboratory data are necessary for effective public health actions
- Close and continuous monitoring for antimicrobial resistance in *N. gonorrhoeae* remain essential
- However, further preparations are needed to detect emergence of cephalosporin-resistant GC

A call for global public health action

- Proposal of what is needed:
 - ◆ Increase global awareness
 - ◆ Enhance global collaboration among laboratorians & epidemiologists to strengthen surveillance in key areas such as the Western Pacific and South-East Asia regions
 - ★ Timely & more formal communication and exchange of information and isolates
 - ★ Consensus on resistance testing methodologies and interpretation
 - ◆ Increase global response (using both epidemiological and laboratory data)
 - ★ Prompt detection (Ex: screening those with risk factors associated with antimicrobial resistance, persons at high risk for GC infections, & screening sexual partners, increased education among medical communities)
 - ★ Effective treatment regimens: Need for development of novel drugs
 - ★ Ongoing research on mechanisms of resistance



Acknowledgements



- ◆ **CDC Atlanta Staff:**
Hillard Weinstock, Stuart Berman, John Papp, David Trees, Ron Ballard, Joan Knapp, Alesia Harvey, Katrina Kramer, Shalini Parekh, Kevin Pettus, Samera Bowers, Manhar Parekh, Michael Grabenstein, & Lori Newman
- ◆ **GISP Principal Investigators & Regional Laboratories:**
 - ★ **Atlanta:** Carlos del Rio, James Thomas, Bianca Humphrey, Tanisha Sullivan
 - ★ **Birmingham:** Ned Hook, Connie Lenderman, Paula Dixon
 - ★ **Cleveland:** Gerrie Hall, Laura Doyle, Gary Procop
 - ★ **Denver:** Frank Judson, Jo Ehret
 - ★ **Seattle:** King Holmes, Wil Whittington, Karen Winterscheid
- **30 GISP Sentinel Sites and their respective local/state public health authorities in 2006 & 2007 (lab, clinic, program staff)**

Required Disclaimer: The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the CDC/ATSDR.

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Additional Information

For more information on GISP:

<http://www.cdc.gov/std/gisp/>

Resource website for information on antimicrobial resistant *Neisseria gonorrhoeae*:

<http://www.cdc.gov/std/Gonorrhea/arg/default.htm>

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