

## Syphilis & Gonorrhea

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### Syphilis

Syphilis is a chronic, systemic infection with protean clinical manifestations. Historically, it has been known as the “great imitator” or “great masquerader” because its appearance can resemble many other diseases. Sir William Osler famously stated, “To know syphilis is to know medicine”. While the rates of syphilis have declined substantially since the availability of penicillin, it remains an important sexually transmitted infection and, in fact, the rates of primary and secondary syphilis (defined below) are beginning to increase again. In the

U.S. during 2014, the last year for which reporting is complete, there were over 20,000 cases, an increase of 15% over the previous year; the calculated rate was 6.3 per 100,000 people, though the geographic distribution of cases is heterogeneous (Figure 1). In Delaware that same year, there were 47 cases reported, for a rate of 5.0 per 100,000. It should be noted that certain populations account for a disproportionate number of cases, including African Americans and men who have sex with men (MSM) (Figures 2 and 3).

Figure 1. Geographic distribution of cases of primary and secondary syphilis, United States, 2014

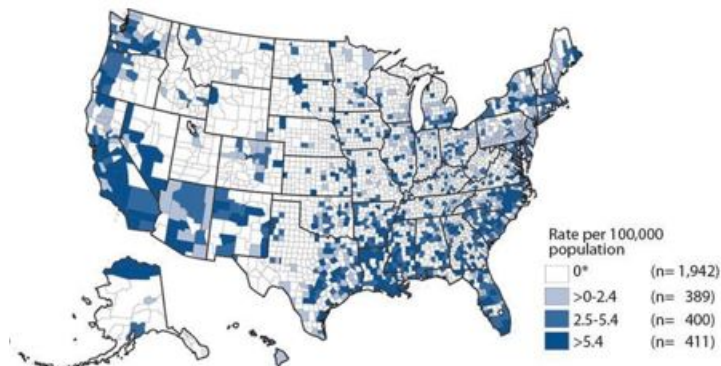


Figure 2. Incidence of primary and secondary syphilis in selected ethnic populations, United States

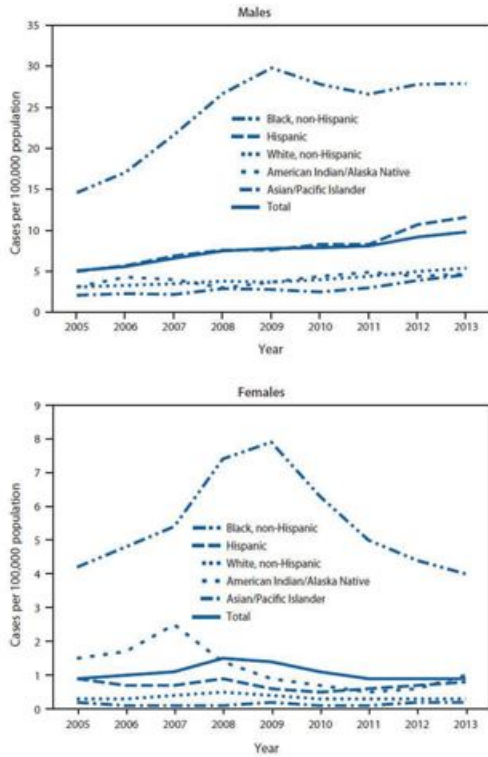
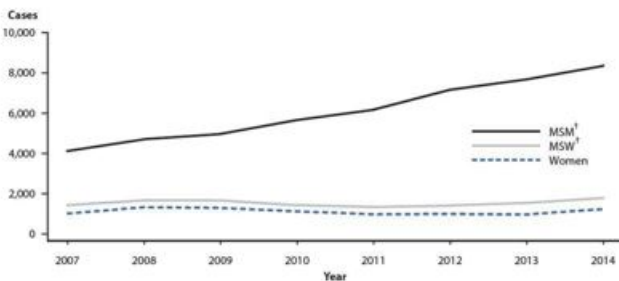


Figure 3. Cases of primary and secondary syphilis in women and in men who have sex with women and men who have sex with men



Clinically, disease is categorized as primary, secondary, and tertiary and there may be a long period of disease inactivity in an infected person, known as latent syphilis. Sexual transmission of the causative organism, the spirochete *Treponema pallidum*, results in the lesion known as a chancre at the infection site, usually after an incubation period of 10-90 days. This characteristic lesion of primary syphilis is highly infectious, but eventually resolves. When the organism gains access to the blood stream, secondary syphilis results. Skin rashes (Figure 4a), mucous membrane lesions and lymphadenopathy are the main clinical manifestations. However, neurologic and other manifestations may occur at this stage of disseminated infection. Recurrences of mucocutaneous manifestations of secondary syphilis are common, and often less pronounced. The organism then becomes latent, usually for a period of years. Tertiary disease may take many forms, with cardiac involvement (e.g. aortitis), central nervous system involvement (e.g. tabes dorsalis and general paresis), and gummatous lesions (skin and internal tissues and organs).

Figure 4. Skin lesions characteristic of secondary syphilis



There is an interesting and bidirectional relationship between syphilis and chronic HIV infection. The chancre and mucocutaneous lesions of syphilis facilitate the transmission of *Treponema pallidum*. Syphilis probably has a negative effect on the HIV viral load. Clinical manifestations of syphilis are often different in HIV-infected persons, with a more rapid clinical course, atypical and severe disease manifestations, and higher risk for neurologic involvement. The diagnosis of syphilis begins with a high index of suspicion, followed by appropriate testing. Direct evidence of the presence of *T. pallidum*, by darkfield examination or polymerase chain reaction testing, provides proof of infection. However, the vast majority of infected persons will be diagnosed using serologic methods. Two different types of tests are used, treponemal and non-treponemal. Treponemal tests (e.g. FTA-ABS, TP-AP and EIAs) detect antigens of the organism and are typically positive for life, once a person is infected. Non-treponemal tests (e.g. RPR or VDRL) may have biologic false positives (for example, in autoimmune disease or other chronic infections), but are useful because the titers correlate with disease activity and a drop in titer in a patient who has been treated is correlated with cure of infection. Historically, testing began with the use of a non-treponemal test, which if positive, was confirmed with a treponemal test. Recently the “reverse algorithm” for testing has been used by some high volume laboratories, because automated treponemal testing is faster and cheaper; positive tests then need to have a reflex non-treponemal test to reflect disease activity.

Because of either a high risk of infection or the risk of severe consequences of infection, certain populations should be routinely screened for syphilis. Examples include, respectively, persons with high risk sexual behaviors and pregnant women.

Congenital syphilis occurs by one of two mechanisms. When pregnant women with early syphilis are bacteremic with the spirochete, infection of the fetus may occur transplacentally. This results in high rates of fetal death and stillbirth. Clinical manifestations may be present at birth and resemble secondary syphilis in adults, with pronounced mucocutaneous manifestations. If the mother has a chancre, the baby may become infected during passage through the birth canal. This mechanism results in a delayed expression of clinical disease. Infected children can go on to have late manifestations of congenital syphilis, which can affect the bones, teeth and nervous system.

The treatment of choice for syphilis is parenteral penicillin G. For most people, one dose given intramuscularly is sufficient, but for late latent syphilis, 3 weekly IM doses are administered. Neurologic disease is treated with intravenous penicillin G. Follow up serologic testing is recommended for two reasons. Importantly, a fall in the non-treponemal test titer is correlated with adequacy of treatment. Secondly, some people with high risk sexual behaviors will become reinfected.

There are several keys to prevention of infection. Education of persons with high risk sexual behaviour should include advice to reduce the number of sexual partners, to correctly and consistently use condoms, and to avoid the use of drugs and alcohol during sexual encounters. The sexual partners of persons diagnosed with syphilis should be notified of their exposure and the importance of evaluation and possible therapy. Departments of public health play an important role in this regard. Education regarding sexually transmitted infections and how to avoid them is an important part of public school health curricula.

## Gonorrhea

*Neisseria gonorrhoeae* causes about 820,000 new infections in the U.S. each year. The vast majority of these infections are sexually transmitted, making gonorrhea the second most common sexually transmitted infection (STI). Delaware has rates of gonorrhea that are among the highest in the United States. Figure 5 shows the age distribution of infection in men and women. African Americans account for a disproportionately high number of cases (Figure 6). Other risk factors for infection include multiple sex partners, a sex partner with multiple partners, other STIs and inconsistent condom use.

Figure 5. Gonorrhea – Reported Cases by Reporting Source and Sex, United States 2005-2014

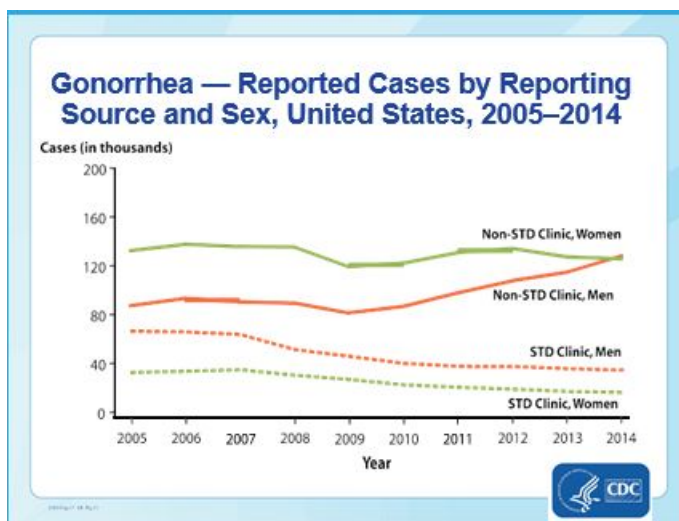
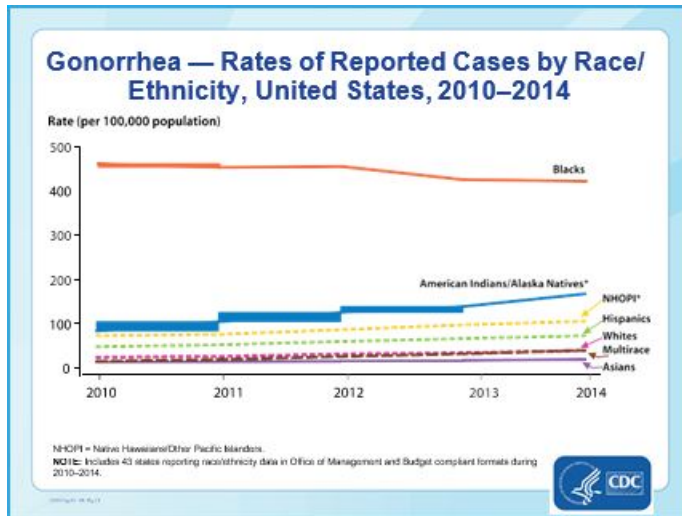


Figure 6. Gonorrhea – Rates of Reported Cases by Race/Ethnicity, United States, 2010-2014



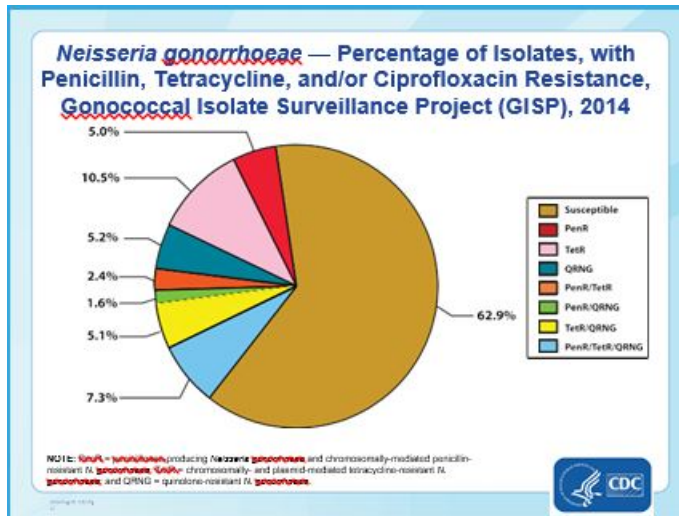
Infection in men usually causes symptomatic urethritis, often causing them to seek medical care. Women often have asymptomatic cervicitis which, if not diagnosed and treated, can progress to pelvic inflammatory disease that can lead to tubal scarring, infertility and tubal pregnancy. Painful perihepatitis (Fitz-Hugh-Curtis syndrome) can also result.

Sex practices, particularly among men who have sex with men (MSM) can lead to infection in the pharynx and rectum, which is usually asymptomatic. Persons of both sexes can experience disseminated infection, which causes skin lesions, tenosynovitis and arthritis. Women with gonococcal infection can transmit the organism to an infant during childbirth causing severe conjunctivitis and sometimes disseminated disease in the baby. Infection at any site can also occur in prepubertal children when seen in this population, sexual abuse should always be considered.

Because infection is often asymptomatic (but with the potential for severe consequences), annual screening is now recommended for sexually active women under 25 years of age, and for older women with additional risk factors. This is typically done using nucleic acid amplification tests (NAAT) which can be used for vaginal swabs, endocervical swabs and urine. MSM are also candidates for periodic screening, typically using urine and extragenital (pharynx and rectum) swabs. Gram stain and cultures can also be used for all of these sites and are the microbiologic tests of choice for disseminated disease. In symptomatic men, a simple and inexpensive Gram stain of urethral discharge which shows intracellular Gram-negative diplococci is highly predictive of the diagnosis of gonorrhea. Among patients with suspected treatment failure, culture must be used (often accompanying NAAT) so that antimicrobial susceptibility testing can be performed.

Over the years, *N. gonorrhoeae*, once uniformly susceptible to penicillin, has become increasingly resistant to antibiotics (Figure 7). In 2007, the development of fluoroquinolone resistance caused the CDC to cease recommending that class of antibiotics, leaving cephalosporins as the most reliable agents. More recently, increasing resistance to cefixime (an oral antibiotic) left parenteral ceftriaxone as the mainstay of treatment. Tragically, in other countries, ceftriaxone resistance is now being reported. Azithromycin is usually active against *N. gonorrhoeae* and is also a recommended treatment for *Chlamydia trachomatis* (which is a frequent co-infection).

Figure 7. *Neisseria gonorrhoeae* – Percentage of Isolates, with Penicillin, Tetracycline, and/or Ciprofloxacin Resistance, Gonococcal Isolate Surveillance Project (GISP), 2014



For these reasons, the current CDC recommendation is for dual therapy for non-neonatal infection, using ceftriaxone and azithromycin. Treatment should be provided in the office or clinic and directly observed to guarantee 100% compliance. Specific recommendations for treatment can be found in the CDC's Sexually Transmitted Infections Treatment Guidelines<sup>1</sup> which are periodically updated.

For neonates born to infected mothers, the use of erythromycin ointment as prophylaxis against ophthalmic gonococcal infection has dramatically reduced the incidence of eye infection. Ceftriaxone and cefotaxime are recommended for neonatal infection.

Any recent (within the preceding two months) sex partners should be evaluated, tested and treated if positive. On site directly observe treatment is preferred, but if a partner is unwilling to be seen, prescriptions for cefixime and azithromycin can be delivered along with appropriate written instructions.

In order to avoid transmission to others, persons treated for gonorrhea should be counseled to abstain from sexual activity for one week after treatment and until all partners have been treated. Unfortunately, those with a history of gonorrhea are likely to experience repeated infection, due to high risk sexual encounters. The current CDC recommendation is to screen patients 3 months after treatment in order to detect recurrences.

## References

1. Workowski, K. A., & Bolan, G. A., & the Centers for Disease Control and Prevention. (2015, June 5). Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Reps*, 64(RR-03, No. RR-3), 1–137. [PubMed](#)

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