

most widely used and studied, it is not the optimal agent because it fails to eradicate carriage in 15–20% of cases, rates of adverse events have been high, compliance is affected by the need for four doses, and emerging resistance has been reported. Ceftriaxone as a single IM or IV injection is highly (97%) effective in carriage eradication and can be used at all ages and in pregnancy. Reduced susceptibility of isolates to ceftriaxone has occasionally been reported. Ciprofloxacin or ofloxacin is preferred in some countries; these agents are highly effective and can be administered by mouth but are not recommended in pregnancy. Resistance to fluoroquinolones has been reported in some meningococci in North America, Europe, and Asia.

In documented serogroup A, C, Y, or W disease, contacts may be offered immunization (preferably with a conjugate vaccine) in addition to chemoprophylaxis to provide protection beyond the duration of antibiotic therapy. Mass vaccination has been used successfully to control disease during outbreaks in closed communities (educational and military establishments) as well as during epidemics in open communities.

## 181 Gonococcal Infections

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### DEFINITION

Gonorrhea is a sexually transmitted infection (STI) of epithelium and commonly manifests as cervicitis, urethritis, proctitis, and conjunctivitis. If untreated, infections at these sites can lead to local complications such as endometritis, salpingitis, tuboovarian abscess, Bartholinitis, peritonitis, and perihepatitis in female patients; periurethritis and epididymitis in male patients; and ophthalmia neonatorum in newborns. Disseminated gonococemia is an uncommon event whose manifestations include skin lesions, tenosynovitis, arthritis, and (in rare cases) endocarditis or meningitis.

### MICROBIOLOGY

*Neisseria gonorrhoeae* is a gram-negative, nonmotile, non-spore-forming organism that grows singly and in pairs (i.e., as monococci and diplococci, respectively). Exclusively a human pathogen, the gonococcus contains, on average, three genome copies per coccal unit; this polyploidy permits a high level of antigenic variation and the survival of the organism in its host. Gonococci, like all other *Neisseria* species, are oxidase positive. They are distinguished from other neisseriae by their ability to grow on selective media and to use glucose but not maltose, sucrose, or lactose.

### EPIDEMIOLOGY



The incidence of gonorrhea has declined significantly in the United States, but there were still ~311,000 newly reported cases in 2012. Gonorrhea remains a major public health problem worldwide, is a significant cause of morbidity in developing countries, and may play a role in enhancing transmission of HIV.

Gonorrhea predominantly affects young, nonwhite, unmarried, less educated members of urban populations. The number of reported cases probably represents half of the true number of cases—a discrepancy resulting from underreporting, self-treatment, and nonspecific treatment without a laboratory-proven diagnosis. The number of reported new cases of gonorrhea in the United States rose from ~250,000 in the early 1960s to a high of 1.01 million in 1978. The recorded incidence of gonorrhea in modern times peaked in 1975, with 468 reported new cases per 100,000 population in the United States. This peak was attributable to the interaction of several variables, including improved accuracy of diagnosis, changes in patterns of contraceptive use, and changes in sexual behavior. The incidence of the disease has since declined gradually and is currently estimated at 120 cases per 100,000,

a figure that is still the highest among industrialized countries. A further decline in the overall incidence of gonorrhea in the United States over the past quarter-century may reflect increased condom use resulting from public health efforts to curtail HIV transmission. At present, the attack rate in the United States is highest among 15- to 19-year-old women and 20- to 24-year-old men; 60% of all reported cases occur in the preceding two groups together. From the standpoint of ethnicity, rates are highest among African Americans and lowest among persons of Asian or Pacific Island descent.

The incidence of gonorrhea is higher in developing countries than in industrialized nations. The exact incidence of any STI is difficult to ascertain in developing countries because of limited surveillance and variable diagnostic criteria. Studies in Africa have clearly demonstrated that nonulcerative STIs such as gonorrhea (in addition to ulcerative STIs) are an independent risk factor for the transmission of HIV (Chap. 226).

Gonorrhea is transmitted from males to females more efficiently than in the opposite direction. The rate of transmission to a woman during a single unprotected sexual encounter with an infected man is ~50–70%. Oropharyngeal gonorrhea occurs in ~20% of women who practice fellatio with infected partners. Transmission in either direction by cunnilingus is rare.

In any population, there exists a small minority of individuals who have high rates of new-partner acquisition. These “core-group members” or “high-frequency transmitters” are vital in sustaining STI transmission at the population level. Another instrumental factor in sustaining gonorrhea in the population is the large number of infected individuals who are asymptomatic or have minor symptoms that are ignored. These persons, unlike symptomatic individuals, may not cease sexual activity and therefore continue to transmit the infection. This situation underscores the importance of contact tracing and empirical treatment of the sex partners of index cases.

### PATHOGENESIS, IMMUNOLOGY, AND ANTIMICROBIAL RESISTANCE

**Outer-Membrane Proteins • Pili** Fresh clinical isolates of *N. gonorrhoeae* initially form piliated (fimbriated) colonies distinguishable on translucent agar. Pilus expression is rapidly switched off with unselected subculture because of rearrangements in pilus genes. This change is a basis for antigenic variation of gonococci. Piliated strains adhere better to cells derived from human mucosal surfaces and are more virulent in organ culture models and human inoculation experiments than nonpiliated variants. In a fallopian tube explant model, pili mediate gonococcal attachment to nonciliated columnar epithelial cells. This event initiates gonococcal phagocytosis and transport through these cells to intercellular spaces near the basement membrane or directly into the subepithelial tissue. Pili are also essential for genetic competence and transformation of *N. gonorrhoeae*, which permit horizontal transfer of genetic material between different gonococcal lineages in vivo.

**OPACITY-ASSOCIATED PROTEIN** Another gonococcal surface protein that is important in adherence to epithelial cells is opacity-associated protein (Opa, formerly called protein II). Opa contributes to intergonococcal adhesion, which is responsible for the opaque nature of gonococcal colonies on translucent agar and the organism’s adherence to a variety of eukaryotic cells, including polymorphonuclear leukocytes (PMNs). Certain Opa variants promote invasion of epithelial cells, and this effect has been linked with the ability of Opa to bind vitronectin, glycosaminoglycans, and several members of the carcinoembryonic antigen-related cell adhesion molecule (CEACAM) receptor family. *N. gonorrhoeae* Opa proteins that bind CEACAM1, which is expressed by primary CD4+ T lymphocytes, suppress the activation and proliferation of these lymphocytes. This phenomenon may serve to explain the transient decrease in CD4+ T lymphocyte counts associated with gonococcal infection. Select Opa proteins can engage CEACAM3, which is expressed on neutrophils, with consequent nonopsonic phagocytosis (i.e., phagocytosis independent of antibody and complement) and killing of bacteria.