

that can differentiate the three subspecies of *T. pallidum* by culture-independent methods based on polymerase chain reaction (PCR), but other sequence signatures cross subspecies boundaries in certain strains. Other *Treponema* species found in the human mouth, genital mucosa, and gastrointestinal tract have been associated with disease (e.g., periodontitis), but their role as primary etiologic agents is unclear.

T. pallidum subspecies *pallidum* (referred to hereafter as *T. pallidum*), a thin spiral organism, has a cell body surrounded by a trilaminar cytoplasmic membrane, a delicate peptidoglycan layer providing some structural rigidity, and a lipid-rich outer membrane containing relatively few integral membrane proteins. Endoflagella wind around the cell body in the periplasmic space and are responsible for motility.



T. pallidum cannot be cultured in vitro, and little was known about its metabolism until the genome was sequenced in 1998. This spirochete possesses severely limited metabolic capabilities, lacking the genes required for de novo synthesis of most amino acids, nucleotides, and lipids. In addition, *T. pallidum* lacks genes encoding the enzymes of the Krebs cycle and oxidative phosphorylation. The organism contains numerous compensatory genes predicted to encode transporters of amino acids, carbohydrates, and lipids. In addition, genome analyses and other studies have revealed the existence of a 12-member gene family (*tpr*) that bears similarities to variable outer-membrane antigens of other spirochetes. One member, *TprK*, has discrete variable (V) regions that undergo antigenic variation during infection, providing a mechanism for immune evasion.

The only known natural host for *T. pallidum* is the human. *T. pallidum* can infect many mammals, but only humans, higher apes, and a few laboratory animals regularly develop syphilitic lesions. Rabbits are used to propagate virulent strains of *T. pallidum* and serve as the animal model that best reflects human disease and immunopathology.

TRANSMISSION AND EPIDEMIOLOGY

Nearly all cases of syphilis are acquired by sexual contact with infectious lesions (i.e., the chancre, mucous patch, skin rash, or condylomata lata; see Fig. 25e-20). Less common modes of transmission include nonsexual personal contact, infection in utero, blood transfusion, and organ transplantation.

SYPHILIS IN THE UNITED STATES

With the advent of penicillin therapy, the total number of cases of syphilis reported annually in the United States declined significantly to a low of 31,575 cases in 2000—a 95% decrease from 1943—with <6000 reported cases of infectious primary and secondary syphilis (the latter being a better indicator of disease activity than total syphilis cases). Since 2000, the number of cases of primary and secondary syphilis has more than doubled, with more than 14,000 cases reported in 2012 (Fig. 206-1). Approximately 70% of these cases were in men who have

sex with men (MSM), 20–70% of whom are co-infected with HIV (depending on geographic location). The number of primary and secondary cases among women in the United States increased from 2004 to 2008 but has since been declining in conjunction with a decline in congenital syphilis. Surveillance of the number of new cases of primary and secondary syphilis has revealed multiple 7- to 10-year cycles, which may be attributed to herd immunity in at-risk populations, changing sexual behaviors, and changes in control efforts.

The populations at highest risk for acquiring syphilis have changed over time, with outbreaks among MSM in the pre-HIV era of the late 1970s and early 1980s as well as at present. It is speculated that recent increases in syphilis and other sexually transmitted infections in MSM may be due to unprotected sex between persons who are HIV concordant and to disinhibition caused by highly effective antiretroviral therapies. The syphilis epidemic that peaked in 1990 predominantly affected African-American heterosexual men and women and occurred largely in urban areas, where infectious syphilis was correlated with the exchange of sex for crack cocaine. The rate of primary and secondary syphilis among African Americans nearly doubled between 2003 and 2009, remains higher than rates for other racial/ethnic groups, but has since declined somewhat (Fig. 206-1).

The incidence of congenital syphilis roughly parallels that of infectious syphilis in women. In 2011, 360 cases in infants <1 year of age were reported, for a decline of 20% since 2008. The case definition for congenital syphilis was broadened in 1989 and now includes all live or stillborn infants delivered to women with untreated or inadequately treated syphilis.

One-third to one-half of individuals named as sexual contacts of persons with infectious syphilis become infected. Many have already developed manifestations of syphilis when they are first seen, and ~30% of asymptomatic contacts examined within 30 days of exposure actually have incubating infection and will later develop infectious syphilis if not treated. Thus, identification and treatment of all recently exposed sexual contacts continue to be important aspects of syphilis control.

GLOBAL SYPHILIS



Syphilis remains a significant health problem globally; the number of new infections is estimated at 11 million per year. The regions that are most affected include sub-Saharan Africa, South America, China, and Southeast Asia. During the past decade, the incidence rate in China has increased by approximately eightfold, and higher rates of infectious syphilis have been reported among MSM in many European countries. Worldwide, there are estimated to be 1.4 million cases of syphilis among pregnant women, with 500,000 adverse pregnancy outcomes annually (e.g., stillbirth, neonatal and early fetal death, prematurity/low birth weight, and infection in newborns). Congenital syphilis rates in China are ~150 cases per 100,000 live births.

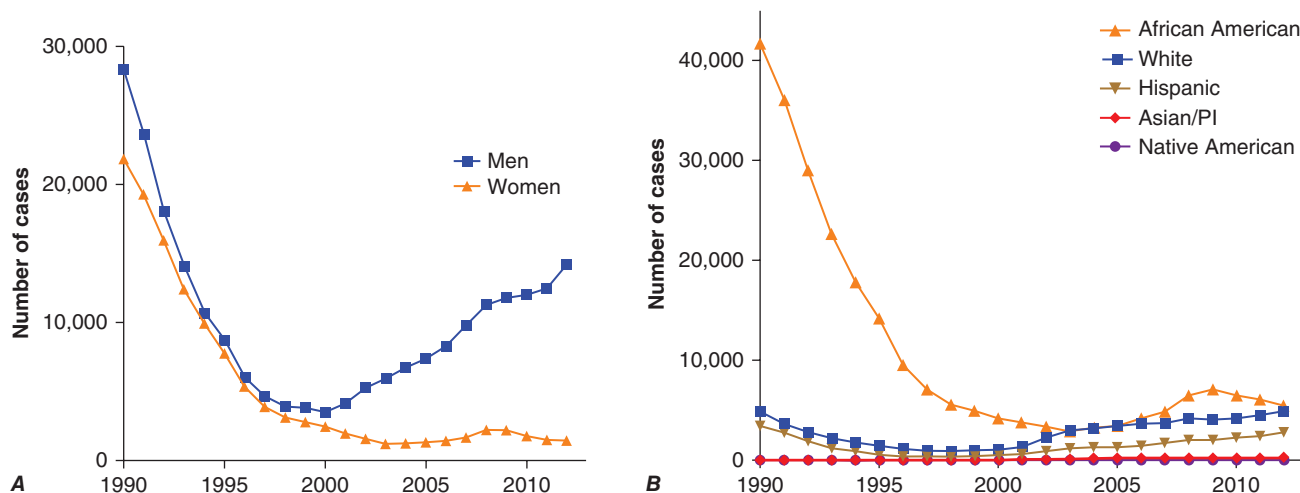


FIGURE 206-1 Primary and secondary syphilis in the United States, 1990–2012, by sex (A) and by race or ethnicity (B). (Data from the Centers for Disease Control and Prevention.)