

Antimicrobial Resistance and <i>Neisseria gonorrhoeae</i>	
Clinical Features	<i>N. gonorrhoeae</i> causes infection of mucosal membranes including the cervix, rectum, and throat. If untreated, gonorrhea remains a major cause of pelvic inflammatory disease (PID), tubal infertility, ectopic pregnancy, and chronic pelvic pain. Epidemiologic studies provide strong evidence that gonococcal infections facilitate HIV transmission.
Incidence	<p>Gonorrhea, caused by <i>Neisseria gonorrhoeae</i>, is second only to chlamydial infections in the number of cases reported to the Centers for Disease Control and Prevention (CDC); 361,705 cases were reported to CDC in 2001 (www.cdc.gov/std/stats/). It is estimated that only one-half of the actual number of infections are reported. The number of reported cases of gonorrhea increased steadily from 1964 to 1975. During 1975-1997, the U.S. gonorrhea rate declined by 73.9%; it increased by 7.9% between 1997 and 1998 and has remained stable with a rate in 2001 of 128.5 cases per 100,000.</p> <p>The incidence of gonorrhea is highest in high-density urban areas among persons under 24 years of age who have multiple sex partners and engage in unprotected sexual intercourse. Increases in gonorrhea prevalence have been noted since 1993 among men who have sex with men.</p>
Costs	In 1997, the estimated annual direct medical cost of gonorrhea treatment in the United States was \$56 million (American Social Health Association. Sexually Transmitted Diseases in America: How many cases and at what cost? December 1998). Direct medical costs are dollars spent within the health care system treating gonorrhea and its complications and do not include nonmedical indirect costs such as lost wages or productivity.
Risk Groups	Because gonococcal infections among women often are asymptomatic, an important component of gonorrhea control in the United States continues to be the screening of women at high risk for STDs. Among women, 15-19 year olds have the highest gonorrhea rates and among men, 20-24 year olds have the highest rates. Gonorrhea rates are highest in the South and among African-Americans.
Opportunities	Ongoing STD prevention efforts, such as the current syphilis elimination campaign and HIV prevention activities, may assist in lowering rates of gonorrhea infection. Additionally, the expanding <i>Chlamydia trachomatis</i> screening program, which often uses combined gonorrhea/chlamydia diagnostic tests, may also result in improved gonorrhea control.

<p>Prevention</p>	<p>When used consistently and correctly, male latex condoms are effective in preventing the sexual transmission of HIV infection and can reduce the risk for other STDs (i.e., gonorrhea, chlamydia, and trichomonas). However, because condoms do not cover all exposed areas, they are likely to be more effective in preventing infections transmitted by fluids from mucosal surfaces (e.g., gonorrhea, chlamydia, trichomonas, and HIV) than in preventing those transmitted by skin-to-skin contact (e.g. herpes simplex virus, HPV, syphilis, and chancroid). Condom failure usually results from inconsistent or incorrect use rather than condom breakage.</p> <p>Patients should be advised that condoms must be used consistently and correctly to be highly effective in preventing STDs. Patients should be instructed in the correct use of condoms.</p>
<p>Treatment Guidelines</p>	<p>2002 STD Treatment Guidelines: http://www.cdc.gov/STD/treatment/</p>
<p>Antimicrobial Resistance, General Information</p>	<p>Antimicrobial resistance in <i>N. gonorrhoeae</i> remains an important challenge to controlling gonorrhea; gonococcal strains may be resistant to penicillins, tetracyclines, spectinomycin, and fluoroquinolones. Resistance to CDC-recommended doses of ciprofloxacin and ofloxacin exceeds 40% in some Asian countries (World Health Organization (WHO) Western Pacific Region Gonococcal Antimicrobial Susceptibility Programme (GASP) Report- 2000. <i>Commun Dis Intell</i> 2001; 25:274-277).</p> <p>Fluoroquinolone-resistant strains of <i>N. gonorrhoeae</i> have also been reported in the United States and Canada. The proportion of gonococcal isolates in Hawaii that are fluoroquinolone-resistant currently exceeds 10% ("Fluoroquinolone-Resistance in <i>Neisseria gonorrhoeae</i>, Hawaii, 1999, and Decreased Susceptibility to Azithromycin in <i>N. gonorrhoeae</i>, Missouri, 1999." <i>MMWR</i>. 2000; 49(37): 833-7) and increasing numbers of resistant strains have been identified in the continental United States.</p> <p>Antimicrobial resistance in <i>N. gonorrhoeae</i> occurs as plasmid-mediated resistance to penicillin and tetracycline, and chromosomally mediated resistance to penicillins, tetracyclines, spectinomycin, and fluoroquinolones.</p>
<p>Surveillance</p>	<p>Surveillance for antimicrobial resistance in <i>N. gonorrhoeae</i> in the United States is conducted through the Gonococcal Isolate Surveillance Project (GISP). The Gonococcal Isolate Surveillance Project (GISP) was established in 1986 to monitor trends in antimicrobial susceptibilities of strains of <i>N. gonorrhoeae</i> in the United States and to establish a rational basis for the selection of gonococcal therapies. Approximately 26 cities participate in GISP. Data from this project have been reported and used to revise the CDC's STD Treatment Guidelines in 1989, 1993, 1998, and 2002.</p> <p>GISP protocol: http://www.cdc.gov/std/gisp/</p> <p>GISP annual reports: http://www.cdc.gov/std/gisp/Reports.htm</p>

Antimicrobial Resistance Trends

Antimicrobial resistance remains an important consideration in the treatment of gonorrhea. Overall, 20.9% of isolates collected in 2001 by the GISP were resistant to penicillin, tetracycline, or both. The percentage of GISP isolates that were penicillinase-producing *Neisseria gonorrhoeae* (PPNG) declined from a peak of 11.0% in 1991 to 1.5% in 2001. In contrast, the percentage of isolates with chromosomally mediated resistance to penicillin had increased from 0.5% in 1988 to 5.7% in 1999 and then declined to 2.9% in 2001. The prevalence of chromosomally mediated tetracycline resistance increased in 1995 to 11.5% and subsequently declined to 4.4% in 2001. However, the prevalence of isolates with chromosomally mediated resistance to penicillin and tetracycline (CMRNG) increased from a low of 3.0% in 1989 to 6.4% in 2001.

Resistance to ciprofloxacin was first identified in GISP in 1991. From 1991 to 1998, fewer than 9 ciprofloxacin-resistant isolates were identified each year and such isolates were identified in only a few GISP clinics. In 2000, similar to 1999, 19 (0.4%) ciprofloxacin-resistant GISP isolates were identified in 7 of the 25 GISP clinics. In 2001, 38 (0.7%) ciprofloxacin-resistant GISP isolates were identified in 6 clinics. Notably, in Honolulu, the proportion of GISP isolates that were resistant to ciprofloxacin continued to increase quite markedly and was 20.3% in 2001. This ongoing trend reinforces the recommendation made by CDC in 2000 that fluoroquinolones not be used to treat gonorrhea acquired in Hawaii. In 2001, elevated proportions of GISP isolates resistant to ciprofloxacin were identified in all four California GISP sites (3.4% in San Francisco, 3.0% in Long Beach, 2.3% in Orange County, and 2.1% in San Diego); as a result, in early 2002, the California STD Program recommended that fluoroquinolones no longer be used for gonorrhea treatment in California.

In 2001, four (0.1%) GISP isolates had decreased susceptibility to cefixime; no GISP isolates had decreased susceptibility to ceftriaxone. The proportion of GISP isolates demonstrating decreased susceptibility to ceftriaxone or cefixime has remained very low over time. To date, no cephalosporin resistance has been identified in GISP. However, it was notable that three of the four isolates with decreased susceptibility to cefixime were also resistant to penicillin, tetracycline, and ciprofloxacin; such multi-drug resistance in combination with decreased susceptibility to cefixime has rarely been identified in the United States (Wang SA, Lee MV, Iverson CJ, O'Connor N, Ohye RG, Hale JA, Knapp JS, Effler PV, Weinstock HS. [Multi-drug resistant *Neisseria gonorrhoeae* with decreased susceptibility to cefixime, Hawaii 2001](#). [Abstract] International Conference on Emerging Infectious Diseases, Atlanta, Georgia, March 25, 2002.) [Note: no NCCLS criteria currently exist for resistance of *N. gonorrhoeae* to cephalosporins].

The proportion of GISP isolates demonstrating elevated minimum inhibitory concentrations (MICs) to azithromycin has been increasing since GISP began monitoring azithromycin susceptibility in 1992. In 1992, 0.9% of GISP isolates had azithromycin MIC ≥ 0.5 $\mu\text{g/ml}$ compared with 1.5% in 2001. In 1992, there were no isolates with azithromycin MIC ≥ 1.0 $\mu\text{g/ml}$, but in 2000 there were 15 such isolates. [Note: no NCCLS criteria currently exist for susceptibility or resistance of *N. gonorrhoeae* to azithromycin].

Challenges	Major challenges to monitoring antimicrobial resistance of <i>N. gonorrhoeae</i> include substantial declines in the use of gonorrhea culture for testing and declines in the number of laboratories performing gonorrhea susceptibility testing. There has been a proliferation of non-culture diagnostic testing for gonorrhea. In many clinical settings, non-culture testing has completely replaced testing using culture. Currently, susceptibility testing can only be performed on <i>N. gonorrhoeae</i> growing in culture. Technology that allows susceptibility testing from non-culture specimens is needed.
Laboratory Issues	Research into determining mechanisms of resistance for the newer antimicrobials and for determining the upper limits of resistance conferred by currently recognized mechanisms of resistance to fluoroquinolones is ongoing.
CDC role	CDC conducts national surveillance for antimicrobial resistance in <i>N. gonorrhoeae</i> via GISP and performs outbreak investigations of resistant gonococcal infections as needed. CDC also performs laboratory confirmation for clinicians who identify or suspect antimicrobial resistance in patients with gonorrhea. CDC publishes updated STD Treatment Guidelines on a regular basis to guide use of appropriate and effective antimicrobial therapy for gonorrhea and other STD treatment.