Multi-drug resistant *Neisseria gonorrhoeae* with decreased susceptibility to cefixime, Hawaii, 2001

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Neisseria gonorrhoeae

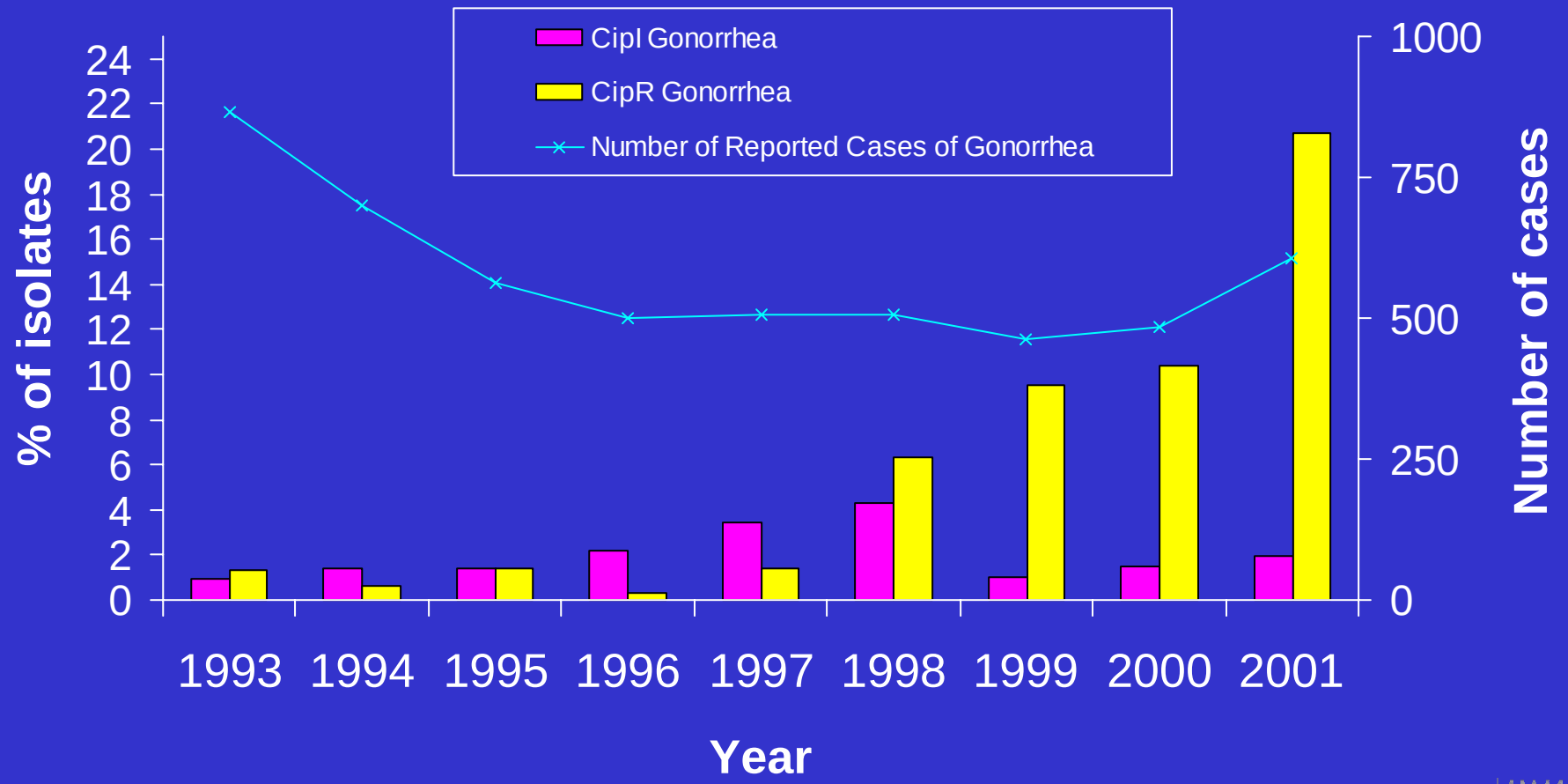
- Gram-negative diplococci
- 62.4 million infections worldwide in 1999
- 718,000 infections in the U.S. in 2000
- Acute clinical infection
  - urethritis, pharyngitis, cervicitis, neonatal ophthalmia
  - increases HIV transmission by 3- to 5- fold
  - asymptomatic in 80% of women and at least 10% of men
- Complications include: pelvic inflammatory disease, ectopic pregnancy, infertility, chronic pelvic pain

History of antimicrobial resistance in *N. gonorrhoeae* in the United States

- 1936: sulfanilamide introduced
- 1945: 1/3 of gonorrhea sulfanilamide-resistant; penicillin (50,000 units) becomes therapy of choice
- 1972: recommended therapeutic penicillin dose reaches 4.8 million units
- 1985: widespread tetracycline-resistance, so tetracycline abandoned
- 1987: penicillin abandoned
- 1993: fluoroquinolones recommended
- 2000: CDC recommends that fluoroquinolones no longer be used to treat gonorrhea acquired in Hawaii, Pacific Islands, or Asia

CDC
Centers for Disease Control and Prevention

Percentage of all gonococcal isolates that were intermediate-resistant or resistant to ciprofloxacin and number of reported cases of gonorrhea, by year, Hawaii, 1993-2001



Gonorrhea Treatment
(from CDC STD Treatment Guidelines, 2002 – *in press*)

Cefixime 400 mg

or

Ceftriaxone 125 mg IM

or

Ciprofloxacin 500 mg or

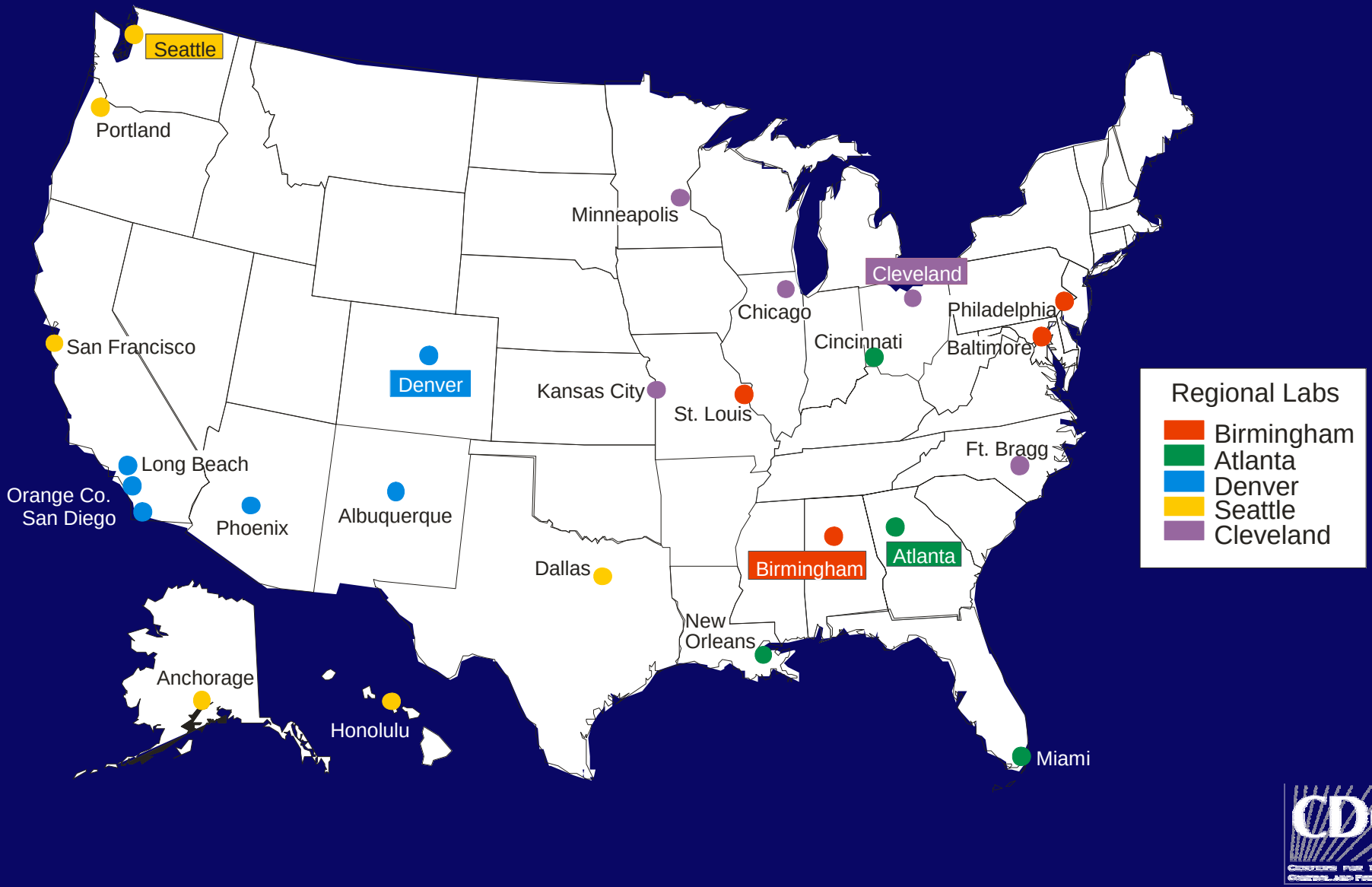
Ofloxacin 400 mg or Levofloxacin 250 mg

[plus, treatment for *Chlamydia trachomatis* infection]

*** Need to obtain travel history from patients suspected to have gonorrhea. A patient who may have acquired gonorrhea in Asia or Hawaii or the Pacific Islands or whose sex partner(s) may have acquired gonorrhea in those places should NOT be treated with fluoroquinolones!

Gonococcal Isolate Surveillance Project (GISP)

Locations of clinics and regional laboratories: United States, 2001



Emergence of multi-drug resistant gonorrhea with decreased susceptibility to cefixime in the United States, 2001

Three patients in Hawaii were diagnosed with four episodes of multi-drug resistant gonorrhea with decreased susceptibility to cefixime:

- resistant to penicillin, tetracycline, and ciprofloxacin
- decreased susceptibility to cefixime
- high azithromycin MICs of 0.125-0.5 mg/L
- susceptible to ceftriaxone and spectinomycin

Patient A, February 2001

35 year old white male residing in Hawaii

- presented to the STD clinic with a 3-day hx of urethritis; Gram stain showed GNID
- treated with cefixime 400 mg and azithromycin 1 gm
- urethral culture grew *N. gonorrhoeae* which was
  - susceptible to spectinomycin and ceftriaxone
  - β-lactamase negative
  - penicillin MIC 8.0 mg/L
  - tetracycline MIC 4.0-8.0 mg/L
  - ciprofloxacin MIC 8.0-16.0 mg/L
  - cefixime MIC 0.5-1.0 mg/L
  - azithromycin 0.25-0.5 mg/L

Patient A, April 2001

Patient A returned to the STD clinic

- reported persistent urethritis symptoms since his Feb visit; Gram stain showed GNID
- treated with spectinomycin 2 gm IM and doxycycline 100 mg BID x 7 days
- urethral culture grew *N. gonorrhoeae* which had the same antibiogram as his Feb culture
- on f/u 3 wks later, Patient A reported complete resolution of symptoms; test-of-cure culture showed no growth
- Patient A reported having 2 female sex partners, both of whom visited Hawaii from Japan

Patient B, May 2001

Patient A's sex partner, Patient B, was a 27 year old Japanese female visitor to Hawaii

- reported having persistent yellow vaginal discharge since Feb 2001, having only Patient A as a sex partner
- treated with ceftriaxone 125 mg IM and azithromycin 1 gm
- endocervical culture grew *N. gonorrhoeae*
- antibiogram matched Patient A's antibiogram except that the cefixime MIC was 0.25 mg/L; susceptible by NCCLS criteria but within one dilution of Patient A's cefixime MIC

Patient C, March 2001

Patient C was a 30 year old Micronesian male residing in Hawaii

- presented to the STD clinic with a 4-day hx of urethritis; Gram stain showed GNID
- treated with cefixime 400 mg and azithromycin 1 gm
- urethral culture grew *N. gonorrhoeae*
- antibiogram similar to those of Patients A and B; cefixime MIC 0.25-1.0 mg/L
- on f/u 3 months later, Patient C reported complete resolution of symptoms; test-of-cure culture was negative
- Patient C reported having only 1 female sex partner

Implications

- Unclear whether Patient A experienced a cefixime treatment failure or not
- These isolates represent the first time that *N. gonorrhoeae* having resistance to penicillin, tetracycline, and ciprofloxacin and decreased susceptibility to cefixime have been identified in the United States
- *N. gonorrhoeae* having resistance to penicillin, tetracycline, and ciprofloxacin and elevated MICs to cefozopran have been identified since 1999 in Kitakyushu, Japan
- Existence and spread of such strains threaten to further limit gonorrhea treatment options and efforts to control gonorrhea transmission

Monitoring Antimicrobial Resistance in *N. gonorrhoeae*

- To supplement GISP data, CDC requests reports of gonorrhea resistant to any of the recommended gonorrhea treatment regimens and reports of suspected treatment failures
- Because prevalence of resistance varies greatly by location, local susceptibility data are necessary to guide local gonorrhea treatment recommendations
- At the local level, maintaining gonococcal culture capacity is crucial!

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Antimicrobial susceptibility results by agar dilution method for *N. gonorrhoeae* specimens from Patients A, B, and C

Isolate source & date	β-lactamase	Pen	Tet	Spc	Cfx	Cro	Cipro	Azi
Pt A Feb 2001	Neg	8.0	4.0-8.0	S	0.5-1.0	0.06-0.25	8.0-16.0	0.25-0.5
Pt A Apr 2001	Neg	8.0	4.0	S	0.5-1.0	0.06-0.125	8.0-16.0	0.125-0.5
Pt B May 2001	Neg	4.0-8.0	2.0-4.0	S	0.25	0.03-0.125	16.0	0.125-0.25
Pt C Mar 2001	Neg	8.0	4.0-8.0	S	0.25-1.0	0.06-0.125	8.0-16.0	0.125-0.5