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**Gonococcal Isolate Surveillance Project (GISP)  
Annual Report - 2004**

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This report is available from the Internet via the CDC home page address at <http://www.cdc.gov/std/GISP2004/>.

The 2004 STD Surveillance Report may be found at <http://www.cdc.gov/std/stats/>.

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# GONOCOCCAL ISOLATE SURVEILLANCE PROJECT (GISP) ANNUAL REPORT – 2004

## Introduction

With 330,132 gonorrhea cases reported in 2004, 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 continued to decrease since 1999 to the current rate of 113.5 per 100,000 persons (**Figure 1**).<sup>1</sup> Gonorrhea rates remain high in the southeastern states, among African-Americans, and among adolescents of all racial and ethnic groups (**Figures 2, 3 and 4**).<sup>1-3</sup> 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.<sup>4</sup> In addition, data suggest that gonorrhea facilitates HIV transmission.<sup>5,6</sup>

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).<sup>8</sup> However, since the 1990s, fluoroquinolone-resistant *N. gonorrhoeae* (QRNG) have been reported from many parts of the world, including the United States<sup>9-14</sup> The increased prevalence of QRNG in Asia (where prevalence in several countries exceeds 60%)<sup>15</sup>, 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.<sup>8,11,12</sup> Data collected during January-September 2003 from all Gonococcal Isolate Surveillance Project (GISP) sites indicated an increase in QRNG among men who have sex with men (MSM) and led CDC to recommend in early 2004 that fluoroquinolones not be used to treat patients who are MSM.<sup>16</sup>

## GISP Overview

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.<sup>17</sup> 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 2004, *N. gonorrhoeae* isolates were collected from the first 25 men with urethral gonorrhea attending STD clinics each month in 28 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 interpreted according to criteria recommended by the National Committee for Clinical Laboratory Standards (NCCLS).<sup>18-20</sup> Clinical and demographic data were abstracted from medical records.

\* cefixime is not currently available in the US<sup>7</sup>

Important GISP findings have included:

- Resistance to penicillin and tetracycline is decreasing, but the prevalence of resistance to one or both agents remains above 15%;
- the emergence and increasing prevalence of resistance to the fluoroquinolones;<sup>9-14,16</sup>
- the appearance, with increasing prevalence, of decreased susceptibility to the macrolides;<sup>21</sup>
- the emergence of multi-drug resistant isolates (resistant to penicillin, tetracycline, and ciprofloxacin) with decreased susceptibility to cefixime;<sup>22</sup> and
- the increasing proportion of gonorrhea cases identified in men who have sex with men.<sup>23,24</sup>

GISP findings contributed to the development of CDC's STD treatment recommendations in 1993, 1998, and 2002.<sup>8,25,26</sup> 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.<sup>16</sup>

## 2004 GISP Sites

Twenty-eight STD clinics contributed 6,322 gonococcal isolates to GISP in 2004 (**Figure 5**). Fifteen of these sites have participated continuously since 1988: Albuquerque, 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 site has had intermittent participation in GISP: St. Louis 1987-1993 and 1995-2004. Sites joining GISP in 2003 included Detroit, Los Angeles, and Oklahoma City; no new sites joined in 2004. Anchorage and Salt Lake City withdrew from GISP in 2004. 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:** When comparing the age distribution of GISP participants to nationally reported cases of male gonorrhea, GISP had proportionally fewer 20-24 year olds and fewer <20 year olds than were reported nationally; otherwise the two groups had similar age distributions. In 2004 GISP participants ranged in age from 13 to 84 years, with a median age of 28 years.

**Race/Ethnicity:** The race/ethnicity distribution of GISP participants compared with nationally reported male gonorrhea patients in 2004 is shown in **Figure 7**. White, Hispanic, and Asian males were slightly over represented in GISP while African-American males were slightly under represented compared with the race/ethnicity distribution of nationally reported male gonorrhea patients in 2004.



**Sexual Orientation:** The proportion of GISP participants who were MSM increased every year from 1993 until 2003, when there was a slight decrease. This proportion increased in 2004 to 20.2% (**Figure 8**). The majority of GISP participants who were MSM were on the west coast, but sites such as Denver, Las Vegas, Minneapolis, Miami and Philadelphia had increases from 2003 in the proportion of GISP participants who were MSM (**Figure 9**).

**Reason for Clinic Attendance:** Most (95.5%) GISP participants in 2004 presented to the clinic on their own initiative (volunteers); others were referred as contacts of sexual partners diagnosed with gonorrhea or presented for tests-of-cure (**Figure 10**). There has been little change in this distribution over time. In 2004 97.4% of GISP participants reported dysuria and/or urethral discharge; 2.6% had no symptoms. These proportions have been relatively stable over time.

**History of Gonorrhea:** The percentage of GISP participants reporting ever having had gonorrhea reached a high point in 2004 with 52.3% reporting having ever had a previous episode. The percentage of GISP participants with a documented previous episode of gonorrhea in the last 12 months peaked at 23.6% in 2000 and decreased to 16.1% in 2004.

**Antimicrobial Treatment:** The antimicrobial agents given to GISP participants for gonorrhea therapy are shown in **Figure 11**. The proportion of GISP patients treated with cephalosporins decreased from a peak of 84.7% in 1990 to 57.0% in 2004. However, 57% represented an increase from the proportion treated with cephalosporins in 2003. The manufacture and distribution of cefixime was halted in 2002;<sup>7</sup> since then, the proportion of GISP participants treated with cefixime decreased from 15.0% in 2003 to 1.5% in 2004. With the discontinuation of cefixime, the use of “other cephalosporins” increased from 4.6% in 2003 to 14.5% in 2004. The proportion of GISP participants treated with fluoroquinolones (ciprofloxacin, ofloxacin or levofloxacin) increased from none in 1988 to a high of 42.0% in 2003 before declining slightly to 40% in 2004. The antimicrobial agents given to GISP participants for treatment of *Chlamydia trachomatis* infection are shown in **Figure 12**. The proportion of GISP patients treated with doxycycline or tetracycline decreased from a high of 99.4% in 1990 to 45.5% in 2004, while the proportion treated with azithromycin increased from 0.2% in 1992 to 52.4% in 2004.

**Supplemental Patient Data:** The proportion of GISP participants who were HIV-positive during 2004 was 8.8% (314/3579). Of 954 MSM reporting HIV testing information, 260 (27.3%) were HIV positive; 2.0% (53/2608) of heterosexuals were HIV positive. During the 60 days prior to diagnosis of gonorrhea, GISP patients reported the following behaviors:

- 5.2% (228/4375) took antibiotics;
- 12.0% (326/2727) traveled outside the state where the sentinel site is located;
- 1.8% (63/3558) used injection recreational drugs;
- 29.1% (923/3177) used non-injection recreational drugs
- 3.4% (108/3194) 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):<sup>18-20</sup>

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

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

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

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

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

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

Cefixime, MIC  $\geq 0.5$   $\mu\text{g/ml}$  (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, 15.9% (1008/6322) of isolates collected in 2004 were resistant to penicillin, tetracycline, or both (**Figure 13**); 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:<sup>8</sup>

- (1) penicillinase-producing *N. gonorrhoeae* (PPNG):  $\beta$ -lactamase-positive and tetracycline MIC  $< 16.0$   $\mu\text{g/ml}$ ;
- (2) plasmid-mediated tetracycline resistant *N. gonorrhoeae* (TRNG):  $\beta$ -lactamase-negative and tetracycline MIC  $\geq 16.0$   $\mu\text{g/ml}$ ;
- (3) PPNG-TRNG:  $\beta$ -lactamase-positive and tetracycline MIC  $\geq 16.0$   $\mu\text{g/ml}$ ;
- (4) chromosomally mediated penicillin-resistant *N. gonorrhoeae* (PenR): non-PPNG and penicillin MIC  $\geq 2.0$   $\mu\text{g/ml}$  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  $\geq 2.0$   $\mu\text{g/ml}$  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 0.6% in 2004 (**Figure 14**). The percentage of PenR isolates increased annually from 0.5% in 1988 to 5.7% in 1999 and subsequently decreased annually to 1.1% in 2004 (**Figure 15**). The prevalence of TRNG, was 3.4% in 2004 (**Figure 14**). TetR prevalence decreased every year since 1995, until 2002, when it slightly increased. In 2004 the prevalence was similar to that in 2003 at 6.1% (**Figure 15**). 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. In 2004 CMRNG increased slightly to 4.3%. The prevalence of PPNG-TRNG continues to be very low and was 0.5% in 2004.

### Susceptibility to Spectinomycin

All isolates were susceptible to spectinomycin in 2004. 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

Susceptibility testing for ceftriaxone began in 1988. There has not been an overall increase in MIC distribution since that time. **Figure 16** demonstrates MIC values for 3 years: the first year of testing, the current year, and a mid-point year (1996). In 2004, 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

Susceptibility testing for cefixime began in 1992. There has been a decrease in the percentage of isolates with higher MIC values since 1992, as demonstrated in **Figure 17**. In 2004, there were 2 isolates with decreased susceptibility to cefixime reported to GISP; both were from Los Angeles and demonstrated resistance to penicillin, tetracycline and ciprofloxacin. Prior to 2004 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  $\geq 4.0 \mu\text{g/ml}$ .<sup>24</sup> Gonococcal isolates with intermediate resistance (MICs 0.125-0.5  $\mu\text{g/ml}$ ) and resistance ( $\geq 1.0 \mu\text{g/ml}$ ) 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  $\geq 2.0 \mu\text{g/ml}$ .<sup>19,20</sup>

Susceptibility testing for ciprofloxacin began in 1990. A total of 7.6% (482/6322) of isolates exhibited intermediate resistance or resistance to ciprofloxacin in 2004 compared with 5.0% (328/6552) of isolates tested in 2003 (**Figure 18**). **Figure 19** demonstrates all MIC values for ciprofloxacin for 3 years: the first year of testing, the current year, and a mid-point year (1997). There was a shift toward higher MIC values from 1997 to 2004.

**Intermediate resistance:** In 2004, 0.8% (53/6322) of all GISP isolates exhibited intermediate resistance to ciprofloxacin. Of these isolates, 22.6% (12/53) came from San Francisco where they accounted for 4.0% (12/300) of isolates; 17.0% (9/53) came from Chicago where they accounted for 3.0% (9/300); 15.1% (8/53) came from Seattle where they accounted for 3.4% (8/235) of isolates tested; and 13.2% (7/53) came from Cleveland, where they accounted for 2.7% (7/264) of isolates tested in 2004. Elsewhere in 2004, 17 isolates of *N. gonorrhoeae* exhibiting intermediate resistance to ciprofloxacin were found in Birmingham (1), Cincinnati (2), Dallas (1), Los Angeles (1), Miami (2), Minneapolis (2), Orange County (3), Phoenix (1), Philadelphia (1), Portland (1), and San Diego (2). Albuquerque, Atlanta, Baltimore, Denver, Detroit, Greensboro, Honolulu, Las Vegas, Long Beach, New Orleans, Oklahoma City, St. Louis and Tripler did not have any isolates with intermediate resistance to ciprofloxacin during 2004.

**Resistance:** Four hundred twenty-nine, or 6.8% of GISP isolates were resistant to ciprofloxacin (MICs  $\geq 1.0$   $\mu\text{g/ml}$ ) in 2004. Ciprofloxacin-resistant isolates were identified in 85% (24/28) of all sentinel sites in 2004 compared with 70% (21/30) in 2003 and 48% (13/27) in 2002. Of note, 51.3% (220/429) of the 2004 isolates were from the California GISP sites, compared with 68.9% (186/270) during 2003. As the prevalence of ciprofloxacin-resistant isolates continues to increase in the United States more geographic variability is observed (**Figure 20**).

Resistance to ciprofloxacin among MSM continued to increase from 7.2% in 2002 to 15% in 2003 to 23.8% in 2004. Ciprofloxacin resistance also increased among heterosexuals from 0.9% in 2002 to 1.5% in 2003 to 2.9% in 2004 (**Figure 21**). When excluding GISP data from Hawaii and California, sites where CDC no longer recommends using fluoroquinolones in the treatment of gonorrhea, ciprofloxacin resistance among MSM continued to increase in 2004 to 17.8%, up from 7.7% in 2003 and 1.8% in 2002. Ciprofloxacin resistance among heterosexuals increased outside California and Hawaii to 1.3% in 2004, up from 0.4% in 2003 and 0.2% in 2002.

In Hawaii, the prevalence of ciprofloxacin resistance remained high. In 2004, 21 (22.8%) of 92 isolates submitted from Honolulu demonstrated ciprofloxacin resistance. At Tripler Army Medical Center, 2 of 7 isolates tested in 2004 demonstrated resistance to ciprofloxacin. In California, increases in the number of isolates resistant to ciprofloxacin were identified in 4 of 5 GISP sites, while one site, Orange County, experienced a decrease from 31.5% in 2003 to 20.5% in 2004. In 2004, 25.0% (25/100) of isolates from Long Beach were ciprofloxacin-resistant; in San Francisco, 24.3% (73/300) were resistant; in San Diego 20.6% (52/253) were resistant; in Los Angeles 13.8% (27/268) were resistant. In other west coast states, GISP sites experienced large increases in ciprofloxacin-resistance. In Seattle the prevalence of resistant isolates submitted to GISP doubled from 18 (7.0%) of 258 in 2003 to 38 (16.2%) of 235 in 2004, while in Portland the prevalence nearly quadrupled, from 4 (3.0%) of 132 in 2003 to 22 (11.5%) of 191 in 2004.

Prevalence of ciprofloxacin resistance also increased in other GISP sites in 2004 (Figure 20). Substantial increases occurred in Denver, Miami, Minneapolis and Phoenix, while smaller increases occurred in 8 other GISP sites. In Denver, ciprofloxacin-resistance increased from 0.7% in 2003 to 8.3% in 2004; in Miami resistance increased from 2.1% in 2003 to 6.8% in 2004; in Minneapolis resistance increased from 2.3% in 2003 to 9.3% in 2004; in Phoenix resistance increased from 2.6% in 2003 to 6.6% in 2004. Baltimore, Chicago, Dallas, New Orleans, and Philadelphia saw increases in QRNG prevalence, but to a lesser extent. Sites which saw ciprofloxacin resistant isolates for the first time in 2004 included Atlanta, Greensboro, and Oklahoma City. The prevalence of ciprofloxacin-resistance did not change from 2003 in Cincinnati – 0.3%, Cleveland – 0.4%, and Las Vegas – 2.4%. Albuquerque, Birmingham, Detroit and St. Louis did not identify ciprofloxacin-resistant isolates during 2004.

## Susceptibility to Azithromycin

Susceptibility testing for azithromycin began in 1992. **Figure 22** demonstrates MIC values for 3 years: the first year of testing, the current year, and a mid-point year (1998). In 2004 there was an increase from 1998 in the percentage of isolates with MIC values greater than 0.25  $\mu\text{g/ml}$ . 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  $\mu\text{g/ml}$ .<sup>27-30</sup>

In 2004 6.7% (426/6322) of isolates had azithromycin MIC  $\geq 0.5 \mu\text{g/ml}$  compared with 2.2% (145/6552) in 2003. In 1992, there were no isolates with azithromycin MIC  $\geq 1.0 \mu\text{g/ml}$  (range, 1.0-4.0  $\mu\text{g/ml}$ ). In 2004 there were 57 such isolates, compared to 26 in 2003. These isolates by location and number are: Atlanta (7); Baltimore (3); Chicago (7); Cincinnati (7); Cleveland (1); Las Vegas (8); Los Angeles (1); Miami (1); Minneapolis (8); New Orleans (1); Orange County (2); Philadelphia (2); Phoenix (2); San Diego (6); and San Francisco (1) .

## SUSCEPTIBILITY REPORTING OUTSIDE OF GISP

During 2004-2005, 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 2004.**

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 <sup>a</sup>
AZ	151	150	0	1	-	-	-	-	151	0	-	-
CA												
San Diego	203	190	0	13 <sup>b</sup>	-	-	-	-	203	0	-	-
San Francisco	110	90	0	20	110	0	110	0	110	0	110	0
FL <sup>c</sup>	39	37	0	2	-	-	-	-	39	0	-	-
HI	318	286	0	32	318	0	318	0 <sup>d</sup>	318	0	317	1
IN												
Indianapolis	1662	1614	0	48	-	-	-	-	1661	1	-	-
MA <sup>e</sup>	339	254	0	85	339	0	-	-	339	0	339	0
MI	750	738	1	11	750	0	-	-	750	0	-	-
MN <sup>f</sup>	88	82	0	6	88	0	88	0	87	1	88	0
MS	442	442	0	0	-	-	-	-	25 <sup>g</sup>	0	-	-
MT	9	8	0	1	9	0	9	0	9	0	6	3
NH	23	18	0	5	23	0	-	-	23	0	-	-
NJ	176	172	0	4 <sup>h</sup>	176	0	176	0	176	0	-	-
NY	77	66	9	2 <sup>h</sup>	77	0	77	0	77	0	67	10
NYC <sup>i</sup>	153	139	1	12	153	0	130	0	152	0	140	0
OR	159	144	0	15	15	0	15	0	15	0	15	0
TX	20	20	0	0	-	-	-	-	20	0	-	-
UT <sup>j</sup>	150	144	0	6	-	-	-	-	150	0	-	-
VA	16	16	0	0	16	0	-	-	16	0	-	-
WA												
Seattle	299	264	0	35	35	0	35	0	35	0	35	0
WI	453	444	3	6	453	0	-	-	448	5	445	8
Total	5637	5318	14	304	2562	0	958	0	4804	7	1562	22

Note:

- Cip=ciprofloxacin; Spc=spectinomycin; Cfx=cefixime; 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 following areas used disk diffusion as their testing methodology: Arizona, San Diego, Massachusetts, Michigan, Minnesota, Mississippi, New Hampshire, New Jersey, New York State, Utah, Virginia, and Wisconsin. Florida, Hawaii, Indianapolis, Montana, New York City, and Texas used the E-test method. Oregon and Washington state initially tested by disk diffusion and resistant isolates were tested by agar dilution. San Francisco tested by agar dilution.

<sup>a</sup>For Table 1, AziDS is defined as an isolate with azithromycin disk inhibition zone size  $\leq$  30mm or minimum inhibitory concentration (MIC)  $\geq$  1.0  $\mu$ g/ml.

<sup>b</sup>San Diego tested all isolates against ofloxacin, rather than against ciprofloxacin. As of August 2004, susceptibility testing for male GC specimens is no longer performed, except on request by the physician, and only female GC specimens are tested for resistance.

<sup>c</sup>Florida tested all isolates against ciprofloxacin, cefditoren, cefnidir, ceftriaxone, levofloxacin, and ofloxacin.

<sup>d</sup>Hawaii tested all isolates against cefpodoxime, rather than cefixime as of February 2004. Hawaii had one isolate with decreased susceptibility to cefpodoxime which was confirmed at the CDC GC laboratory.

<sup>e</sup>Massachusetts tested all isolates against azithromycin, cefotaxime, cefpodoxime, ceftriaxone, ciprofloxacin, ceftioxin, penicillin, and spectinomycin. As of November 2004, GC susceptibility testing stopped for cefotaxime and penicillin.

<sup>f</sup>Minnesota tested all isolates against azithromycin, cefixime, ceftriaxone, ciprofloxacin, penicillin, and spectinomycin and tetracycline.

<sup>g</sup>Mississippi screened all 442 isolates for QRNG using ciprofloxacin; 25 of the 442 isolates were also tested against penicillin, tetracycline, and ceftriaxone.

<sup>h</sup>New Jersey and New York tested isolates against ofloxacin and ciprofloxacin.

<sup>i</sup>New York City Public Health Laboratories performed GC culture for the Bureau of STD Control beginning the 3rd quarter of 2004. Specimens cultured before September 1st were tested for fluoroquinolone resistance using levofloxacin and ciprofloxacin, after September 1st ofloxacin and ciprofloxacin were utilized. Number of isolates tested against a given antibiotic varies.

<sup>j</sup>Utah tested isolates against ofloxacin and ciprofloxacin.

## Observations

The STD project areas and APHL laboratories which previously provided *Neisseria gonorrhoeae* susceptibility testing data<sup>31</sup>, were asked to share their 2004 testing results; data from a total of 6096 isolates were available. Isolates from most represented 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 contrast to GISP, multiple non-GISP isolates from various anatomic sites may be submitted from a single patient, so the 6096 non-GISP isolates likely represent fewer than 6096 patients with gonorrhea.

These data demonstrate that 5.6% (340/6096) of non-GISP isolates were resistant to ciprofloxacin or ofloxacin. Fluoroquinolone-resistant isolates were identified in Arizona (0.7%); San Diego, California (6.4%); San Francisco, California (18.2%); Florida (5.1%); Hawaii (10.1%); Indiana (2.9%); Massachusetts (25.1%); Michigan (1.5%); Minnesota (6.8%); Montana (11.1%); New Hampshire (21.7%); New Jersey (2.3%); New York State (2.6%); New York City (7.8%); Oregon (9.4%); Utah (4%); Seattle, Washington (11.7%); and Wisconsin (1.3%).

For the first time in 2004, information on gender was requested and was provided by 15 of the 21 sites providing susceptibility testing data. Information was provided on 4347 isolates from males, of which 307 demonstrated resistance to quinolones (7.1%). Information was provided on 1086 isolates from women, of which 14 (from 2 sites) were resistant to quinolones (1.3%). The 7.1% prevalence obtained from male isolates in sites outside GISP was comparable to the 6.8% prevalence obtained from sites within GISP.

## Acknowledgments

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## ADDITIONAL RESOURCES

Recent publications using GISP data include an article in EID<sup>32</sup> and a late-2004 article in Sexually Transmitted Diseases.<sup>33</sup> Presentations of GISP data were made at the Tracking Resistant Organisms: Workshop for Improving State-based Surveillance Programs in Atlanta, Georgia in April 2004, at the 16<sup>th</sup> biennial meeting of the International Society for Sexually Transmitted Diseases Research (ISSTD), in Amsterdam, the Netherlands in July 2005<sup>34</sup>, and at the Annual Meeting of the Infectious Diseases Society of America (IDSA) in San Francisco, California in October 2005.<sup>35</sup>

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 2004 STD Surveillance Report<sup>1</sup> (<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/drugresistance/publications/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_5](http://www.who.int/drugresistance/publications/WHO_CDS_CSR_DRS_2001_5));
- 3) the UNAIDS/WHO Guidelines for Sexually Transmitted Infections Surveillance (<http://www.who.int/hiv/pub/sti/pubstiguideines>);
- 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_resistance_in_Neisseria_gonorrhoeae.pdf)).



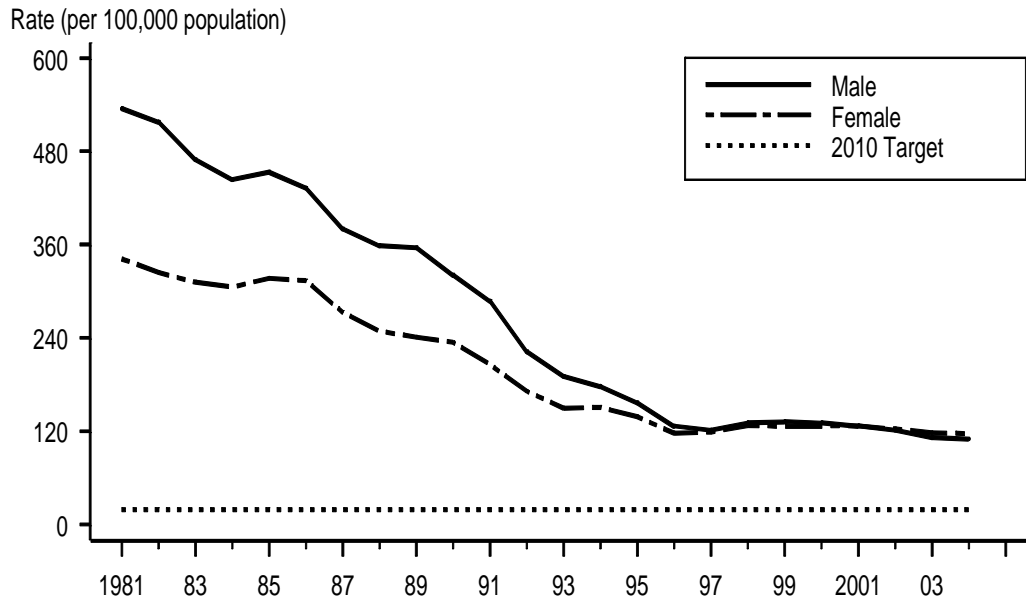
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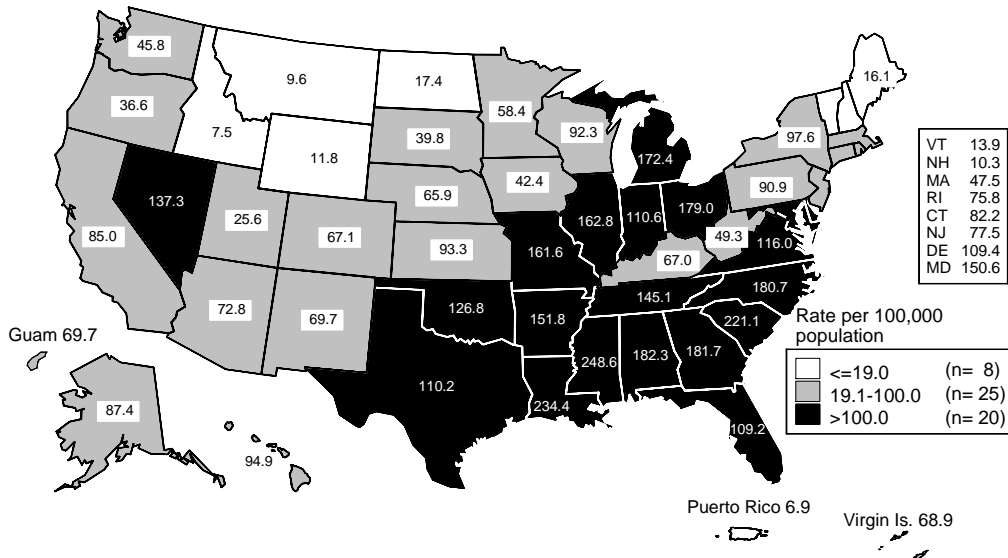
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**Figure 1. Gonorrhea — Rates by sex: United States, 1981–2004 and the Healthy People 2010 target**



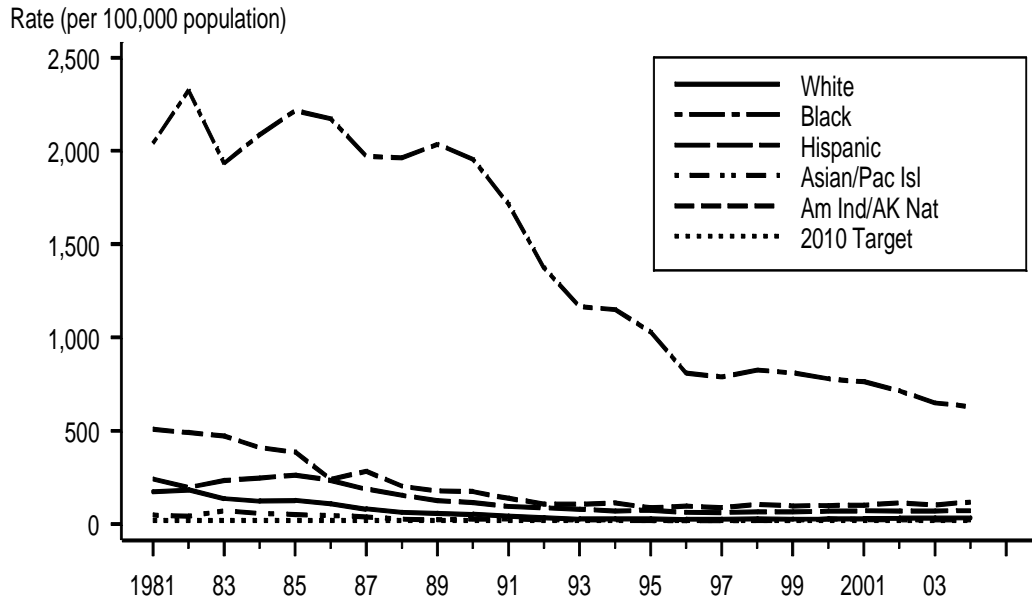
Note: The Healthy People 2010 objective for gonorrhea is 19.0 cases per 100,000 population.

**Figure 2. Gonorrhea — Rates by state: United States and outlying areas, 2004**

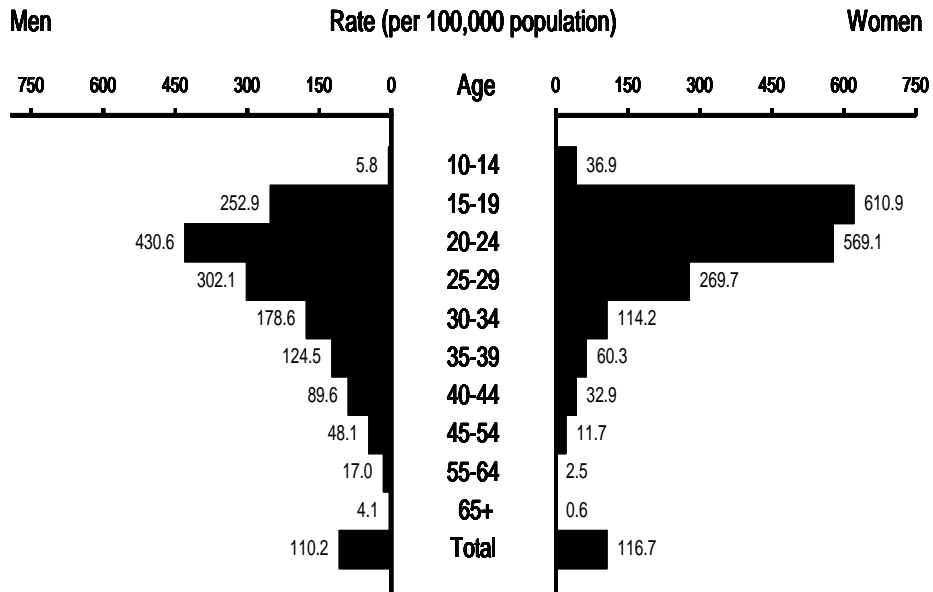


Note: The total rate of gonorrhea for the United States and outlying areas (Guam, Puerto Rico and Virgin Islands) was 112.1 per 100,000 population. The Healthy People 2010 target is 19.0 cases per 100,000 population.

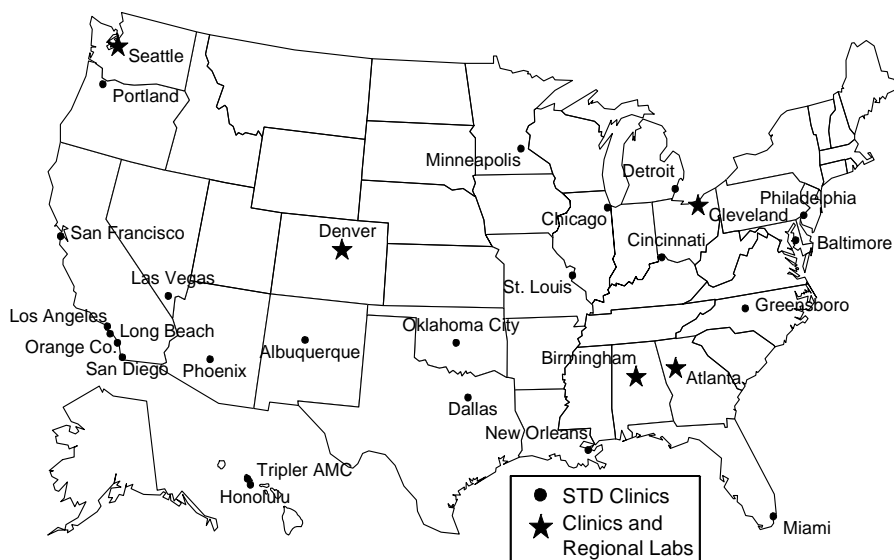
**Figure 3. Gonorrhea — Rates by race and ethnicity: United States, 1981–2004 and the Healthy People 2010 target**



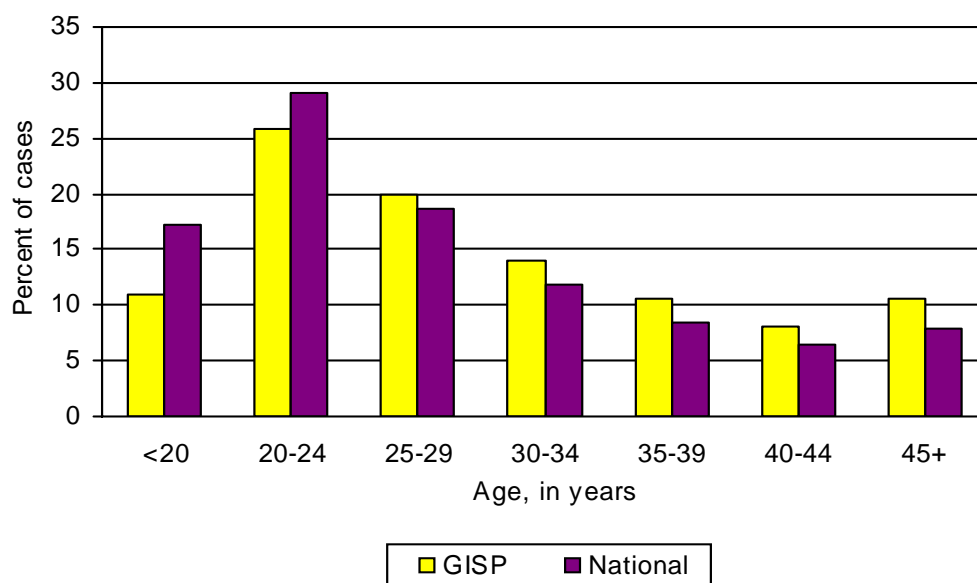
**Figure 4. Gonorrhea — Age- and sex-specific rates: United States, 2004**



**Figure 5. Gonococcal Isolate Surveillance Project (GISP) — Location of participating clinics and regional laboratories: United States, 2004**

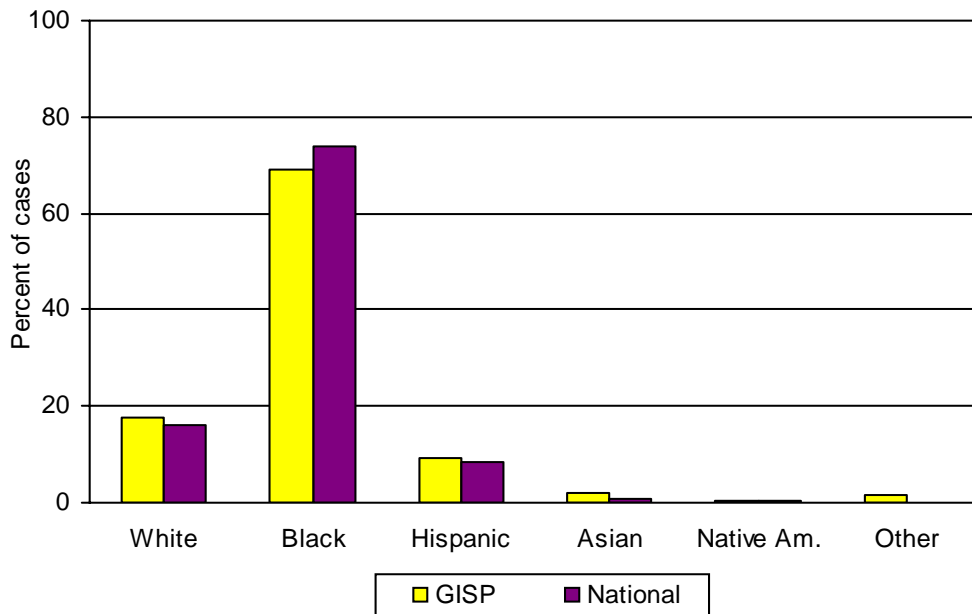


**Figure 6. Age distribution of GISP participants and nationally reported gonorrhea cases in men, 2004**



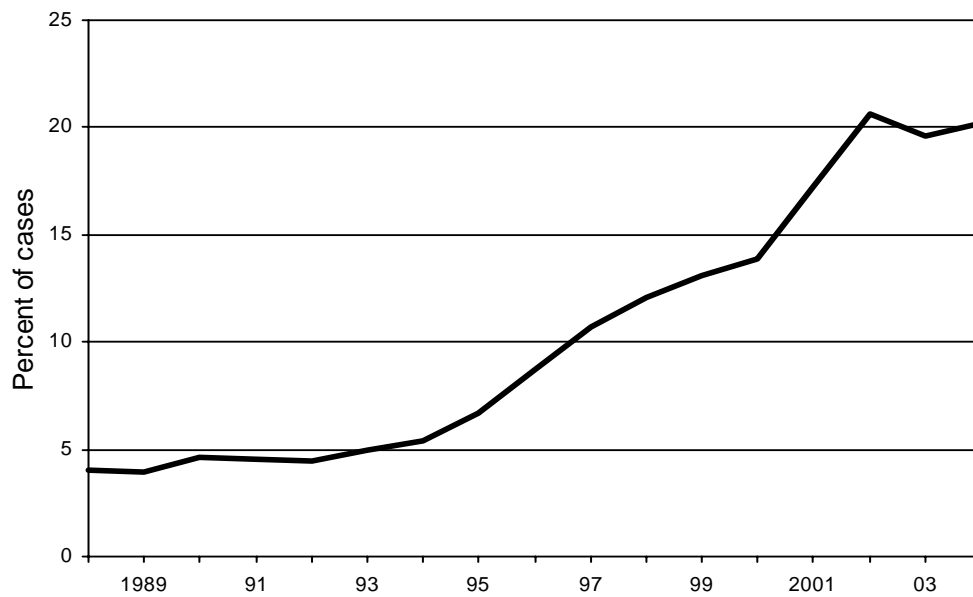
Note: The age<20 category includes ages 10-19 for national cases, and ages 13-19 for GISP; over 98% of the GISP cases in the <20 category are ages 15-19. National cases with unknown ages were excluded.

**Figure 7. Race distribution of GISP participants and nationally reported cases of gonorrhea in men, 2004**

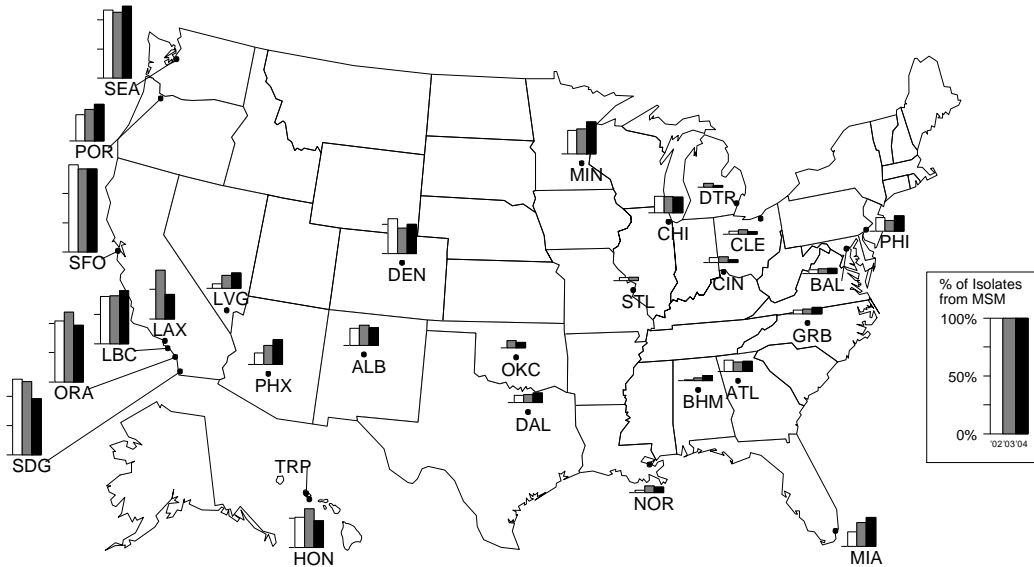


Note: The "Other" category is not used in national gonorrhea reporting. National cases with unknown race were excluded. Asian includes Native Hawaiians and Other includes participants who selected more than one race category.

**Figure 8. Percentage of GISP cases that occurred among men who have sex with men (MSM), 1988-2004**

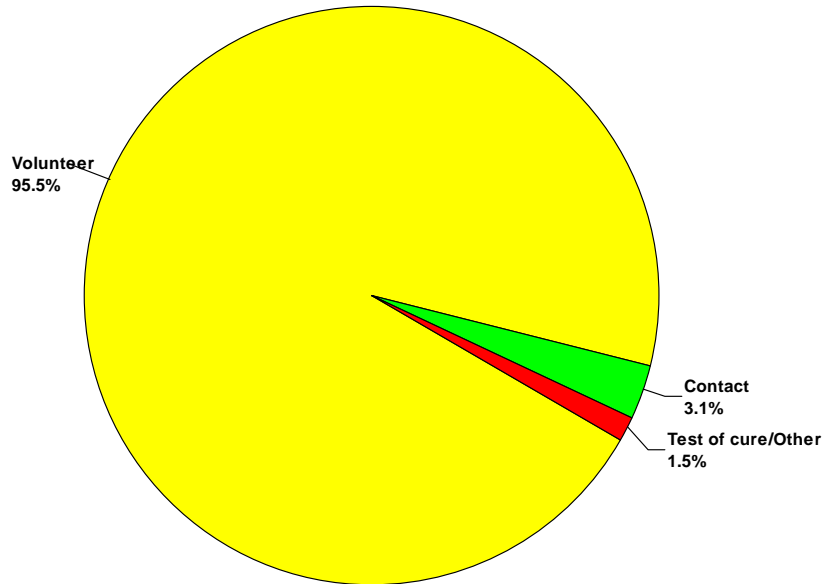


**Figure 9. Gonococcal Isolate Surveillance Project (GISP) — Percent of *Neisseria gonorrhoeae* isolates obtained from MSM attending STD clinics, 2002–2004**



Note: Not all clinics participated in GISP for the last 3 years. Clinics include: ALB=Albuquerque, NM; 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; GRB=Greensboro, NC; HON=Honolulu, HI; LAX=Los Angeles, CA; LBC=Long Beach, CA; LVC=Las Vegas, NV; MIA=Miami, FL; MIN=Minneapolis, MN; NOR=New Orleans, LA; OKC=Oklahoma City, OK; ORA=Orange County, CA; PHI=Philadelphia, PA; PHX=Phoenix, AZ; POR=Portland, OR; SDG=San Diego, CA; SEA=Seattle, WA; SFO=San Francisco, CA; STL=St. Louis, MO (only has data through 2003); and TRP=Tripler Army Medical Center, HI (does not provide sexual risk behavior data).

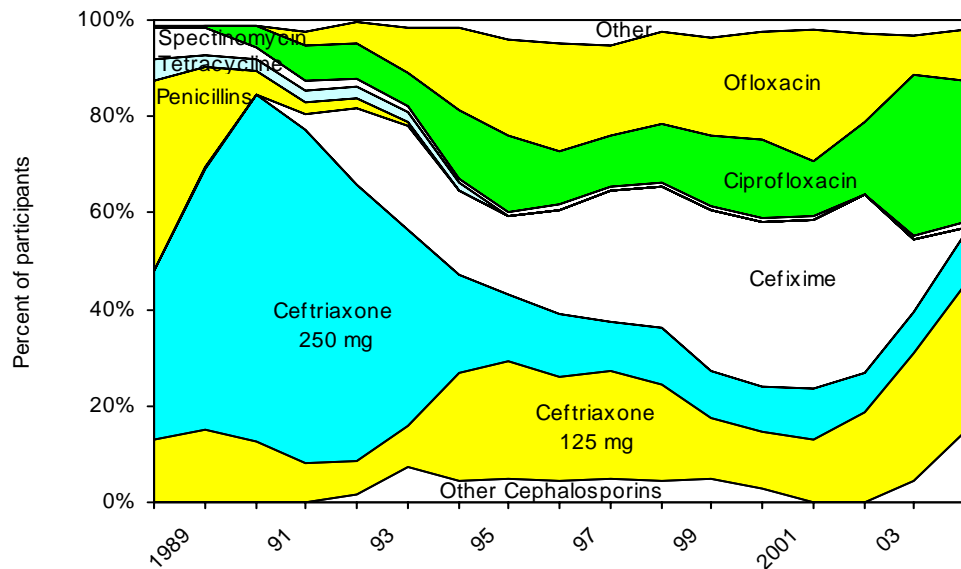
**Figure 10. Reason for clinic attendance among GISP participants, 2004**



Note: Contact=has sexual partner with gonorrhea

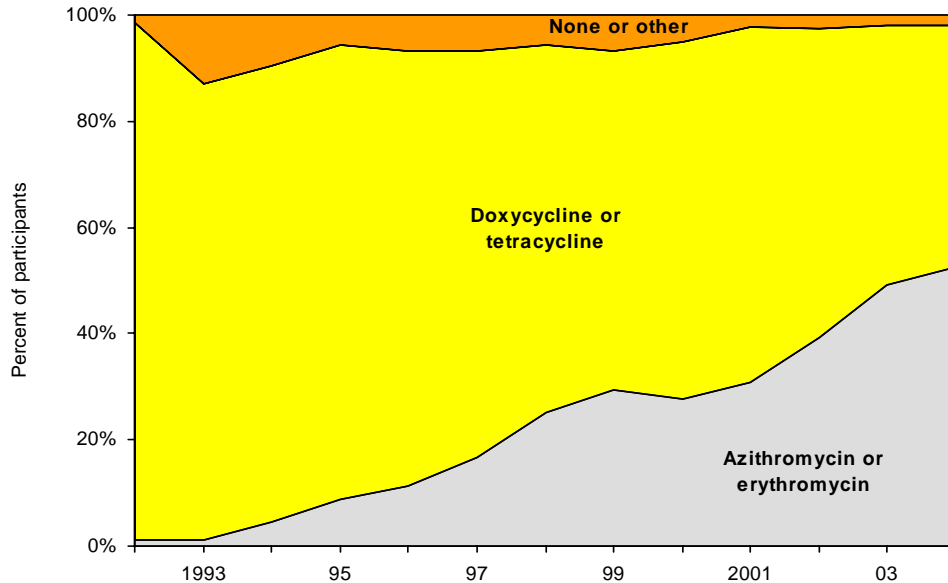


**Figure 11. Drugs used to treat gonorrhea in GISP participants, 1988–2004**



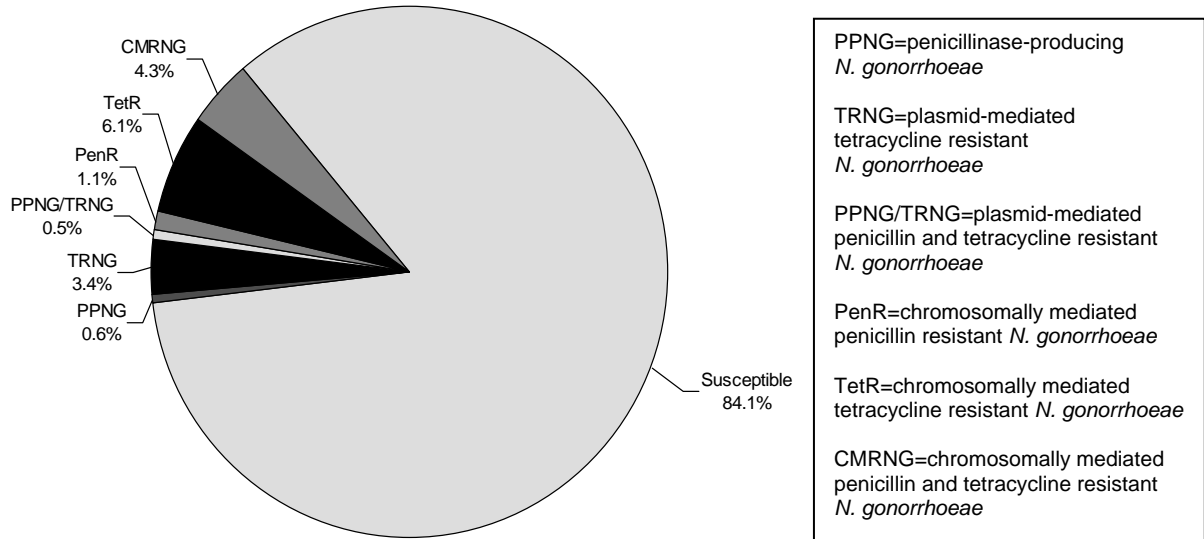
Note: For 2004, “Other” includes no therapy (1.6%), azithromycin 2 g (0.3%), levofloxacin (0.2%), and other less frequently used drugs.

**Figure 12. Drugs used to treat *Chlamydia trachomatis* infection in GISP participants, 1992-2004**

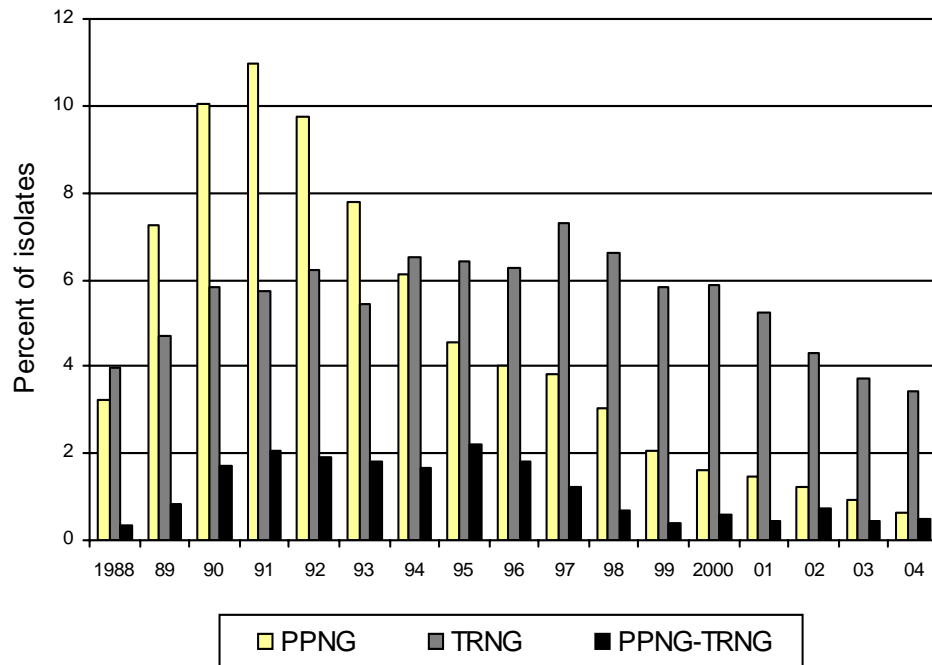


Note: For each year, “Other” accounted for only 0 – 0.9% of *C. trachomatis* treatment and erythromycin accounted for only 0.1 – 1.0% of *C. trachomatis* treatment.

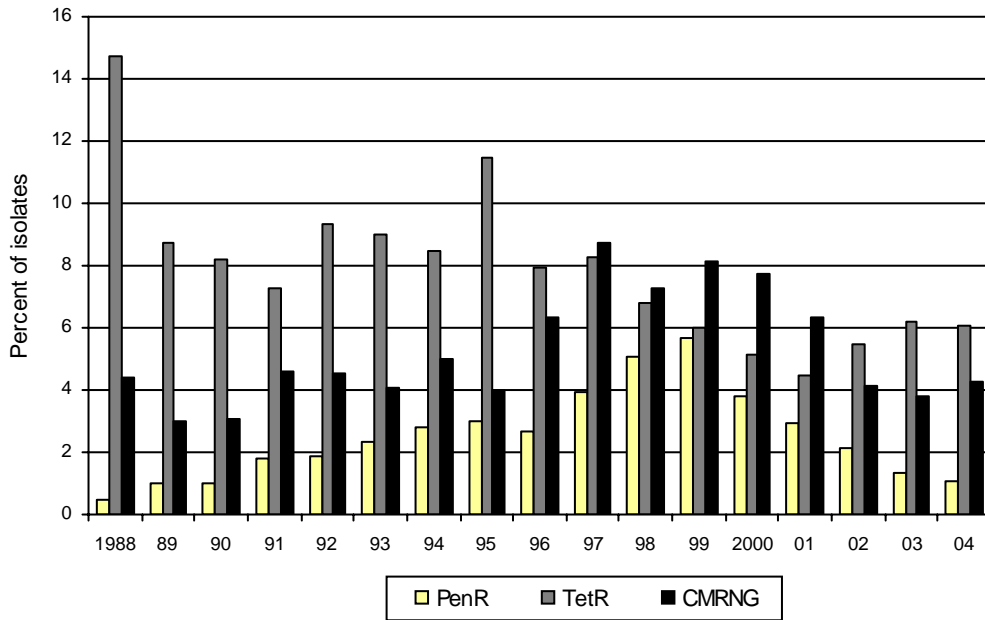
**Figure 13. Penicillin and tetracycline resistance among GISP isolates, 2004**



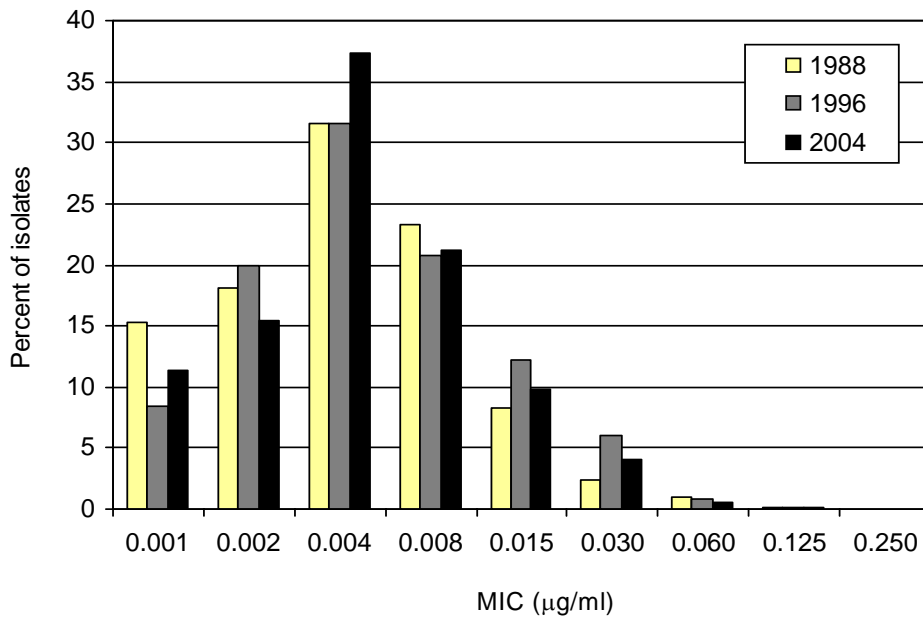
**Figure 14. Plasmid-mediated resistance to penicillin and tetracycline among GISP isolates, 1988–2004**



**Figure 15. Chromosomally mediated resistance to penicillin and tetracycline among GISP isolates, 1988-2004**

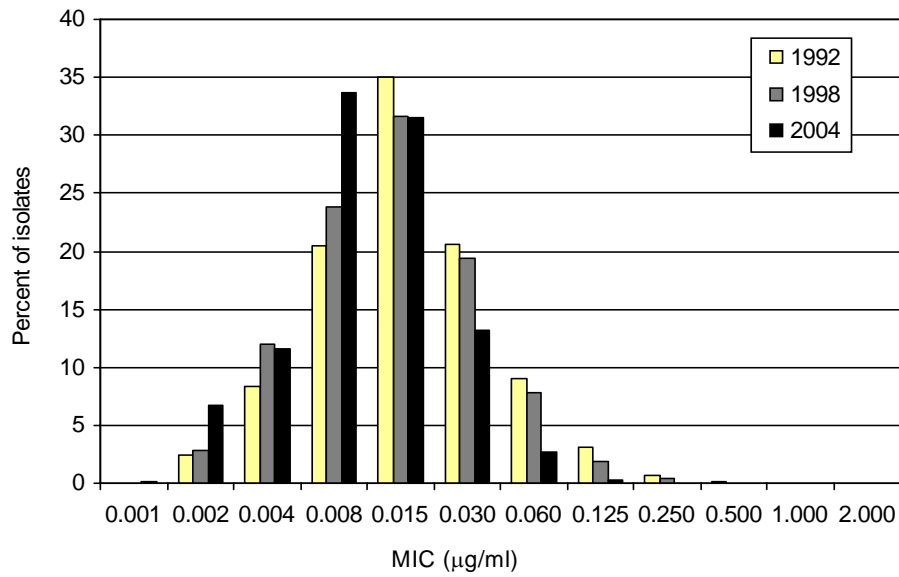


**Figure 16. Distribution of MICs to ceftriaxone among GISP isolates, 1988, 1996, and 2004**



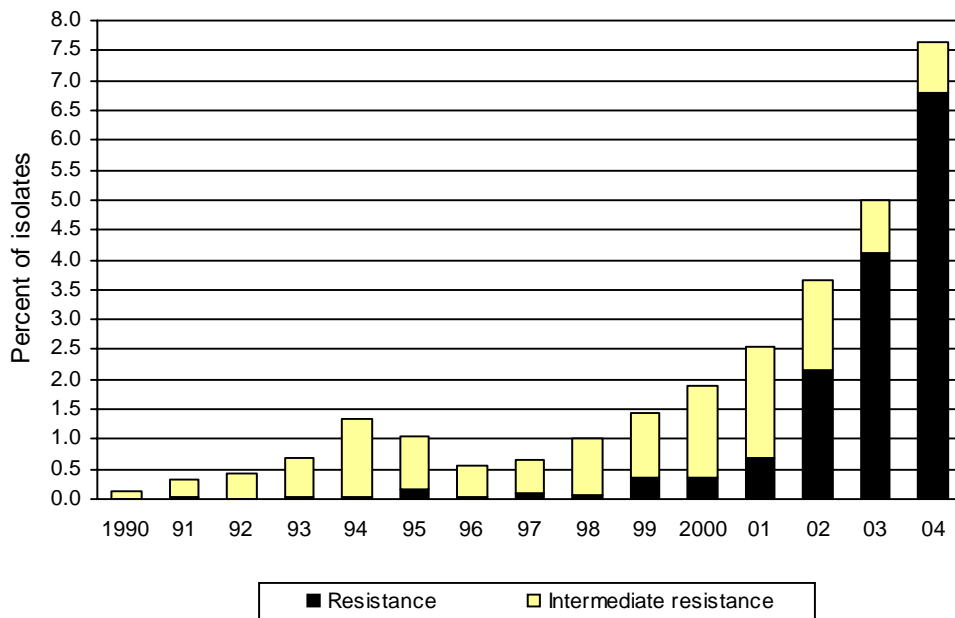
Note: In 1988, there was one isolate with MIC 0.25 µg/ml. In 1996 and 2004, there were no isolates with MIC 0.25 µg/ml.

**Figure 17. Distribution of MICs to cefixime among GISP isolates, 1992, 1998, and 2004**

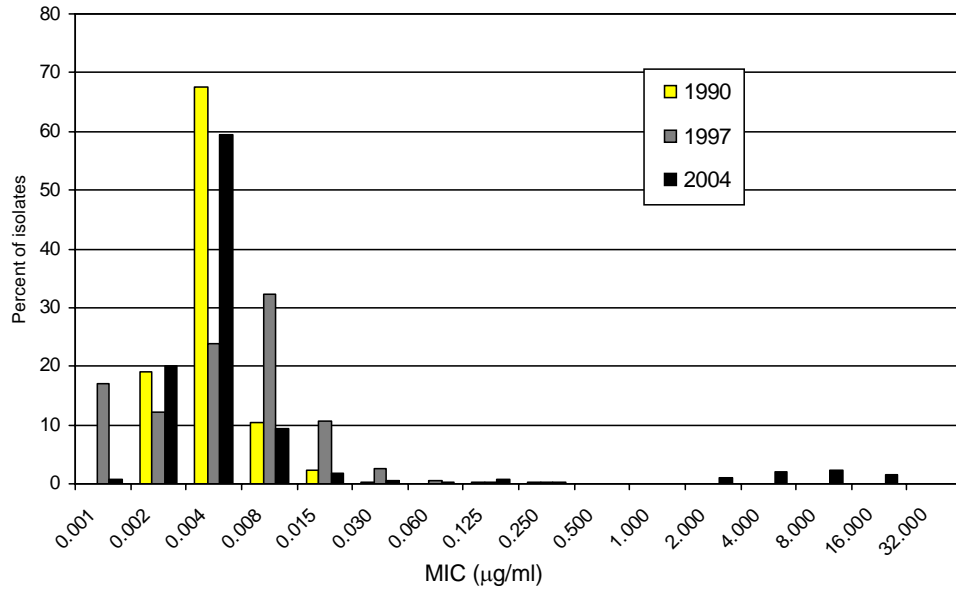


In 1992, there were six isolates with MIC 0.5 µg/ml, three isolates with MIC 1.0 µg/ml, and two isolates with MIC 2.0 µg/ml. In 1998, there were two isolates with MIC 0.5 µg/ml and three isolates with MIC 1.0 µg/ml. In 2004, there were two isolates with MIC 0.5 µg/ml.

**Figure 18. Percentage of GISP isolates with intermediate resistance or resistance to ciprofloxacin, 1990-2004**

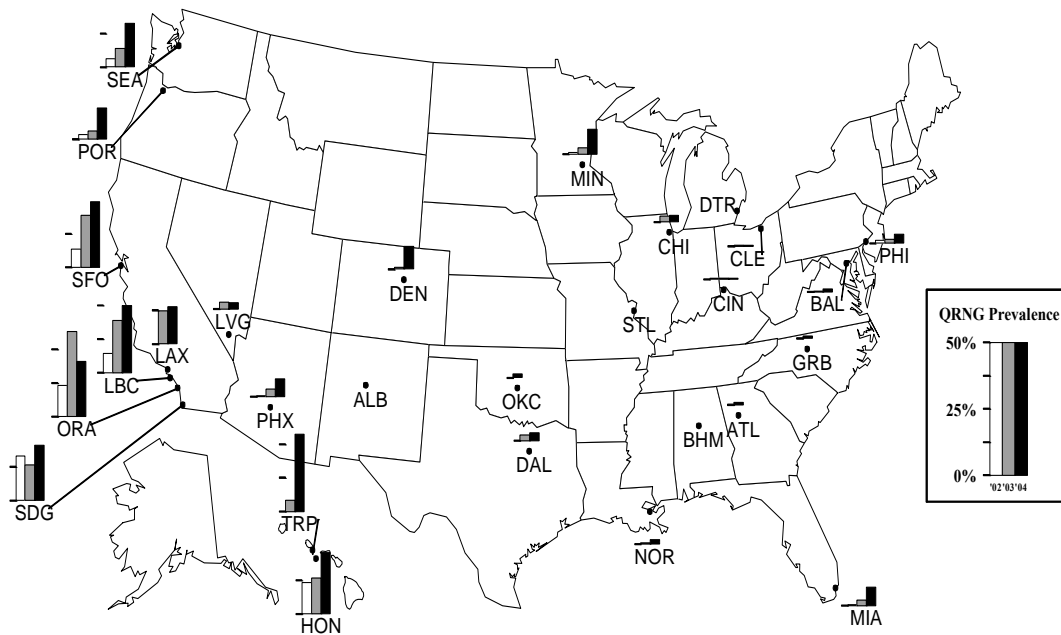


**Figure 19. Distribution of MICs to ciprofloxacin among GISP isolates, 1990, 1997, and 2004**

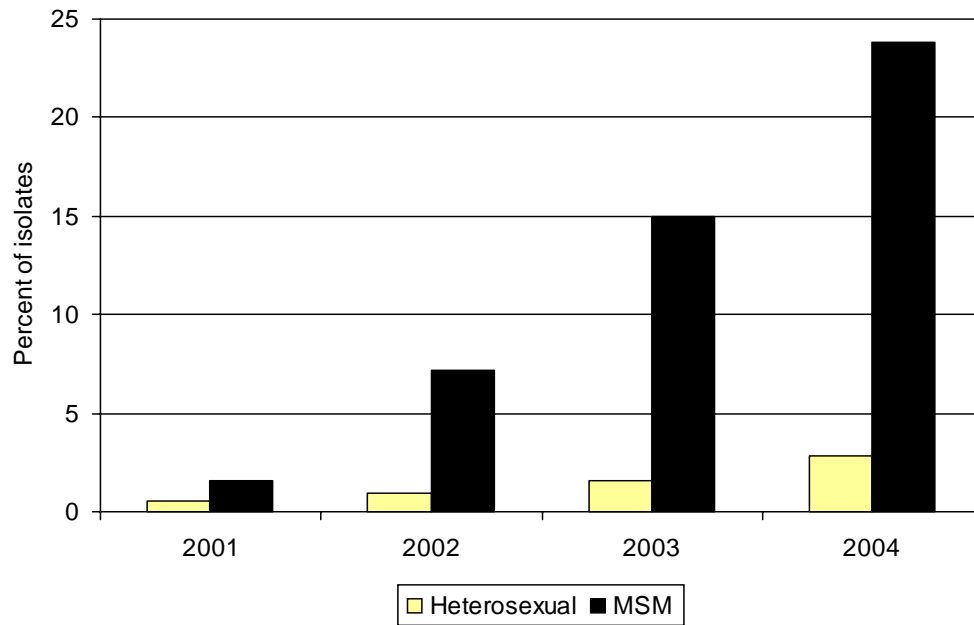


Note: In 1990, there were no isolates with MIC > 0.25 µg/ml. In 1997 there was one isolate with MIC 0.5 µg/ml, one isolate with MIC 1.0 µg/ml, two isolates with MIC 2.0 µg/ml, and two isolates with MIC 16.0 µg/ml. In 2004, there were two isolates with MIC 0.5 µg/ml, six isolates with MIC 1.0 µg/ml, sixty isolates with MIC 2.0 µg/ml, one hundred twenty-seven isolates with MIC 4.0 µg/ml, one hundred forty isolates with MIC 8.0 µg/ml, ninety-two isolates with MIC 16.0 µg/ml and four isolates with MIC 32.0 µg/ml.

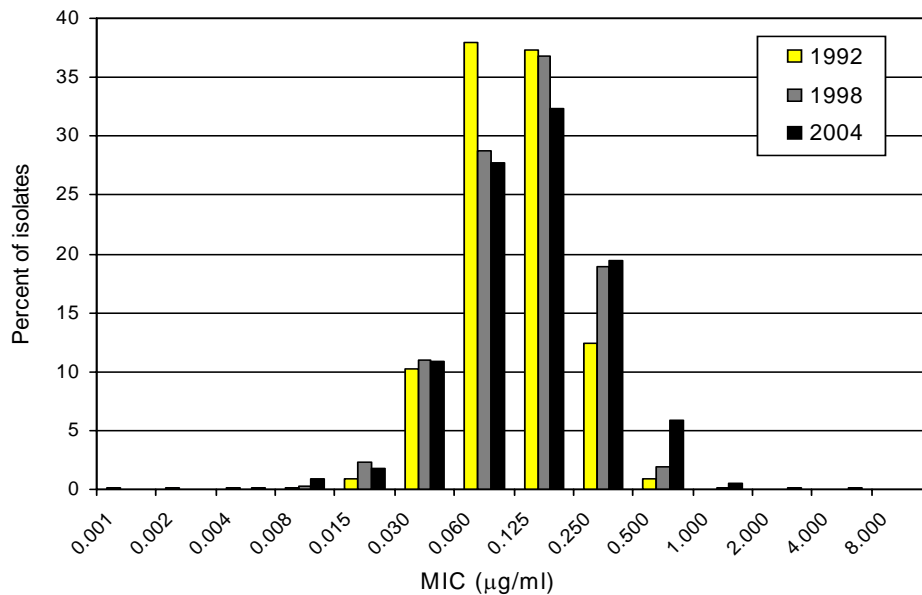
**Figure 20. Prevalence of ciprofloxacin resistant *Neisseria gonorrhoeae* by site, 2002-2004**



**Figure 21. Percentage of GISP isolates with resistance to ciprofloxacin by sexual behavior, 2001-2004**



**Figure 22. Distribution of MICs to azithromycin among GISP isolates, 1992, 1998, and 2004**



Note: In 1992, there were no isolates with MIC > 0.5 µg/ml. In 1998, there were four isolates with MIC 1.0 µg/ml, two isolates with MIC 2.0 µg/ml, and one isolate with MIC 4.0 µg/ml. In 2004, there were thirty-three isolates with MIC 1.0 µg/ml, ten isolates with MIC 2.0 µg/ml, eleven isolates with MIC 4.0 µg/ml, and three isolates with MIC 8.0 µg/ml.

## CLINIC-SPECIFIC DEMOGRAPHIC, CLINICAL, AND LABORATORY DATA

The remainder of this report provides clinic-specific figures for each of the 28 clinics that participated in GISP in 2004. 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 2004 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*