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## Congenital and heterosexual syphilis: Still part of the problem

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### Short summary:

Although the U.S. syphilis epidemic is concentrated among men who have sex with men, the number of congenital syphilis cases and the primary and secondary syphilis rate among women both doubled in recent years.

### Keywords

congenital syphilis; syphilis

In the United States (U.S.), diagnoses of syphilis fell dramatically after the introduction of penicillin, but concurrent with the sexual revolution, began increasing during the 1960s. Cases continued to rise, hitting a peak in 1990 with over 135,000 cases reported.(1,2) At the time, syphilis appeared to be less common among gay, bisexual and other men who have sex with men (collectively referred to as MSM), perhaps due to changes in sexual behavior related to the AIDS epidemic,(3) and was primarily reported among heterosexuals, likely tied to the crack cocaine epidemic.(4,5) Following intensive public health interventions, including targeted screening and intensive partner services, syphilis rates fell and by the late 1990s, syphilis was nearing elimination in the U.S.(6) In 2000, fewer than 6,000 cases of primary and secondary (P&S) syphilis were reported, down from 50,000 cases in 1990. Cases of congenital syphilis, syphilitic infection in a newborn, had decreased from over 4,400 cases in 1991 to fewer than 600 cases in 1999. Before elimination could be declared, cases of P&S syphilis began climbing again, doubling to over 15,000 cases in 2012. But this time, the epidemic appeared to be primarily among MSM. Congenital syphilis cases remained low, reaching a nadir of 334 cases in 2012. Then in 2013, the epidemic shifted slightly and concurrent with continued increases among MSM, syphilis increased among both women and newborns. During 2012–2016, the number congenital syphilis cases (334 to 628 cases) and the P&S syphilis rate among women (0.9 to 1.9 cases per 100,000 females) both doubled. (1)

The current U.S. syphilis epidemic remains concentrated among MSM with 58% of P&S syphilis cases occurring among MSM in 2016;(1) however, rising rates among females and

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the increased number of congenital syphilis cases is a growing public health concern. Like other bacterial sexually transmitted infections, syphilis in adults can be prevented by consistent use of condoms and/or mutual monogamy with a negative partner. Although early signs and symptoms of syphilis in women (e.g., a vaginal or oral chancre) can be missed or mistaken for another infection (e.g., herpes), syphilis among women can be diagnosed with a simple blood test and can be cured with antibiotics. However, if undiagnosed and untreated, syphilis can facilitate HIV acquisition (7) and, although rare, can lead to severe complications, such as ocular syphilis and neurosyphilis. (8) Syphilitic infection in pregnant women has even more severe consequences, including miscarriage and stillbirth, and infants born with a syphilitic infection can suffer from bone deformities, jaundice, and neurological problems including blindness and deafness.(8) Congenital syphilis is preventable by 1) preventing women with syphilis from getting pregnant, 2) preventing pregnant women from getting syphilis, and 3) identifying and treating pregnant women with syphilis prior (>30 days) to delivery. Additionally, the long-term consequences of congenital syphilis can be minimized by ensuring that infants exposed to syphilis are treated appropriately. Congenital syphilis is completely avoidable. Therefore, a case of congenital syphilis represents a failure of the health care system and should be considered a sentinel event. As congenital syphilis requires an infection in a pregnant woman, heterosexual and congenital syphilis are inextricably linked providing multiple opportunities for prevention and control.

This section of the current issue focuses on heterosexual and congenital syphilis in the U.S. Kidd and colleagues provide an in-depth review of recent trends in congenital syphilis and present a novel congenital syphilis prevention cascade, estimating the proportion of potential congenital syphilis cases averted, and identifying opportunities for intervention.(10) Plotzker and colleagues conduct a review of current interventions to prevent congenital syphilis, highlighting both evidence-based interventions, such as routine screening during pregnancy, as well as promising strategies, such as using point-of care syphilis tests in settings that might reach women of reproductive age who are not linked to prenatal care.(11) Finally, Berruti and colleagues investigate the cost-effectiveness of antenatal syphilis screening using a decision tree model to estimate costs and outcomes of timing of antenatal screening.(12) Although these manuscripts will help inform and refine prevention and control of congenital syphilis in the U.S., it is also critical to consider what might have caused the epidemic to shift back to the heterosexual population after nearing elimination in the 1990s and to identify key areas for future research.

In the 36 states that reliably reported sex of sex partner data for P&S syphilis cases during 2012–2016, 31% of all P&S cases were reported among women and men who have sex with women only (MSW) in 2016, a 17% increase from the proportion of cases that were among heterosexuals in 2012. (1) This increased proportion of heterosexual cases reflects an increasing number of cases diagnosed among both MSW (99% increase during 2012–2016; 1,616 to 3,211 cases) and women (112% increase; 1,216 to 2,579 cases). The number of cases among MSM showed a slower increase (64% increase; 7,728 to 12,654 cases). These changes in the syphilis epidemic may be a result of several intertwined factors, including failure to control the epidemic in MSM, changes in sexual networks, and changes in health care access.

One hypothesis for the increasing rates among heterosexual populations is increased mixing between sexual networks, with an increased number of men who have sex with both men and women (MSMW) serving as “bridges” between MSM and heterosexual networks. In a recent analysis of over 40,000 HIV nucleotide sequences from 25 jurisdictions, HIV infection among heterosexual women likely originated from both heterosexual men (about 21% of linked pairs) and MSM (about 29% of linked pairs) in potential transmission pairs (i.e., those with close genetic distance), with the remainder of women linked to heterosexual females (likely representing an indirect connection to a man) and persons who inject drugs. (13) This finding suggests that bridging between MSM and heterosexual networks may play an important role in HIV transmission dynamics in the U.S. Syphilis transmission dynamics differ from HIV, as sexual transmission of syphilis requires exposure to a mucosal or cutaneous syphilitic lesion, which are self-limiting (e.g., a few weeks or months). (14) Additionally, lesions may occur in the rectum of MSM, limiting the potential to expose female partners. Consequently, more frequent mixing may be required to transmit syphilis across MSM and heterosexual networks. But bridging may have contributed to the recent shift in the syphilis epidemic, similar to the HIV patterns. Given the large increase in the number of MSM with syphilis (64% increase in the last 5 years), the number of MSM who also have sex with women who have acquired syphilis has likely increased (even if the overall proportion that are MSMW in the population has stayed stable), increasing the probably of bridging between sexual networks. The delayed increase in the heterosexual population may be attributable, at least in part, to the short window of infectiousness of syphilis and the proportionately small number of MSMW in the population. These factors would limit bridging events. Nonetheless, these explanations are hypothetical—the frequency of bridging events and the resulting impact on observed syphilis rates are unknown. Understanding the role of bridging in the current syphilis epidemic could inform allocation of prevention resources. For example, will it be possible to control the growing heterosexual epidemic using prevention strategies from the 1990s (e.g., partner services, screening), or will it be necessary to control syphilis among MSM to control syphilis among heterosexual populations?

Increases in syphilis among heterosexuals may also be independent of increases among MSM. In the concurrent crack cocaine and syphilis epidemics in the 1990s, drug use and sexual transmitted infections (STIs) were intimately intertwined. The use of prescription pain relievers, heroin, other opioids, and methamphetamine has increased nationwide (15) and may be contributing to current syphilis rates. Drug use can be linked to often coercive sexual behaviors associated with STIs, such as trading sex for drugs/money, survival sex, and sex trafficking. Drug use can also result in poverty, homelessness, and reduced access to health care, all of which can affect the risk of acquiring syphilis. Persons actively using illegal drugs may be hesitant to seek medical care, even when they have symptoms of syphilis; as a result, their duration of infection is longer, increasing the probability of transmitting the infection to their partners. Pregnant women who are using drugs may also delay seeking health care, as some states consider substance use during pregnancy to be considered child abuse. (16) For pregnant women with syphilis, this delay may lead to continued transmission to sexual partners and increase the risk of congenital syphilis. The impact of the current opioid crisis on STIs, including syphilis, in rural areas of the U.S. is

the focus of eight ongoing cooperative agreements with support from the National Institute of Drug Abuse, the Centers for Disease Control and Prevention (CDC), Substance Abuse and Mental Health Services Administration, and the Appalachian Regional Commission.(17)

Understanding factors, such as risk behaviors, associated with the current syphilis epidemic is critical to identifying intervention opportunities; however, it is difficult to monitor trends in reported behaviors among persons diagnosed with syphilis. Behavioral information, such as sex of sex partners, may not be systematically captured in medical records and is often missing on provider case report forms. Although many syphilis cases are interviewed by public health staff for partner services, providing an opportunity to capture patient-reported behaviors, social desirability bias may limit accurate disclosure. Consequently, some men reported as heterosexual may be men who have sex with men. If over time men became less likely to disclose that they have had sex with men, heterosexual rates could increase independent of changes in morbidity. Similarly, more complete disclosure of behaviors over time could distort trends. As efforts to control the opioid epidemic in the U.S. grow, it is likely that more healthcare providers and public health staff will discuss substance use with patients resulting in more complete information on drug-related behaviors in syphilis case reports. Consequently, trends in reported drug abuse could increase independent of changes in actual drug use. It is important to consider the inherent limitations of surveillance data when using case report data to identify intervention opportunities.

Increases in rates of syphilis among women have been noted in all regions of the U.S. in recent years. In 2016, at least one case of congenital syphilis was reported in 37 states and Washington DC.(1) But the epidemics of heterosexual and congenital syphilis remain concentrated. In 2016, 47% of all P&S syphilis cases among women and 61% of all congenital syphilis cases were reported from four states (California, Florida, Louisiana, and Texas). Understanding local drivers of the syphilis epidemic in these high prevalence areas is key to controlling national rates. Recently the CDC awarded funding to nine jurisdictions with high rates of congenital syphilis. These supplemental funds will be used to bolster local congenital syphilis control and prevention efforts, including using local congenital syphilis case review boards to identify root causes of congenital syphilis in the jurisdiction and to identify opportunities for individual- or systems-level strengthening to prevent future cases. (18)

The surge in syphilis observed among MSM has recently been paired with corresponding increases in syphilis among women and consequently, congenital syphilis. The underlying factors contributing to the heterosexual syphilis and congenital syphilis cases are unclear, but bridging from the MSM epidemic and substance use may play a role. More distal factors, such as poverty and access to quality healthcare, as well as social vulnerabilities, such as incarceration and homelessness, are additional contributors (19, 20). Stemming the current epidemic will require a multi-level approach, combining individual-level interventions, such as ensuring all pregnant women are screened for syphilis during the first prenatal care visit, as well as interventions that address underlying socioeconomic factors. (21) Regardless, one thing is clear—congenital syphilis is entirely preventable and its control should be a high priority for sexually transmitted disease prevention efforts.

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