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Annual Report - 2003**

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This report is available from the Internet via the CDC home page address at <http://www.cdc.gov/std/GISP2003/>.

The 2003 STD Surveillance Report may be found at <http://www.cdc.gov/std/stats/>.

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GONOCOCCAL ISOLATE SURVEILLANCE PROJECT (GISP) ANNUAL REPORT – 2003

Introduction

With 335,104 gonorrhea cases reported in 2003, gonorrhea is the second most frequently reported communicable disease in the United States. Gonorrhea rates in the United States declined 73.8% during 1975-1997. After a small increase in the rate in 1998, the gonorrhea rate has decreased 10.1% since 1999 to the current rate of 116.2 per 100,000 persons (**Figure 1**).¹ Gonorrhea rates remain high in the southeastern states, among minorities, and among adolescents of all racial and ethnic groups (**Figures 2, 3 and 4**).¹⁻³ The health impact of gonorrhea is largely related to its role as a major cause of pelvic inflammatory disease, which frequently leads to infertility or ectopic pregnancy.⁴ In addition, data suggest that gonorrhea facilitates HIV transmission.^{5,6}

The treatment and control of gonorrhea has been complicated by the ability of *Neisseria gonorrhoeae* to develop resistance to antimicrobial agents. The appearance of penicillinase-producing *N. gonorrhoeae* (PPNG) and chromosomally mediated penicillin- and tetracycline-resistant *N. gonorrhoeae* (CMRNG) in the 1970s eventually led to the abandonment of these drugs as therapies for gonorrhea. The current CDC-recommended primary therapies for gonorrhea are two broad-spectrum cephalosporins (ceftriaxone and cefixime), and three fluoroquinolones (ciprofloxacin, ofloxacin, and levofloxacin).⁷ However, since the 1990s, fluoroquinolone-resistant *N. gonorrhoeae* (QRNG) have been reported from many parts of the world, including the United States.^{8-10,12} The increased prevalence of QRNG in Asia (where prevalence in several countries exceeds 40%)¹³, the Pacific Islands, Hawaii, and California, prompted CDC to recommend that fluoroquinolones not be used to treat patients with gonorrhea acquired in these areas with high QRNG prevalence.^{7,11,12} Preliminary data collected during January-September 2003 from all GISP sites indicating an increase in QRNG among men who have sex with men (MSM) led CDC to recommend in early 2004 that fluoroquinolones not be used to treat patients who are MSM.¹⁴

GISP Overview

The Gonococcal Isolate Surveillance Project (GISP) was established in 1986 to monitor trends in antimicrobial susceptibilities of strains of *N. gonorrhoeae* in the United States to establish a rational basis for the selection of gonococcal therapies.¹⁵ GISP is a collaborative project among selected sexually transmitted diseases (STD) clinics, five regional laboratories, and the Centers for Disease Control and Prevention (CDC).

In GISP during 2003, *N. gonorrhoeae* isolates were collected from the first 25 men with urethral gonorrhea attending STD clinics each month in 30 cities in the United States. Using agar dilution, regional laboratories determined the susceptibilities of these isolates to penicillin, tetracycline, spectinomycin, ciprofloxacin, ceftriaxone, cefixime, and azithromycin. Minimum inhibitory concentrations (MICs) were measured, and values are interpreted according to criteria

recommended by the National Committee for Clinical Laboratory Standards (NCCLS).¹⁶⁻¹⁸ Clinical and demographic data were abstracted from medical records.

Important GISP findings have included:

- the ongoing high prevalence of resistance to penicillin and tetracycline;
- the emergence and increasing prevalence of resistance to the fluoroquinolones;^{8-10,12,14}
- the appearance, with low level prevalence, of decreased susceptibility to the macrolides;¹¹
- the absence of resistance to the broad-spectrum cephalosporins;
- the emergence of multi-drug resistant isolates (resistant to penicillin, tetracycline, and ciprofloxacin) with decreased susceptibility to cefixime;⁹ and
- the increasing proportion of gonorrhea cases identified in men who have sex with men.^{20,21}

GISP findings contributed to the development of CDC's STD treatment recommendations in 1993, 1998, and 2002.^{7,22,23} Additionally, GISP findings led to a change in treatment recommendations in 2004, when it was recommended that MSM no longer receive fluoroquinolone treatment for their gonococcal infections.¹⁴

2003 GISP Sites

A total of 30 STD clinics contributed 6,552 gonococcal isolates to GISP in 2003 (**Figure 5**). Sixteen sites have participated continuously since 1988: Albuquerque, Anchorage, Atlanta, Baltimore, Birmingham, Cincinnati, Denver, Honolulu, Long Beach, New Orleans, Philadelphia, Phoenix, Portland, San Diego, San Francisco, and Seattle. Nine sites joined GISP after 1988: Cleveland and Orange County in 1991; Minneapolis in 1992; Chicago in 1996; Miami in 1998; Dallas in 2000, Tripler in 2001, and Greensboro and Las Vegas in 2002. One 2003 site has had intermittent participation in GISP: St. Louis 1987-1993 and 1995-2002. New sites joining GISP in 2003 included Detroit, Los Angeles, Oklahoma City and Salt Lake City. The GISP Regional Laboratories are located in Atlanta, Birmingham, Cleveland, Denver, and Seattle.

Description of GISP Data

Aggregate data from all GISP sites are described and illustrated in the first part of this report. The clinic-specific data illustrate substantial geographic variation in patient characteristics and antimicrobial susceptibility of gonococcal strains; clinic-specific figures are provided in the second part of this report.

Demographic and Clinical Characteristics

Age: The age distribution of GISP participants compared with nationally reported male gonorrhea patients in 2003 is shown in **Figure 6**. In 2003, GISP had proportionally fewer 20-24 year olds and fewer <20 year olds than were reported nationally for male gonorrhea cases; otherwise the two groups had similar age distributions. GISP participants in 2003 ranged in age from 13 to 79 years.

Race/Ethnicity: The race/ethnicity distribution of GISP participants compared with nationally reported male gonorrhea patients in 2003 is shown in **Figure 7**. White, Hispanic, and Asian males were slightly over represented in GISP while Black males were slightly under represented compared with the race/ethnicity distribution of nationally reported male gonorrhea patients in 2003.

Sexual Orientation: The proportion of GISP participants who were MSM increased every year since 1993 until 2003, when there was a slight (1%) decrease from 20.6% in 2002 to 19.6% in 2003. (**Figure 8**). The majority of MSM cases occurred on the west coast, with cases from MSM decreasing from west to east (**Figure 9**).

Reason for Clinic Attendance: Most (96.3%) GISP participants in 2003 presented to the clinic on their own initiative (volunteers); others were referred as contacts of sexual partners diagnosed with gonorrhea or presented for test-of-cure cultures (**Figure 10**). There has been little change in this distribution over time. Dysuria and/or urethral discharge were present in 96.7% of GISP participants in 2003 and 3.3% had no symptoms; these proportions have been stable over time.

History of Gonorrhea: The percentage of GISP participants who reported a history of gonorrhea (ever) was 48.4% in 2003. The percentage of GISP participants with a documented previous episode of gonorrhea in the last 12 months peaked at 23.6% in 2000 and was 16.9% in 2003 (**Figure 11**).

Antimicrobial Treatment: The antimicrobial agents given to GISP participants for gonorrhea therapy are shown in **Figure 12**. The proportion of GISP patients treated with cephalosporins decreased from a peak of 84.7% in 1990 to 54.5% in 2003, while the proportion treated with fluoroquinolones (ciprofloxacin, ofloxacin or levofloxacin) increased from none in 1988 to a high of 42.0% in 2003. The antimicrobial agents given to GISP participants for treatment of *Chlamydia trachomatis* infection are shown in **Figure 13**. The proportion of GISP patients treated with doxycycline or tetracycline decreased from a high of 99.4% in 1990 to 48.8% in 2003, while the proportion treated with azithromycin increased from 0.2% in 1992 (the first year of GISP that azithromycin was identified as being used for *C. trachomatis* therapy) to 49.1% in 2003.

Supplemental Patient Data: In 2002 six new GISP data elements were implemented to collect additional patient information; 2003 was the first year this data was collected for the entire year. The proportion of GISP participants who were HIV-positive was 7.7% (294/3842). Twenty-six percent (230/886) of MSM were HIV positive, and 1.5% (38/2572) of heterosexuals were HIV positive. During the 60 days prior to diagnosis of gonorrhea, GISP patients reported the following behaviors:

- 5.5% (246/4494) took antibiotics;
- 5.0% (126/2500) traveled or had a sex partner who traveled outside the U.S. or to Hawaii;
- 2.2% (79/3516) used injection recreational drugs;
- 33.7% (1023/3039) used non-injection recreational drugs;
- 3.7% (122/3262) exchanged money or drugs for sex or vice versa.

Susceptibility to Antimicrobial Agents

Antimicrobial Resistance Criteria

Antimicrobial resistance in *N. gonorrhoeae* is defined by the criteria recommended by the National Committee on Clinical Laboratory Standards (NCCLS):¹⁶⁻¹⁸

Penicillin, MIC ≥ 2.0 $\mu\text{g/ml}$

Tetracycline, MIC ≥ 2.0 $\mu\text{g/ml}$

Spectinomycin, MIC ≥ 128.0 $\mu\text{g/ml}$

Ciprofloxacin, MIC 0.125 - 0.5 $\mu\text{g/ml}$ (intermediate resistance)

Ciprofloxacin, MIC ≥ 1.0 $\mu\text{g/ml}$ (resistance)

Ceftriaxone, MIC ≥ 0.5 $\mu\text{g/ml}$ (decreased susceptibility)

Cefixime, MIC ≥ 0.5 $\mu\text{g/ml}$ (decreased susceptibility)

NCCLS criteria for resistance to ceftriaxone, cefixime, erythromycin, and azithromycin and for susceptibility to erythromycin and azithromycin have not been established for *N. gonorrhoeae*.

Susceptibility to Penicillin and Tetracycline

Overall, 16.4% (1075/6552) of isolates collected in 2003 were resistant to penicillin, tetracycline, or both (**Figure 14**); this proportion peaked at 34% in 1992 and has been decreasing annually since 1998. For GISP analyses, six mutually exclusive categories of resistance are used for describing chromosomally and plasmid-mediated resistance to penicillin and tetracycline:⁸

- (1) penicillinase-producing *N. gonorrhoeae* (PPNG): β -lactamase-positive and tetracycline MIC < 16.0 $\mu\text{g/ml}$;
- (2) plasmid-mediated tetracycline resistant *N. gonorrhoeae* (TRNG): β -lactamase-negative and tetracycline MIC ≥ 16.0 $\mu\text{g/ml}$;
- (3) PPNG-TRNG: β -lactamase-positive and tetracycline MIC ≥ 16.0 $\mu\text{g/ml}$;
- (4) chromosomally mediated penicillin-resistant *N. gonorrhoeae* (PenR): non-PPNG and penicillin MIC ≥ 2.0 $\mu\text{g/ml}$ and tetracycline MIC < 2.0 $\mu\text{g/ml}$;
- (5) chromosomally mediated tetracycline-resistant *N. gonorrhoeae* (TetR): non-PPNG and penicillin MIC < 2.0 $\mu\text{g/ml}$ and tetracycline MIC 2.0-8.0 $\mu\text{g/ml}$; and
- (6) chromosomally mediated resistance to both penicillin and tetracycline (CMRNG): non-PPNG and penicillin MIC ≥ 2.0 $\mu\text{g/ml}$ and tetracycline MIC 2.0-8.0 $\mu\text{g/ml}$.

The percentage of PPNG declined annually from a peak of 11.0% in 1991 to 1.0% in 2003 (**Figure 15**). In contrast, the percentage of PenR isolates increased annually from 0.5% in 1988 to 5.7% in 1999 and subsequently decreased annually to 1.3% in 2003 (**Figure 16**). The prevalence of TRNG, which was 3.7% in 2003, has varied little since 1988 (**Figure 15**). TetR prevalence decreased every year since 1995, until 2002, when it slightly increased. In 2003 there was another slight increase to 6.2% (**Figure 16**). The prevalence of CMRNG increased from 3.0% in 1989 to a peak of 8.7% in 1997, and then declined to 3.8% in 2003. The prevalence of PPNG-TRNG continues to be very low and was 0.4% in 2003.

Susceptibility to Spectinomycin

All isolates were susceptible to spectinomycin in 2003. There have been five spectinomycin-resistant isolates in GISP; their locations and years were: St. Louis-1988, Honolulu-1989, San Francisco-1989, Long Beach-1990, and West Palm Beach-1994.

Susceptibility to Ceftriaxone

The distributions of MICs to ceftriaxone in 1988 and 2003 are shown in **Figure 17**. Over this time period, there has been a subtle shift towards higher ceftriaxone MICs. In 2003, all isolates were susceptible to ceftriaxone. There have been four isolates with decreased susceptibility to ceftriaxone in GISP; all four had MICs of 0.5 $\mu\text{g/ml}$. Their locations and years were: San Diego-1987, Cincinnati-1992 and 1993, and Philadelphia-1997.

Susceptibility to Cefixime

The distributions of MICs to cefixime in 1992 (the first year of cefixime susceptibility testing) and 2003 are shown in **Figure 18**. In 2003, all isolates were susceptible to cefixime. There have been 45 isolates with decreased susceptibility to cefixime in GISP; their MICs have ranged from 0.5-2.0 $\mu\text{g/ml}$.

Susceptibility to Ciprofloxacin

The correlation of ciprofloxacin MICs of 0.125-0.5 $\mu\text{g/ml}$ with treatment failure when a fluoroquinolone is used to treat a gonococcal infection is not well established. However, one study of infections with resistant strains treated with ciprofloxacin 500 mg orally showed a treatment failure rate of 45% for strains with MICs of $\geq 4.0 \mu\text{g/ml}$.²⁴ Gonococcal isolates with intermediate resistance and resistance to ciprofloxacin also have intermediate resistance and resistance to other fluoroquinolones. Criteria recommended for interpreting ofloxacin MICs are: intermediate resistance, MICs 0.5-1.0 $\mu\text{g/ml}$; resistance, MICs $\geq 2.0 \mu\text{g/ml}$.^{17,18}

The distributions of MICs to ciprofloxacin in 1990 (the first year of ciprofloxacin susceptibility testing) and 2003 are shown in **Figure 19**. A total of 5.0% (328/6552) of isolates exhibited intermediate resistance or resistance to ciprofloxacin (MICs $\geq 0.125 \mu\text{g/ml}$) in 2003 compared with 3.7% (196/5367) of isolates tested in 2002 (**Figure 20**). Resistance to ciprofloxacin continued to increase from 7.2% in 2002 among MSM to 15% in 2003. Ciprofloxacin resistance also increased among heterosexuals from 0.9% in 2002 to 1.5% in 2003 (**Figure 21**). When GISP data from the states of Hawaii and California, where fluoroquinolones are no longer recommended for treating gonorrhea, are excluded, ciprofloxacin resistance among MSM increased from 1.8% in 2002 to 7.7% in 2003; ciprofloxacin resistance among heterosexuals increased from 0.2% in 2002 to 0.4% in 2003.

Intermediate resistance: In 2003, 0.9% (58/6552) of all GISP isolates exhibited intermediate resistance to ciprofloxacin (MICs 0.125-0.5 $\mu\text{g/ml}$). Of these isolates, 17.2% (10/58) came from San Francisco where they accounted for 3.6% (10/276) of isolates; 15.5% (9/58) came from Seattle where they accounted for 3.5% (9/258) of isolates tested; 13.8% (8/58) came from Chicago where they accounted for 2.8% (8/284); and 12.1% (7/58) came from Honolulu, where they accounted for 5.8% (7/120) of isolates tested in 2003. In 2003, 24 isolates of *N. gonorrhoeae* exhibiting intermediate resistance to ciprofloxacin were also found in Cincinnati (4), Cleveland (1), Denver (1), Las Vegas (1), Los Angeles (1), Long Beach (1), Miami (4), Orange County (1), Phoenix (1), Philadelphia (1), Portland (4), and San Diego (4). Albuquerque, Anchorage, Atlanta, Baltimore, Birmingham, Dallas, Detroit, Greensboro, Minneapolis, New Orleans, Oklahoma City, Salt Lake City, St. Louis and Tripler did not have any isolates with intermediate resistance to ciprofloxacin.

Resistance: Two hundred seventy, or 4.1% of GISP isolates were resistant to ciprofloxacin (MICs $\geq 1.0 \mu\text{g/ml}$) in 2003, which was two times the proportion identified in 2002 (2.2%; 116/5367). Ciprofloxacin-resistant isolates were identified in 70% (21/30) of all sentinel sites in 2003 compared with 23% (6/26) of all sentinel sites in 2001 and 48% (13/27) in 2002. Of note, 68.9% (186/270) of these isolates were from the California GISP sites; the proportion of ciprofloxacin-resistant GISP isolates by California site was: San Diego – 13.2% (34/257), Orange County – 31.5% (56/178), Long Beach – 19.4% (18/93), Los Angeles 12.4% (25/202) and San Francisco – 19.2% (53/276). Honolulu experienced a decline in the proportion of ciprofloxacin-resistant isolates from 20.3% (16/79) in 2001 to 11.7% (11/94) of GISP isolates in 2002 but the percentage increased again in 2003 to 13.3% (16/120) (see Honolulu, Hawaii, **Figure K**). In Seattle, 6.9% (18/258) of isolates were ciprofloxacin-resistant compared to 3% in 2002 and none in 2001. Cities which did not demonstrate ciprofloxacin resistant isolates during 2002, but which did in 2003 include Baltimore (1), Chicago (6), Cleveland (1), Dallas (6), Denver (2), Las Vegas (7), New Orleans (1), and Tripler AMC (1). The remaining 25 ciprofloxacin-resistant 2003 GISP isolates came from Cincinnati (1), Miami (5), Minnesota (5), Philadelphia (4), Phoenix (6), and Portland (4).

Susceptibility to Azithromycin

The correlation of azithromycin MICs $\geq 0.5 \mu\text{g/ml}$ with clinical treatment failure when the 2.0 gm azithromycin dose is used to treat a gonococcal infection is not known. However, clinical treatment failures have been reported with the 1.0 gm azithromycin dose for strains with MICs of 0.125-0.5 $\mu\text{g/ml}$.²⁵⁻²⁸

The distributions of MICs to azithromycin in 1992 (the first year of azithromycin susceptibility testing) and in 2003 are shown in **Figure 22**. Over this time period, there has been a shift towards higher azithromycin MICs. In 1992, 0.9% (34/3928) of isolates had azithromycin MIC $\geq 0.5 \mu\text{g/ml}$ compared with 2.2% (145/6552) of such isolates in 2003. In 1992, there were no isolates with azithromycin MIC $\geq 1.0 \mu\text{g/ml}$. In 2003, there were 26 isolates with azithromycin MIC $\geq 1.0 \mu\text{g/ml}$ (range, 1.0-4.0 $\mu\text{g/ml}$); these isolates by location and number are: Atlanta (9); Birmingham (2); Cincinnati (1); Dallas (1); Greensboro (3); Las Vegas (2); New Orleans (1); Orange County (1); Philadelphia (1); Salt Lake City (3); San Francisco (1) and Seattle (1).

SUSCEPTIBILITY REPORTING OUTSIDE OF GISP

During 2003-2004, Association of Public Health Laboratories (APHL) and STD project areas were informally surveyed to identify city or state public health laboratories which routinely performed antimicrobial susceptibility testing of *N. gonorrhoeae*. Data from 21 project areas and other laboratories which performed antimicrobial susceptibility testing are presented in **Table 1**.

Table 1. Non-GISP antimicrobial susceptibility testing of *N. gonorrhoeae* during 2003.

Reporting Areas	Total # Isolates Tested	Cip S	Cip I	Cip R	Spc S	Spc R	Cfx S	Cfx DS	Cro S	Cro DS	Azi S	Azi DS ^a
AZ	22	22 ^b	0	0	-	-	-	-	22 ^b	0	0	0
CA San Diego	193	158	0	35 ^c	-	-	-	-	193	0	-	-
FL	31	31 ^d	0	0	-	-	-	-	31	0	31	0
Guam ^e	5	4	0	1	-	-	-	-	5	0	-	-
HI	380	358	1	21	380	0	377	3	380	0	380	0
IL Chicago	85	83	0	2 ^d	-	-	83	2	-	-	-	-
IN Indianapolis	491	488	1	2	-	-	-	-	491	0	-	-
MA	402	346	0	56 ^f	-	-	-	-	402	0	-	-
MI	582	564	1	17	582	0	582	0	582	0	-	-
MN	146	146	0	0	146	0	146	0	146	0	141	5
MS ^g	748	748	0	0	-	-	-	-	17	0	-	-
MT	13	13	0	0	-	-	13	0	13	0	13	0
NH	21	14	1	6	21	0	-	-	21	0	-	-
NJ	209	209 ^h	0	0	209	0	209	0	209	0	-	-
NY	29	28	0	1 ⁱ	29	0	28	1	29	0	25	4
NYC	1026	995	1	30 ^c	1026	0	-	-	1026	0	-	-
TX	49	49	0	0	-	-	-	-	49	0	-	-
UT	98	97 ^j	0	1	-	-	-	-	98	0	-	-
VA	2	2	0	0	2	0	-	-	2	0	-	-
WA Seattle ^k	269	252	1	16	-	-	128 ^k	0	-	-	-	-
WI Milwaukee ^l	386	384	0	2	386	0	-	-	386	0	384	2
Total	5187	4991	6	190	2781	0	1566	6	4102	0	974	11

Note:

- Cip=ciprofloxacin; Spc=spectinomycin; Cfx=cefexime; Cro=ceftriaxone; Azi=azithromycin; S=susceptible; DS=decreased susceptibility; I=intermediate resistant; R=resistant.
- Cells containing only “-“ indicate that the antimicrobial for that column was not tested.
- The testing methodology for all sites except Florida, Hawaii, Indianapolis, Montana, and Texas was by disk diffusion; Florida, Hawaii, Indianapolis, Montana, and Texas used the E-test method.

^aFor this table, AziDS is defined as an isolate with azithromycin disk inhibition zone size ≤ 30 mm or minimum inhibitory concentration (MIC) $\geq 1.0 \mu\text{g/ml}$.

^bArizona tested isolates against ciprofloxacin and ceftriaxone from September until December 2003.

^cNew York City and San Diego tested all isolates against ofloxacin, rather than against ciprofloxacin. The 35 isolates reported from San Diego were resistant to ofloxacin. The 30 isolates reported from NYC were resistant to ofloxacin and tested against ciprofloxacin at the CDC.

^dFlorida tested all isolates against levofloxacin, gatafloxacin, and ciprofloxacin.

^eData from Guam reflects isolates tested from January to June 2003.

^fMassachusetts tested all isolates against norfloxacin, ofloxacin, ciprofloxacin, cefotaxime, and cefoxitin.

^gMississippi tested 748 isolates against ciprofloxacin only; 17 isolates were screened for penicillin, ciprofloxacin, ceftriaxone, and tetracycline resistance.

^hNew Jersey tested all isolates against ofloxacin.

ⁱNew York state tested all 29 isolates against ofloxacin and 20/29 isolates against ciprofloxacin.

^jUtah tested all isolates against ofloxacin and ciprofloxacin

^kData from Seattle, WA came from the University of Washington and reflects isolates tested from June until December 2003; Seattle, WA tested 128 isolates against cefixime, cefuroxime, and cefpodoxime.

^lData from Milwaukee, WI came from Milwaukee Health Department Laboratories and does not reflect GC resistance testing procedures of Wisconsin State Laboratory of Hygiene.

Discussion

Susceptibility data from a total of 5187 non-GISP isolates were available. Non-GISP isolates from most STD project areas do not consist of a representative or systematic sample of patients with gonorrhea but rather a convenience sample of patients who happen to undergo culture rather than non-culture testing. In addition, in contrast to GISP, multiple non-GISP isolates from various anatomic sites may be submitted from a single patient, so the 5187 non-GISP isolates are likely to represent fewer than 5187 patients with gonorrhea.

These data reveal that 3.7% (190/5187) of non-GISP isolates were resistant to ciprofloxacin or ofloxacin, which is comparable to the 4.1% (270/6552) identified for GISP isolates in 2003. Fluoroquinolone-resistant isolates were identified in San Diego, California (35/193, 18.1%); Guam (1/5, 20%); Hawaii (21/380, 5.5%); Chicago, Illinois (2/85, 2.4%); Indianapolis, Indiana (2/491, 0.4%); Massachusetts (56/402, 13.9%); Michigan (17/582, 2.9%); New Hampshire (6/21, 28.6%); New York State (1/29, 3.4%); New York City (30/1026, 2.9%); Seattle, Washington (16/269, 5.9%), Utah (1/98, 1%); and Milwaukee, Wisconsin (2/386; 0.5%).

2003-2004 Survey results

During 2003-2004, 66 STD project areas and APHL laboratories were surveyed to determine the extent of antimicrobial susceptibility testing. Of the 66 laboratories surveyed, 25 reported performing susceptibility testing, while 35 did not perform such testing. Six sites did not respond to the survey.

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ADDITIONAL RESOURCES

Recent publications using GISP data include an April 2004 MMWR article¹⁴, a 2004 article in *Clinical Infections Diseases*,²⁹ and a 2004 article in *Sexually Transmitted Diseases*.¹¹ Presentations of GISP data were made at the British Association of Sexual Health & HIV and American Sexually Transmitted Disease Association Spring meeting held in Bath, England, May 29, 2004,³⁰ and at the National STD Prevention Conference, Philadelphia, Pennsylvania, March 8, 2004,³¹ and at the Annual Meeting of the Infectious Diseases Society of America in Boston, Massachusetts in October 2004.³²

Additional information on GISP, as well as useful resources and links, may be found on the GISP website (<http://www.cdc.gov/std/gisp/>). Additional United States surveillance data on *N. gonorrhoeae* and other STDs may be found in the 2003 STD Surveillance Report¹ (<http://www.cdc.gov/std/stats/>).

Information on the U.S. Public Health Action Plan to Combat Antimicrobial Resistance may be found on the CDC webpage (<http://www.cdc.gov/drugresistance/actionplan/>).

The World Health Organization (WHO) webpage contains information on:

- 1) the WHO Global Strategy for Containment of Antimicrobial Resistance (<http://www.who.int/emc/amr.html>);
- 2) the WHO Surveillance Standards for Antimicrobial Resistance (<http://www.who.int/emc/pdfs/CDSsurveillance1.pdf>);
- 3) the UNAIDS/WHO Guidelines for Sexually Transmitted Infections Surveillance (<http://www.who.int/emc-documents/STId/docs/whocdscsredc993.pdf>); and
- 4) Antimicrobial Resistance in *Neisseria gonorrhoeae* ([http://www.who.int/csr/drugresist/Antimicrobial resistance in Neisseria gonorrhoeae.pdf](http://www.who.int/csr/drugresist/Antimicrobial%20resistance%20in%20Neisseria%20gonorrhoeae.pdf)).

REFERENCES

1. CDC. Sexually Transmitted Disease Surveillance, 2003. Atlanta, Georgia: U.S. Department of Health and Human Services, Public Health Service, September 2004
2. CDC. Gonorrhea — United States, 1998 MMWR 2000;49:538-542.
3. Fox KK, Whittington WL, Levine WC, Moran JS, Zaidi AA, Nakashima AK. Gonorrhea in the United States, 1981-1996: Demographic and geographic trends. *Sex Transm Dis* 1998;386-93.
4. McCormack WM. Pelvic inflammatory disease. *N Engl J Med* 1994;330:115-119.
5. Laga M, Manoka A, Kivuvu M, Malele B, Tuliza M, Nzila N, Goeman J, Behets F, Batter V, Alary M. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. *AIDS* 1993;7:95-102.
6. Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Daly CC, Zimba D, Vernazza PL, Maida M, Fiscus SA, Eron JJ. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. AIDSCAP Malawi Research Group. *Lancet* 1997;349:1868-73.
7. CDC. Sexually transmitted diseases treatment guidelines 2002. MMWR 2002;51(No. RR-6).
8. Fox KK, Knapp JS, Holmes KK, Hook EW, Judson FN, Thompson SE, Washington JA, Whittington WL. Antimicrobial resistance in *Neisseria gonorrhoeae* in the United States 1988-1994: the emergence of resistance to the fluoroquinolones. *J Infect Dis* 1997;175:1396-1403.
9. CDC. Fluoroquinolone-resistance in *Neisseria gonorrhoeae* - Colorado and Washington, 1995. MMWR 1995;44:761-4.
10. CDC. Fluoroquinolone-resistant *Neisseria gonorrhoeae* - San Diego, California, 1997. MMWR 1998;47:405-408.
11. McLean CA, Wang SA, Hoff GL, Dennis LY, Trees DL, Knapp JS, Markowitz LE, Levine WC. The emergence of *Neisseria gonorrhoeae*, with decreased susceptibility to azithromycin in Kansas City, Missouri, 1999-2000. *Sexually Transmitted Diseases* 2004;31:73-78.
12. CDC. Increases in fluoroquinolone-resistant *Neisseria gonorrhoeae* – Hawaii and California, 2001. MMWR 2002;51:1041-1044.
13. WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme. Surveillance of antibiotic resistance in *Neisseria gonorrhoea* in the WHO Western Pacific Region, 2001. *Communicable Disease Intelligence* 2002;26:541-545.
14. CDC. Increases in Fluoroquinolone-Resistant *Neisseria gonorrhoeae* Among Men Who Have Sex with Men --- United States, 2003, and Revised Recommendations for Gonorrhea Treatment, 2004. MMWR 2004;53:335-338.

15. Schwarcz SK, Zenilman JM, Schnell D, Knapp JS, Hook EW, Thompson S, Judson FN, Holmes KK, The Gonococcal Isolate Surveillance Project. National surveillance of antimicrobial resistance in *Neisseria gonorrhoeae*. JAMA 1990;264:1413-1417.
16. National Committee for Clinical Laboratory Standards. 1993. Approved standard M7 - A3. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. National Committee for Clinical Laboratory Standards, Villanova, PA.
17. National Committee for Clinical Laboratory Standards. 1998. Approved standard M100-38. Performance standards for antimicrobial susceptibility testing. National Committee for Clinical Laboratory Standards, Wayne, PA.
18. National Committee for Clinical Laboratory Standards. 2002. Approved standard M100-S12, 22. Performance standards for antimicrobial susceptibility testing. National Committee for Clinical Laboratory Standards, Wayne, PA.
19. Wang SA, Lee MVC, O'Connor N, Iverson CJ, Ohye RG, Whitticar PM, Hale JA, Knapp JS, Effler PV, Weinstock HS. Multi-drug resistant *Neisseria gonorrhoeae* with decreased susceptibility to cefixime – Hawaii, 2001. Clin Infect Dis 2003;37:849-852.
20. CDC. Gonorrhea among men who have sex with men--selected sexually transmitted diseases clinics, 1993-1996. MMWR 1997;46:889-892.
21. Fox KK, del Rio C, Holmes KK, Hook EW, Judson FN, Knapp JS, Procop GW, Wang SA, Whittington WL, and Levine WC. Gonorrhea in the HIV era: a reversal in trends among men who have sex with men. Am J Public Health 2001;91:959-64.
22. CDC. 1993 Sexually transmitted diseases treatment guidelines. MMWR 1993;42(No. RR-14).
23. CDC. 1998 Guidelines for treatment of sexually transmitted diseases. MMWR 1998;47(No. RR-1).
24. Aplasca MR, Pato-Mesola V, Klausner JD, Manalastas R, Tuazon CU, Dallabetta G, Whittington WL, Holmes KK. A randomized trial of ciprofloxacin versus cefixime for treatment of gonorrhea after rapid emergence of gonococcal ciprofloxacin resistance in the Philippines. Clin Infect Dis 2001; 32:1313-8.
25. Steingrimsson O, Olafsson JH, Thorarinsson H, Ryan RW, Johnson RB, Tilton RC. Azithromycin in the treatment of sexually transmitted disease. J Antimicrob Chemother 1990;25(Suppl A):109-114.
26. Waugh MA. Open study of the safety and efficacy of a single dose of azithromycin for the treatment of uncomplicated gonorrhea in men and women. J Antimicrob Chemother 1993;31(Suppl E):193-198.
27. Young H, Moyes A, McMillan A. Azithromycin and erythromycin resistant *Neisseria gonorrhoeae* following treatment with azithromycin. Int J STD AIDS 1997;8:299-302.

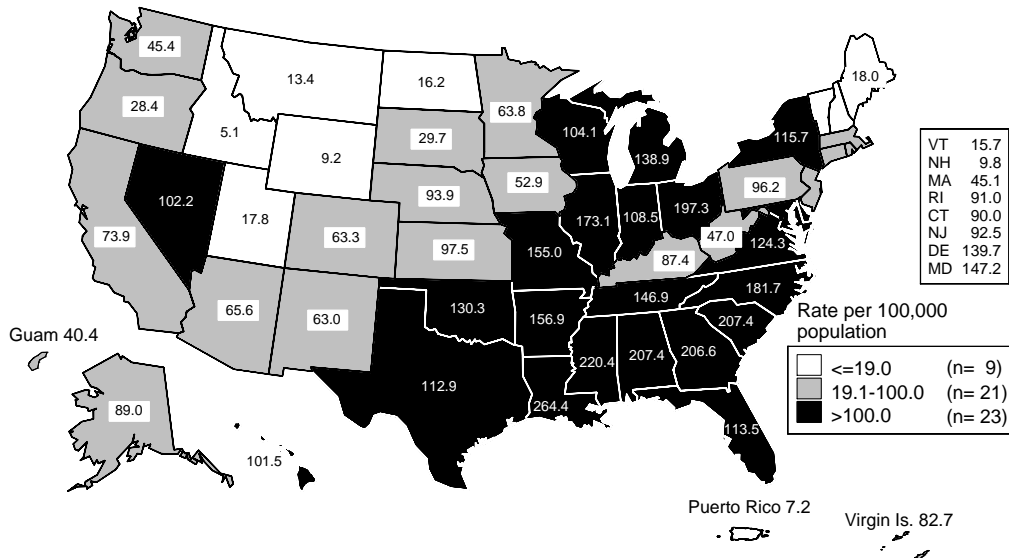
28. Tapsall JW, Shultz TR, Limnios EA, Donovan B, Lum G, Mulhall BP. Failure of azithromycin therapy in gonorrhea and dis correlation with laboratory test parameters. *Sex Transm Dis* 1998;25:505-508.
29. Newman LM, Wang SA, Ohye RG, O'Connor N, Lee MV, Weinstock HS. The epidemiology of fluoroquinolone-resistant *Neisseria gonorrhoeae* in Hawaii, 2001. *Clinical Infectious Diseases* 2004;38:649-54.
30. Wang SA. Gonococcal resistance in the United States: current data and challenges. British Association of Sexual Health and HIV and American Sexually Transmitted Disease Association Spring Meeting, Bath, England, May 19, 2004.
31. Wang SA. Update on gonococcal resistance in the United States. National STD Prevention Conference, Philadelphia, Pennsylvania, March 8, 2004.
32. Wang SA, Harvey AB, Conner SM, Gonococcal Isolate Surveillance Project Investigators. Trends in antimicrobial susceptibilities of *Neisseria gonorrhoeae* in the United States: Increases in fluoroquinolone-resistance. [Abstract 811]. 42nd Annual Meeting of the Infectious Diseases Society of America, Boston, Massachusetts, September 30-October 3, 2004.

Figure 1. Gonorrhea — Rates: United States, 1970–2003 and the Healthy People 2010 target



Note: The Healthy People 2010 objective for gonorrhea is 19.0 cases per 100,000 population.

Figure 2. Gonorrhea — Rates by state: United States and outlying areas, 2003



Note: The total rate of gonorrhea for the United States and outlying areas (Guam, Puerto Rico and Virgin Islands) was 114.7 per 100,000 population. The Healthy People 2010 target is 19.0 cases per 100,000 population.

Figure 3. Gonorrhea — Rates by race and ethnicity: United States, 1981–2003 and the Healthy People 2010 target

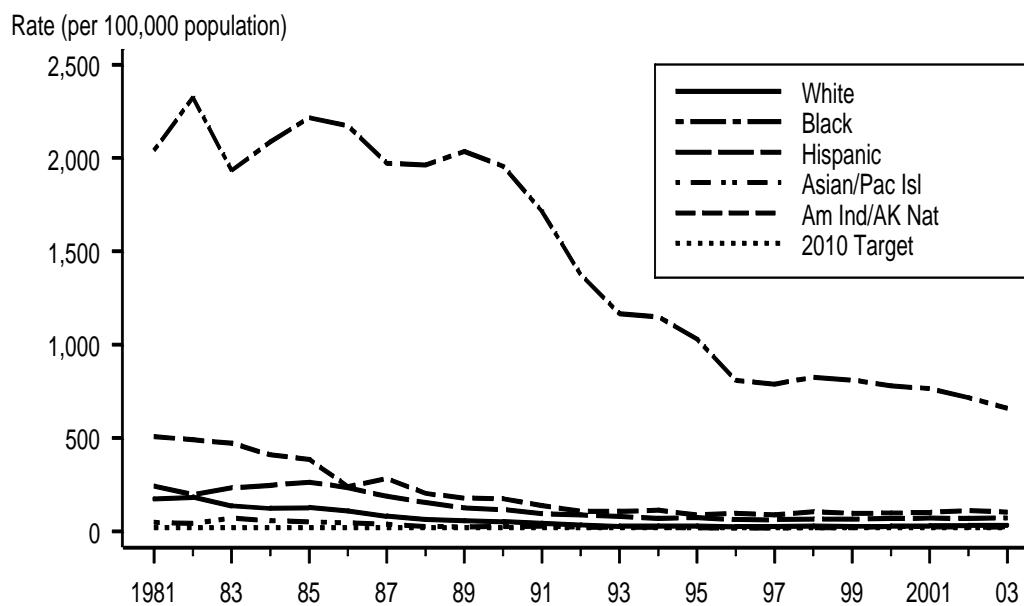


Figure 4. Gonorrhea — Age- and sex-specific rates: United States, 2003

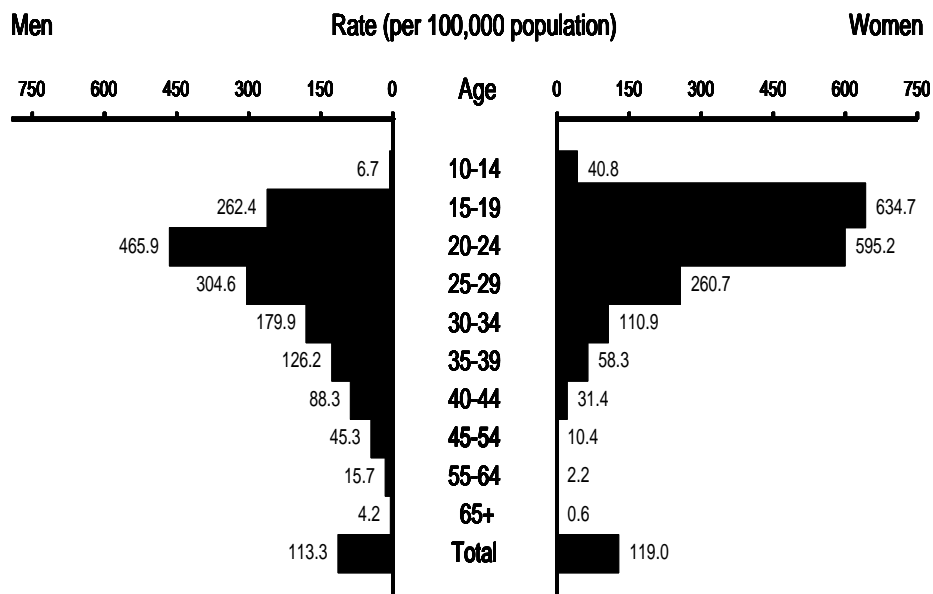


Figure 5. Gonococcal Isolate Surveillance Project (GISP) — Location of participating clinics and regional laboratories: United States, 2003

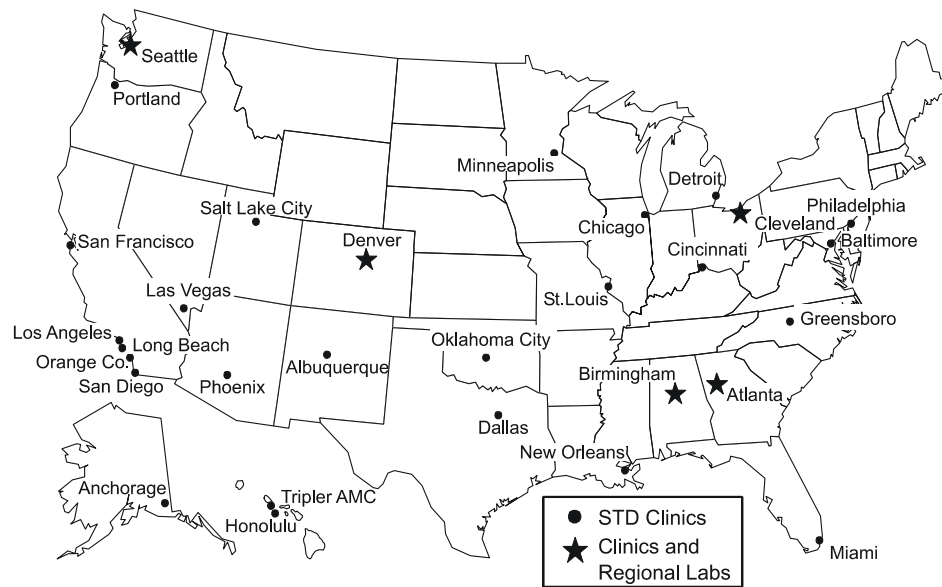
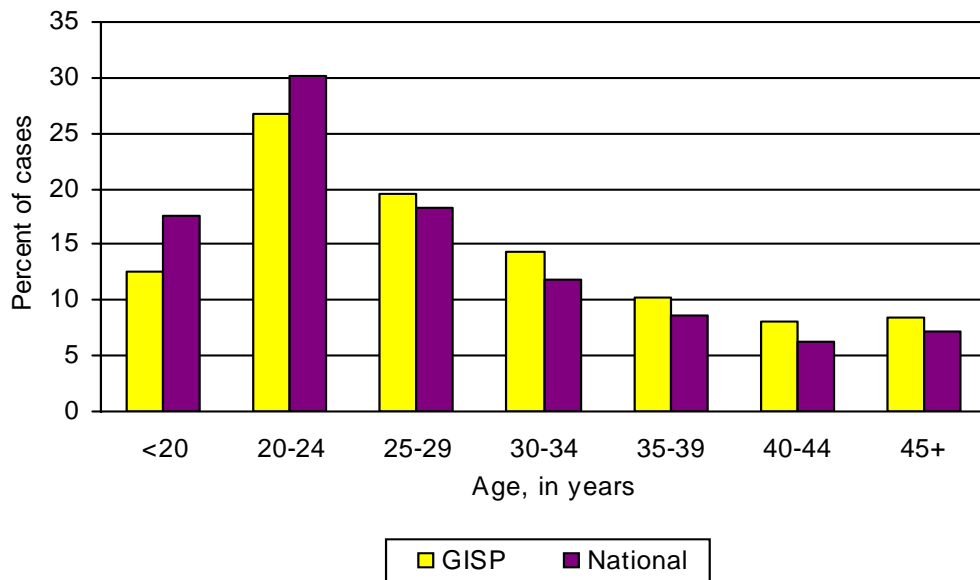
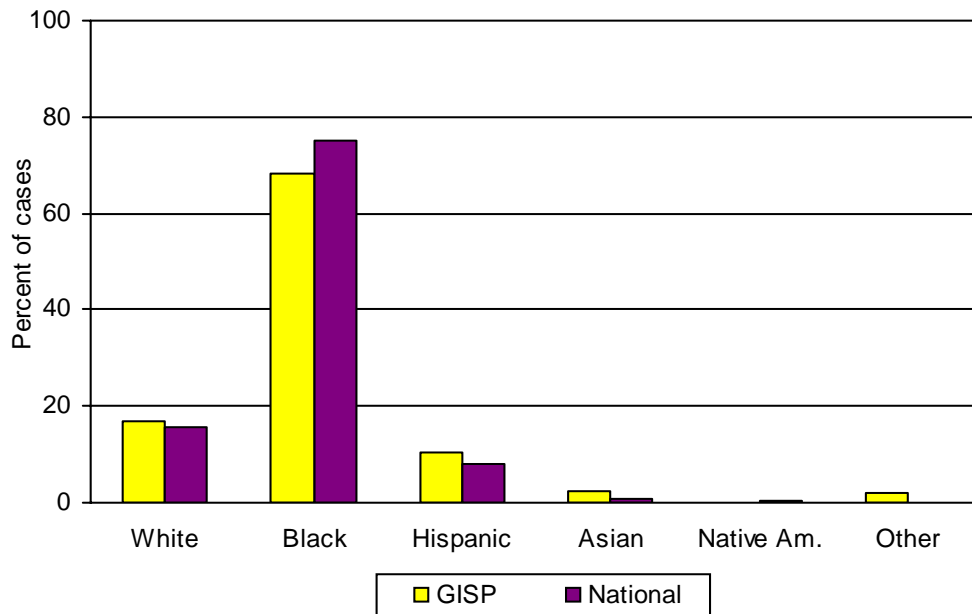


Figure 6. Age distribution of GISP participants and nationally reported gonorrhea cases in men, 2003



Note: The age<20 category includes ages 10-19 for national cases, and ages 13-19 for GISP; over 99% of the GISP cases in the <20 category are ages 15-19. National cases with unknown ages were excluded.

Figure 7. Race distribution of GISP participants and nationally reported cases of gonorrhea in men, 2003



Note: The "Other" category is not used in national gonorrhea reporting. National cases with unknown race were excluded. Asian includes Native Hawaiians and Other includes participants who selected more than one race category.

Figure 8. Percentage of GISP cases that occurred among men who have sex with men (MSM), 1988-2003

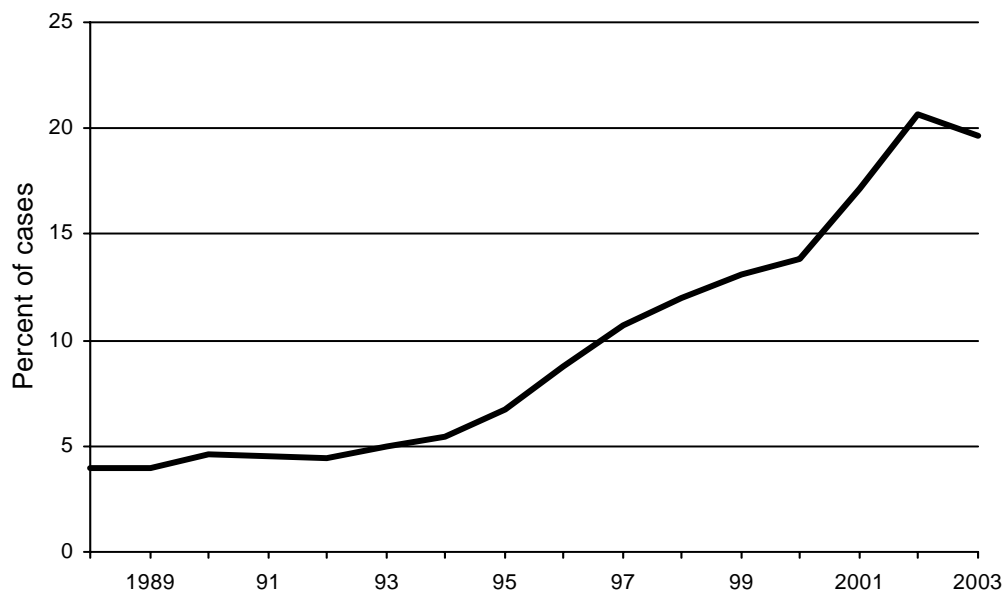
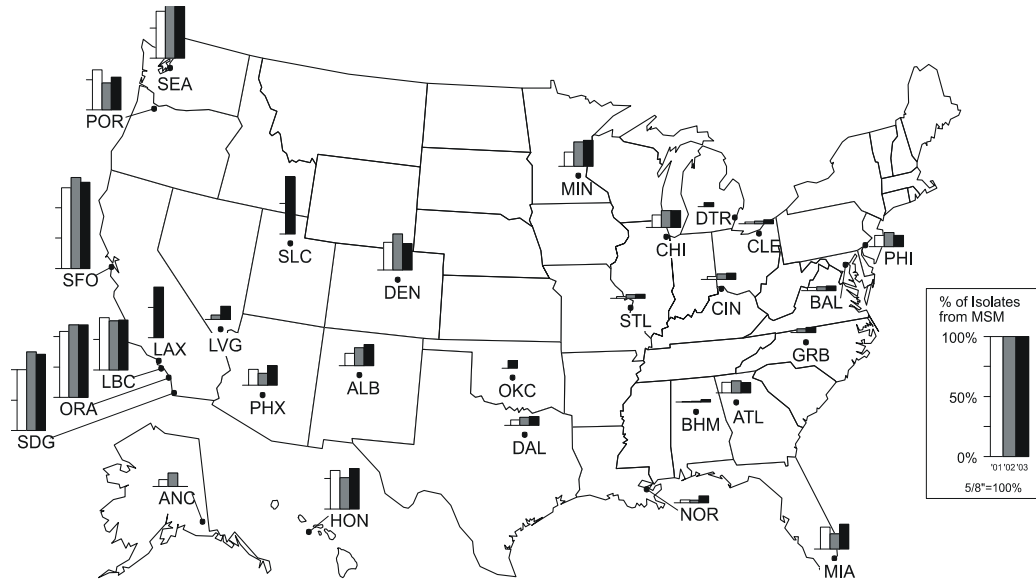
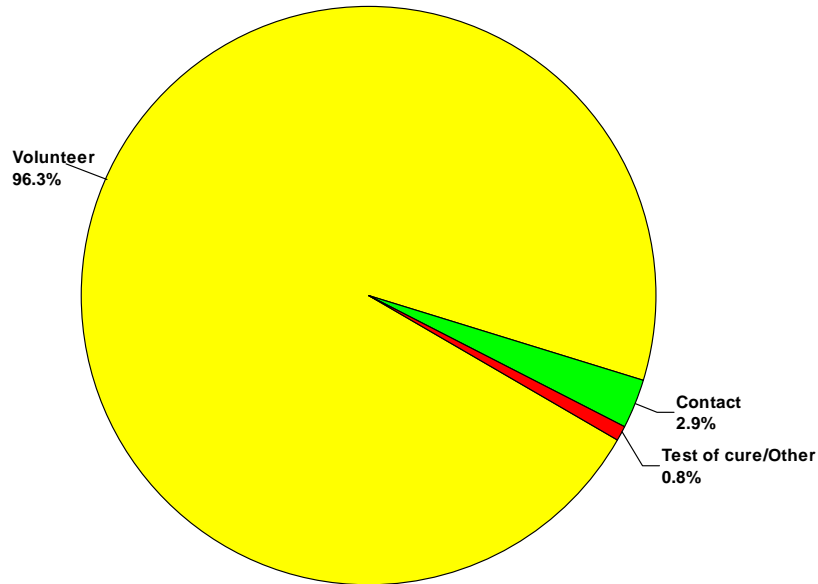


Figure 9. Gonococcal Isolate Surveillance Project (GISP) — Percent of *Neisseria gonorrhoeae* isolates obtained from MSM attending STD clinics, 2001–2003



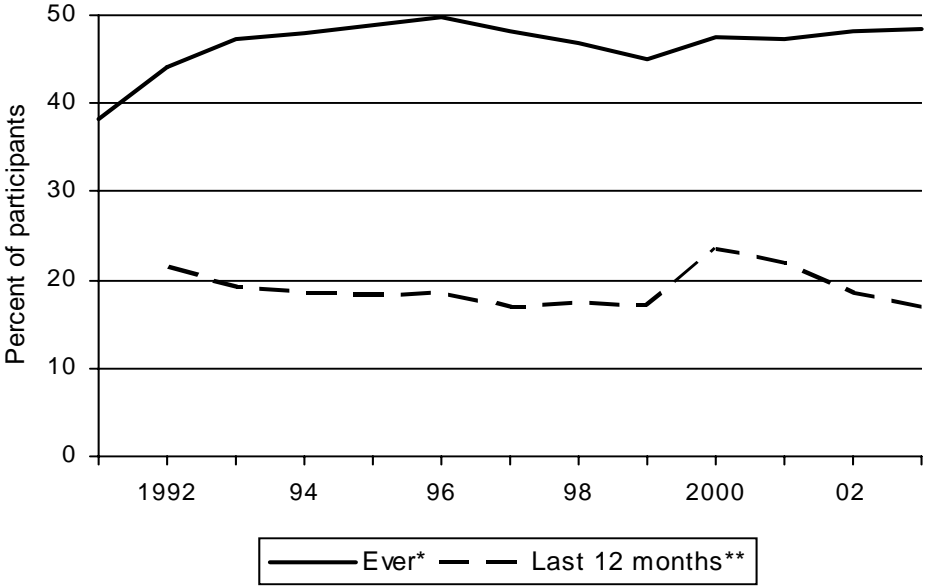
Note: Not all clinics participated in GISP for the last 3 years. Clinics include: ALB=Albuquerque, NM; ANC=Anchorage, AK; ATL=Atlanta, GA; BAL=Baltimore, MD; BHM=Birmingham, AL; CHI=Chicago, IL; CIN=Cincinnati, OH; CLE=Cleveland, OH; DAL=Dallas, TX; DEN=Denver, CO; DTR=Detroit, MI; HON=Honolulu, HI; LAX=Los Angeles, CA; LBC=Long Beach, CA; LVC=Las Vegas, NV; MIA=Miami, FL; MIN=Minneapolis, MN; GRB=Greensboro, NC; NOR=New Orleans, LA; OKC=Oklahoma City, OK; ORA=Orange County, CA; PHI=Philadelphia, PA; PHX=Phoenix, AZ; POR=Portland, OR; SLC=Salt Lake City, UT; STL=St Louis, MO; SDG=San Diego, CA; SEA=Seattle, WA; and SFO=San Francisco, CA. Tripler Army Medical Center, HI does not provide sexual risk behavior data.

Figure 10. Reason for clinic attendance among GISP participants, 2003



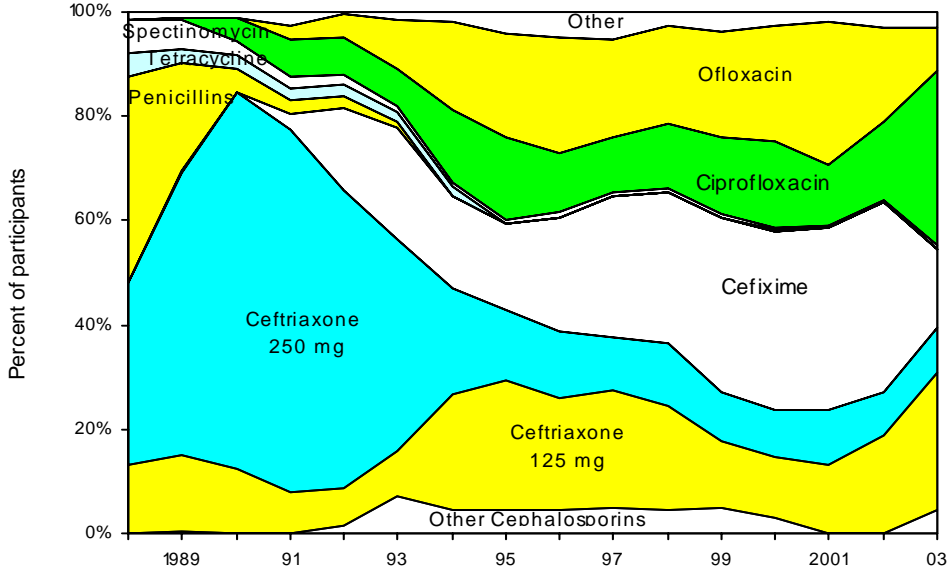
Note: Contact=has sexual partner with gonorrhea

Figure 11. History of gonorrhea in GISP participants, 1991–2003



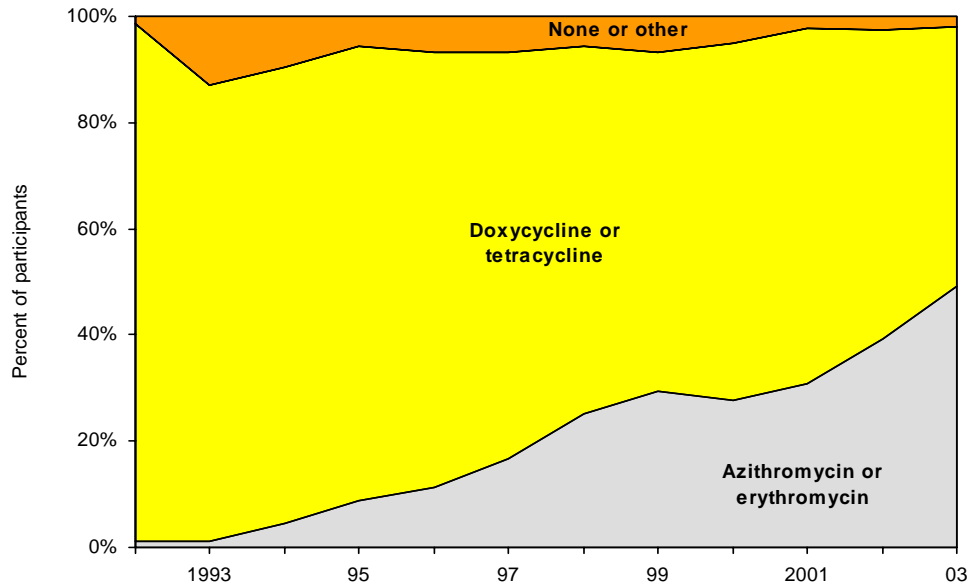
*Data first collected in 1991.
 **Data first collected in 1992.

Figure 12. Drugs used to treat gonorrhea in GISP participants, 1988–2003



Note: For 2003, “Other” includes no therapy (1.8%), azithromycin 1 g (0.1%), azithromycin 2 g (0.5%), levofloxacin (0.4%), and other less frequently used drugs.

Figure 13. Drugs used to treat *Chlamydia trachomatis* infection in GISP participants 1992–2003



Note: For each year, “Other” accounted for only 0 - 0.9% of *C. trachomatis* treatment and erythromycin accounted for only 0.1 - 1.0% of *C. trachomatis* treatment.

Figure 14. Penicillin and tetracycline resistance among GISP isolates, 2003

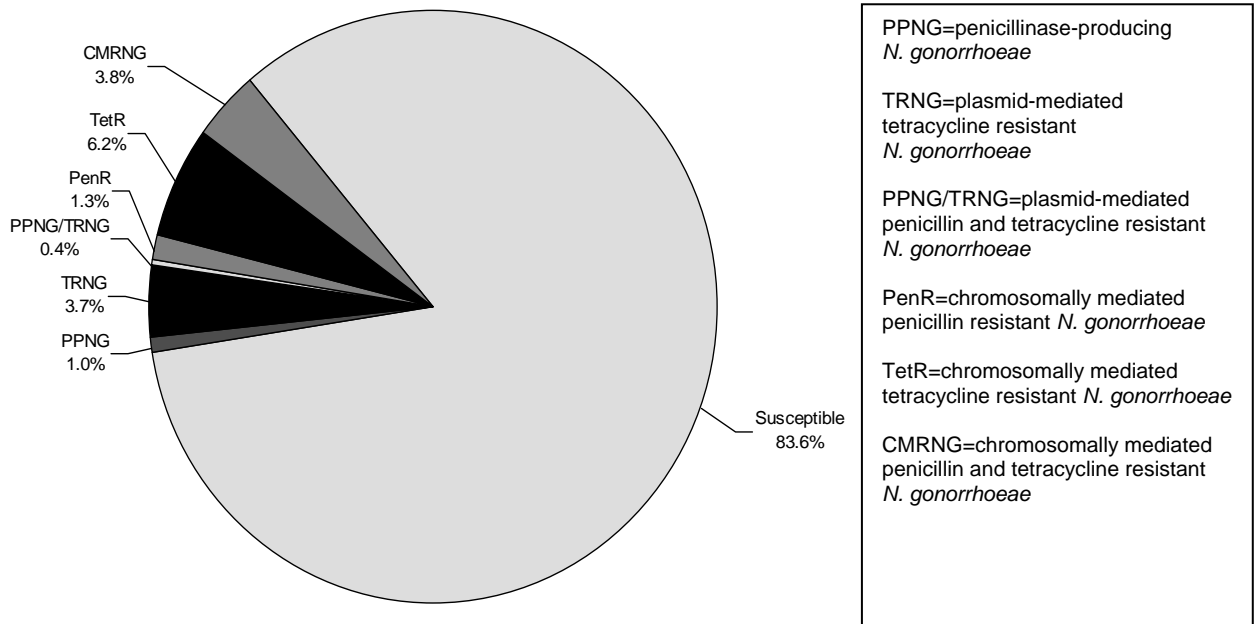


Figure 15. Plasmid-mediated resistance to penicillin and tetracycline among GISP isolates, 1988–2003

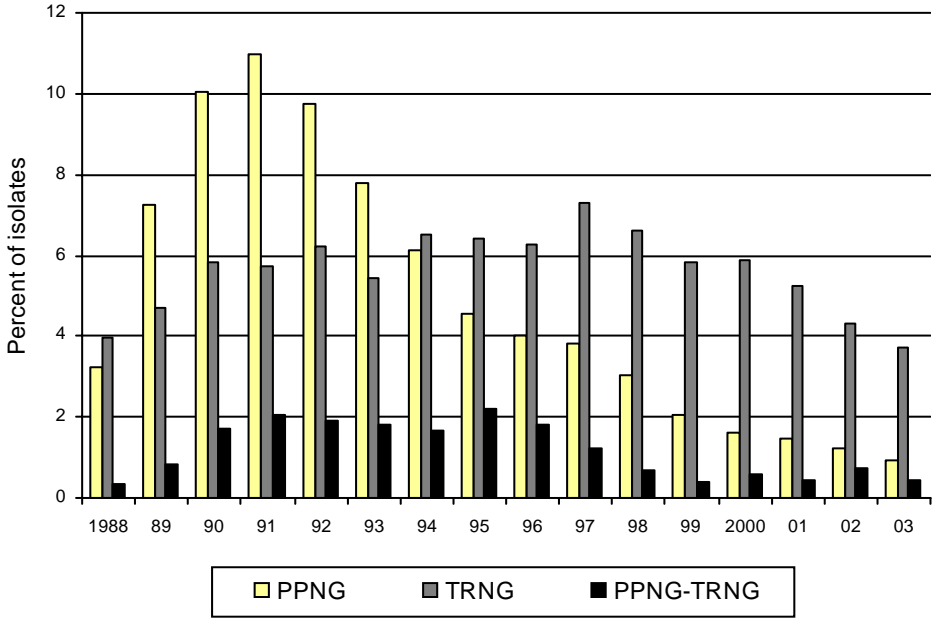


Figure 16. Chromosomally mediated resistance to penicillin and tetracycline among GISP isolates, 1988–2003

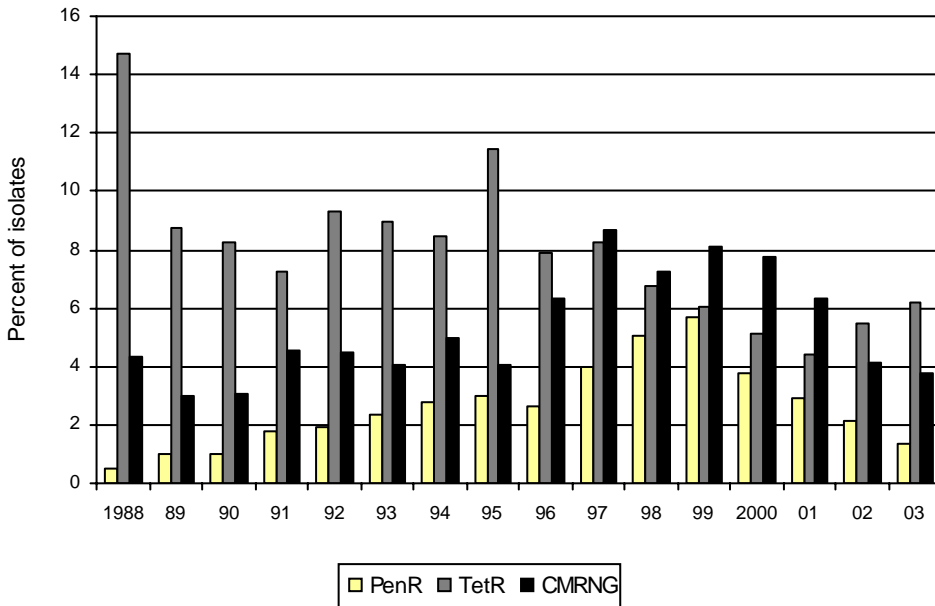
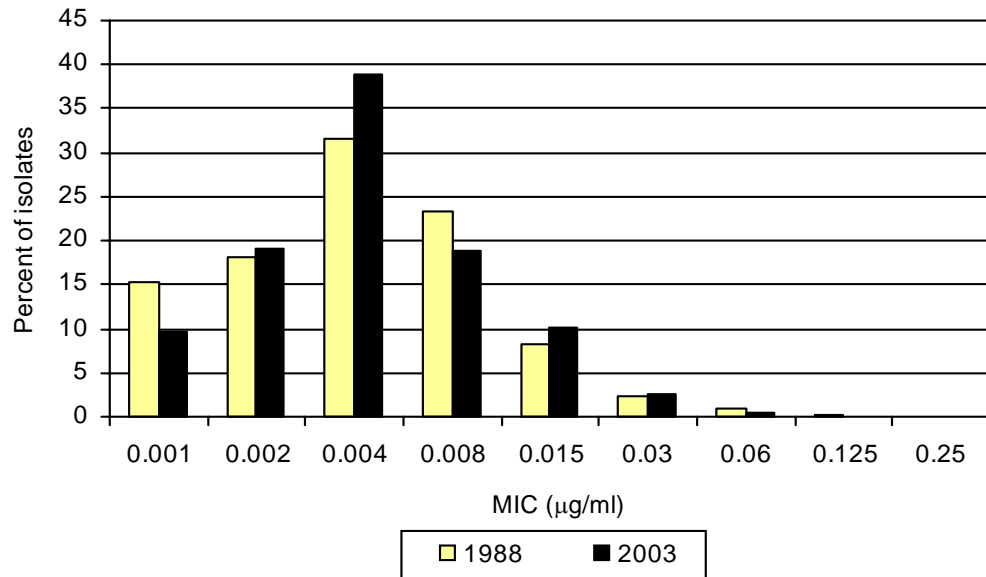
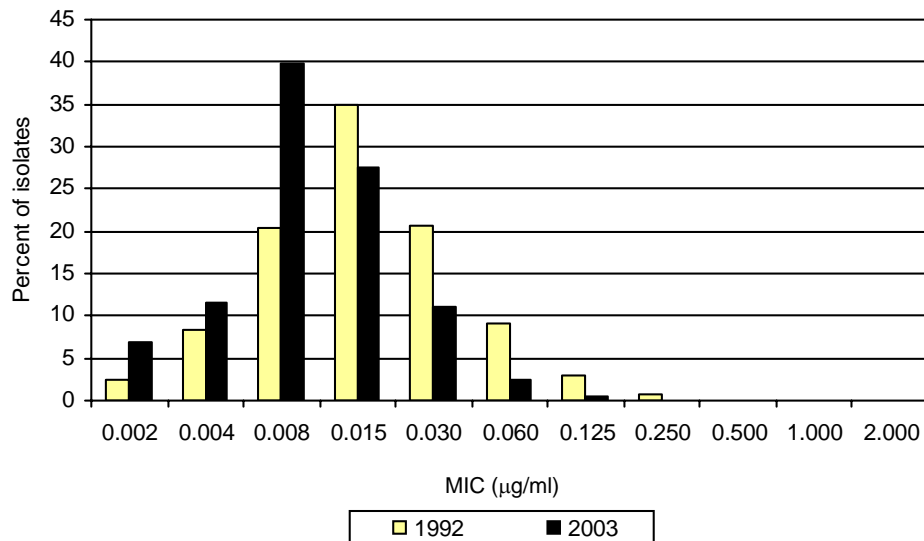


Figure 17. Distribution of MICs to ceftriaxone among GISP isolates, 1988 and 2003



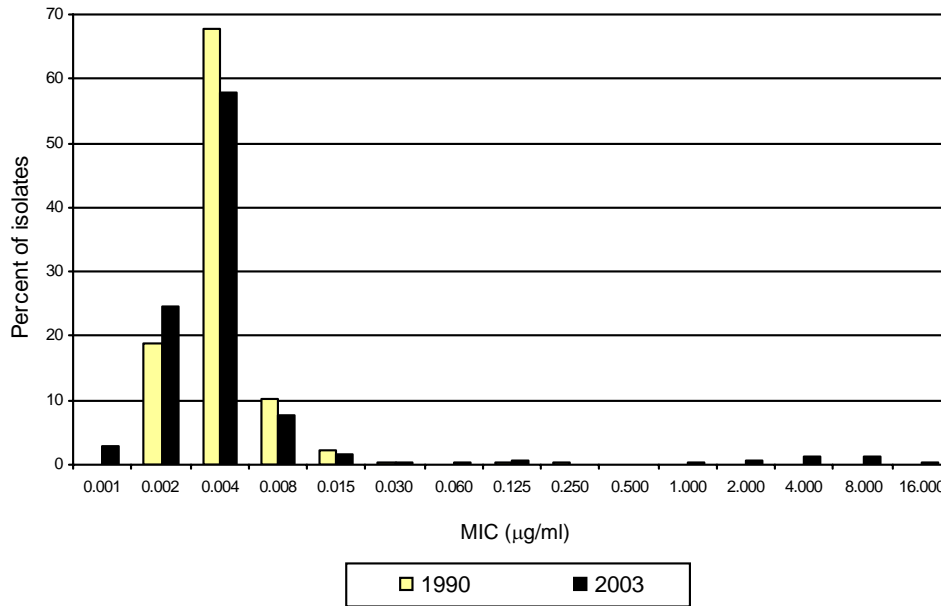
Note: In 1988, there was one isolate with MIC 0.25 µg/ml. In 2003, there were no isolates with MIC 0.25 µg/ml.

Figure 18. Distribution of MICs to cefixime among GISP isolates, 1992 and 2003



Note: In 1992, there were six isolates with MIC 0.5 µg/ml, three isolates with MIC 1.0 µg/ml, and two isolates with MIC 2.0 µg/ml. In 2003, there were no isolates with MIC > 0.25 µg/ml.

Figure 19. Distribution of MICs to ciprofloxacin among GISP isolates, 1990 and 2003



Note: In 1990, there were no isolates with MIC > 0.25 µg/ml. In 2003, there were six isolates with MIC 0.5 µg/ml, fifteen isolates with MIC 1.0 µg/ml, forty-three isolates with MIC 2.0 µg/ml, ninety-four isolates with MIC 4.0 µg/ml, ninety-four isolates with MIC 8.0 µg/ml, and twenty-four isolates with MIC 16.0 µg/ml.

Figure 20. Percentage of GISP isolates with intermediate resistance or resistance to ciprofloxacin, 1990–2003

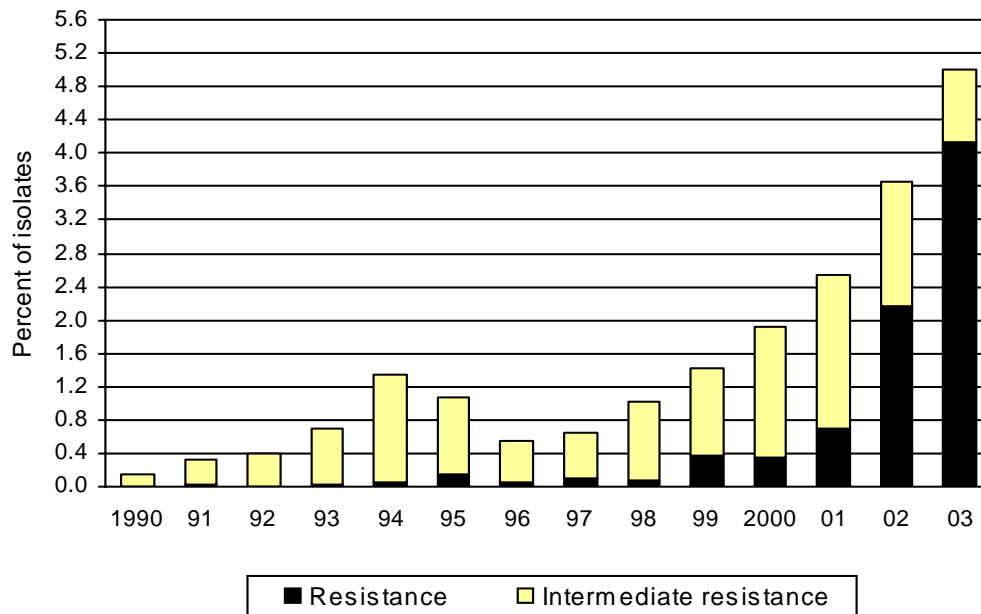


Figure 21. Percent of *Neisseria gonorrhoeae* isolates with resistance to ciprofloxacin by sexual behavior, 2001–2003

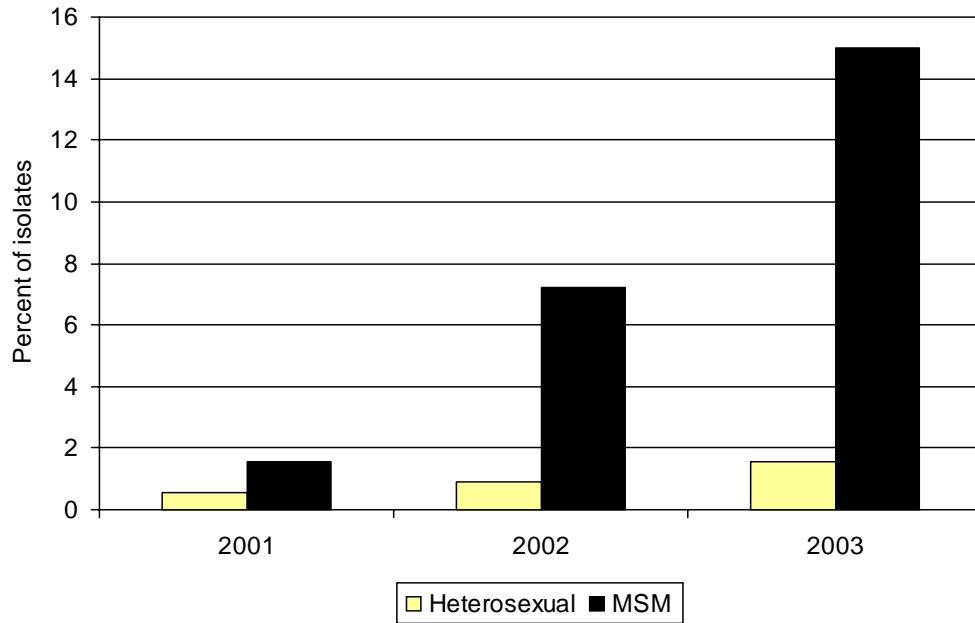
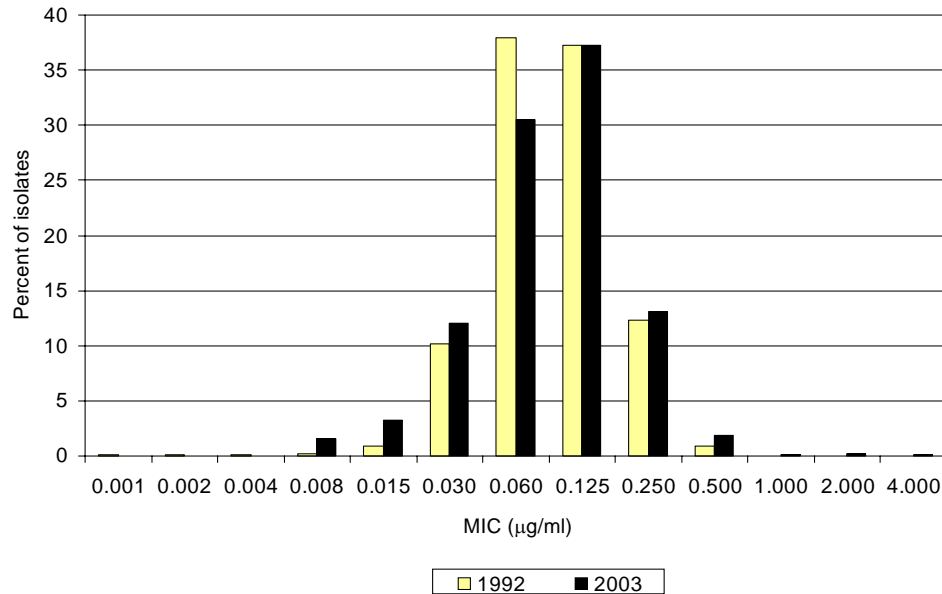


Figure 22. Distribution of MICs to azithromycin among GISP isolates, 1992 and 2003



Note: In 1992, there were no isolates with MIC > 0.5 µg/ml. In 2003, there were six isolates with MIC 1.0 µg/ml, twelve isolates with MIC 2.0 µg/ml, and eight isolates with MIC 4.0 µg/ml.

CLINIC-SPECIFIC DEMOGRAPHIC, CLINICAL, AND LABORATORY DATA

The remainder of this report provides clinic-specific figures for each of the 30 clinics that participated in GISP in 2003. Individual figures for each clinic show demographic and clinical characteristics of the men with gonorrhea enrolled in GISP, as well as antimicrobial susceptibilities for the *N. gonorrhoeae* isolates. The number of isolates submitted by each clinic is 300 when the full sample of 25 isolates per month is obtained. However, the number of isolates submitted is lower for many clinics located in areas with low gonorrhea rates. Each page of figures is labeled with the city of the participating clinic and the actual number of isolates on which the clinic's 2003 data are based.

Definitions of terms and abbreviations used in the clinic-specific figures are given below.

- Figure B:** National cases with unknown race were excluded. The "Asian" category includes Native Hawaiians and the "Other" category includes participants who selected more than one race category. The "Other" category is not used in national gonorrhea reporting.
- Figure D:** Contact=has sexual partner with gonorrhea
TOC/Other=test of cure/other
- Figure G:** Azi/Ery=azithromycin/erythromycin
Doxy/Tet=doxycycline/tetracycline
- Figure H:** PPNG=penicillinase-producing *N. gonorrhoeae*
TRNG=plasmid-mediated tetracycline resistant *N. gonorrhoeae*
PPNG-TRNG=plasmid-mediated penicillin and tetracycline resistant *N. gonorrhoeae*
PenR=chromosomally mediated penicillin resistant *N. gonorrhoeae*
TetR=chromosomally mediated tetracycline resistant *N. gonorrhoeae*
CMRNG=chromosomally mediated penicillin and tetracycline resistant *N. gonorrhoeae*