Increasing Syphilis in Rhode Island: Return of an Old Foe

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ABSTRACT

The number of people diagnosed with syphilis has increased significantly in the United States over the last decade. In Rhode Island, the number of new diagnoses has increased more than four-fold since 2008. Syphilis disproportionately impacts gay, bisexual, and other men who have sex with men (MSM), with those from African American and Hispanic/Latino communities most affected. Given these trends, physicians need to be aware of current prevention, diagnosis, and treatment practices for syphilis, especially when working with populations who are most at risk.

KEYWORDS: syphilis, prevention, screening, MSM, Rhode Island

INTRODUCTION

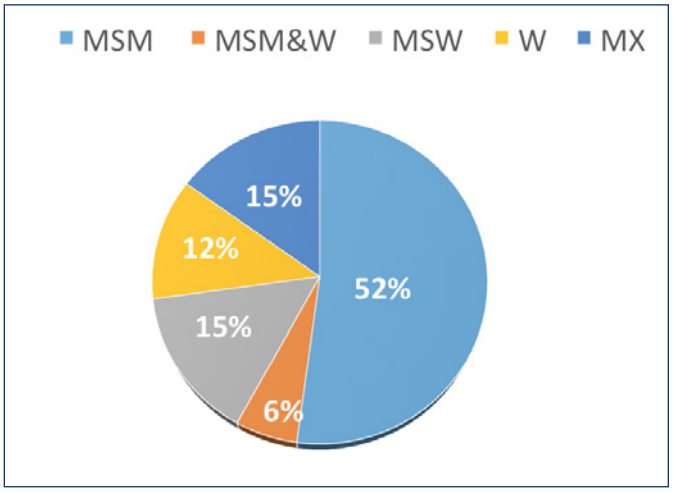
Syphilis is a sexually transmitted disease (STD) caused by the bacterium *Treponema pallidum*. Transmission typically occurs through direct contact with a syphilis chancre during condomless vaginal, anal, or oral sex, and complications of the disease may appear in untreated patients. Syphilis is highly sensitive to penicillin and successful treatment largely results in cure. At the beginning of the twenty-first century, the number of reported syphilis cases reached a historic low in the United States (US).[1] However, the number of people diagnosed with syphilis has steadily increased since 2005. Gay, bisexual, and other men who have sex with men (MSM) are disproportionately affected by syphilis infection. In addition, syphilis is characterized by a high rate of HIV co-infection, particularly among MSM.[2] Racial and ethnic disparities, stigma, sociodemographic factors, access to care, and risky sexual behaviors all contribute to increased rates of syphilis. These trends are observed in Rhode Island (RI) as well as across New England and the US.[3,4]

Primary care physicians (PCPs) play an important role in the screening and diagnosis of syphilis. PCPs often have close relationships with patients and are responsible for providing comprehensive preventive care. Additionally, the increasing burden of syphilis has led to a wide variety of clinical manifestations that medical subspecialists may encounter in their practice.[5] Therefore, it is essential that PCPs and other medical providers are aware of the changing epidemiology of syphilis and current screening and treatment approaches. Such awareness is necessary to prevent further spread of syphilis and prevent late and severe complications.

EPIDEMIOLOGY OF SYPHILIS

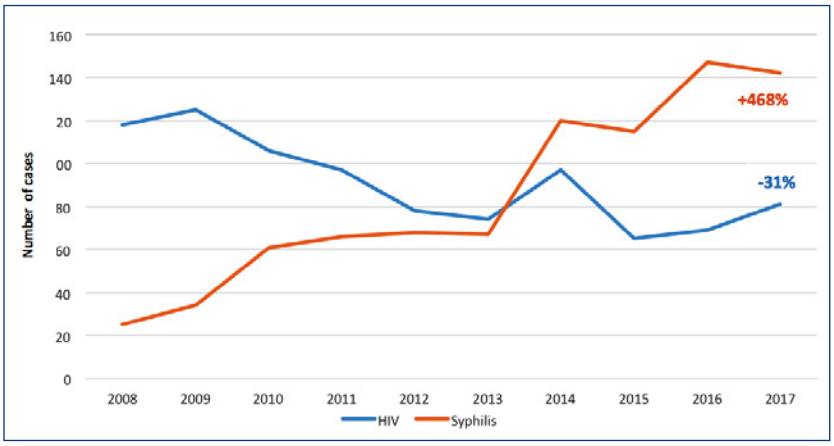
In the US, a total of 6,103 primary and secondary (P&S) syphilis cases were reported in 2001, the lowest number of cases ever.[1] However, the number of reported P&S syphilis cases in 2017 rose to 30,644.[1] Increasing numbers of congenital infections are also being reported (from 334 in 2012 to 918 cases in 2017).[1] Men, and especially MSM, accounted for almost 90% of all cases of reported syphilis in 2017 (**Figure 1**). A large number of new syphilis diagnoses also occur among people living with HIV (PLWH); 45.5% of MSM with P&S syphilis in 2017 were HIV positive.[1] Racial and ethnic minority populations are also disproportionately affected by syphilis in the US. African American, Native Hawaiian and other Pacific Islander, and Hispanic/Latino populations

Figure 1. Rates of reported primary and secondary syphilis cases in the US in 2017 by sex and sexual behavior. (n= 30,644). MSM (Men who had Sex with Men only); MSM&W (Men who had Sex with both Men and Women); MSW (Men who had Sex with Women only); W (Women); MX (Men without information about sex of sex partner).



Source: Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2017. Atlanta, GA: US. Department of Health and Human Services; 2018.

Figure 2. Annual number of newly diagnosed cases of HIV and infectious syphilis – Rhode Island, 2008–2017. Ten-year trend is indicated by percent difference in the number of cases from 2008 to 2017.



Sources: 1. Rhode Island Department of Health. Rhode Island HIV, sexually transmitted disease, and hepatitis C surveillance report 2016. Providence, RI; 2017 Dec.

2. Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2017. Atlanta, GA: US. Department of Health and Human Services; 2018.

had significantly higher rates of syphilis compared to white populations in 2017.[1]

In RI, there were a total of 71 cases of P&S syphilis in 2017.[1] The municipalities with the most reported syphilis cases were Providence, Central Falls, and Pawtucket.[6] Syphilis cases in RI were highest among young adults, with persons aged 20–29 years most affected. There have been no cases of congenital syphilis reported in RI in the last six years.[1]Although the number of new HIV diagnoses has declined by 31% over the last 10 years, the number of infectious syphilis cases (including primary, secondary, and early latent) has increased by 468%, from 25 cases in 2008 to 142 cases in 2017 (**Figure 2**).[1,6] The opposite trends in HIV and syphilis prevalence may be due to advances in HIV treatment and prevention, including pre-exposure prophylaxis (PrEP), which is very effective in preventing HIV but does not protect against other STDs.[7] Other factors may include increased risky sexual behaviors such as condomless sex.[8] Widespread use of the internet and mobile apps to meet sex partners may also be associated with STD transmission, particularly among MSM.[9]

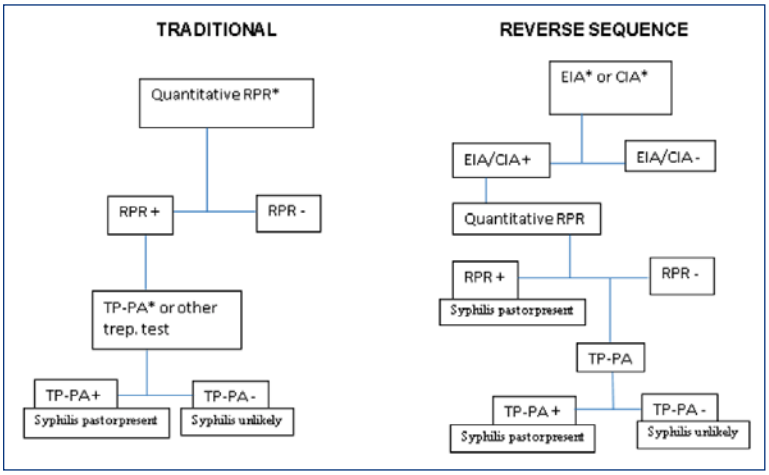
CLINICAL MANIFESTATIONS

The natural history of syphilis includes primary, secondary, latent, and tertiary stages.[5] However, symptoms of syphilis may not always fall into clearly defined categories and previously rare presentations are becoming more frequent with increasing rates of infection.[5,10,11] The classic symptom of primary syphilis is a painless chancre, which may be present in the oropharynx, genitalium or rectum.[11] Chancres may be easily missed, as they are typically painless and may be located within the oropharynx or rectum. Transmission normally occurs during condomless vaginal, anal or oral sex, through direct contact with chancres, which have a high concentration of *T. pallidum* and are extremely infectious.[5] In addition, T. pallidum can cross the placenta during P&S syphilis. Though very rare, the infection can also be transmitted through transfused blood.[5] Secondary syphilis symptoms are observed in approximately 25% of infected individuals and typically present four to eight weeks after infection.[5,12] Symptoms may include a maculopapular rash involving the trunk and extremities, the palms of the hands and soles of the feet, and mucous patches in or around the mouth, vagina, or penis. Fever, muscle and joint pain, and nodular lesions may also occur.[11,13] During the latent phase, syphilis enters a dormant state, which may last for years. During this time, syphilis is rarely transmitted.[5] Up to 25–40% of untreated syphilis infections progress to late or tertiary disease, which may occur 3–15 years after the initial infection. Symptoms of tertiary syphilis include infiltration of skin, bone, or liver tumors (gummas); cardiovascular syphilis that affects the aorta and causes aneurysms or valvulopathy; and disorders of the central nervous system (neurosyphilis).[14] Manifestations of neurosyphilis may include general paresis, tabes dorsalis, and ocular syphilis. General paresis is a progressive illness that usually occurs 10–25 years after infection, with typical findings of dysarthria and intentional tremors of the face, tongue, and hands.[5] Tabes dorsalis is a condition of the posterior columns of the spinal cord. The most common symptoms include sensory ataxia, pupillary irregularities and lancinating pains of the limbs, back or face. Importantly, increased prevalence of ocular syphilis is being observed across the US; these cases typically present as posterior uveitis and panuveitis.[10] Vertical transmission from mother to child during pregnancy results in congenital syphilis. Approximately 80% of untreated syphilis infections in pregnant women lead to fetal infection through placental transmission, and up to 40% of fetal infections result in stillbirth or death of the infant.[1,15]

DIAGNOSIS AND TREATMENT

Given that syphilis may not always present with symptoms, it can be difficult to diagnose. Therefore, screening for syphilis should be a routine part of healthcare for sexually active persons, especially MSM and PLWH. In addition, all pregnant women should be tested for syphilis during the first trimester with rescreening in the third trimester if at risk.[16] *T. pallidum* cannot typically be cultured. The CDC

Figure 3. Recommended algorithms for traditional sequence and reverse sequence syphilis screening. CDC recommends that a specimen with reactive EIA/CIA results be tested reflexively with a quantitative nontreponemal test (e.g., RPR or VDRL). If test results are discordant, the specimen should be tested reflexively using the TP-PA test as a confirmatory treponemal test.



Note: RPR – rapid plasma reagin; TP-PA – treponemal pallidum particle agglutination; EIAs – enzyme immunoassays; CIAs – chemiluminescence immunoassays

Source: Centers for Disease Control and Prevention. Discordant results from reverse sequence syphilis screening – five laboratories, United States, 2006-2010. Morbidity and Mortality Weekly Report 2011;60(5):133-7.

recommends a "traditional" algorithm to diagnose syphilis, which uses a non-treponemal test followed by a treponemal test.[17] Treponemal tests detect antibodies to specific antigenic components of *T. pallidum*, and non-treponemal tests detect antibodies to a non-specific cardiolipin-cholesterol-lecithin reagin antigen produced by the host in response to syphilis.[17] The non-treponemal tests include the Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests.[18] These tests are non-specific and may have false positive results. A positive result by either RPR or VDRL requires confirmation by a treponemal-specific test, such as the fluorescent treponemal antibody-absorbed (FTA-ABS) or the *T. pallidum* particle agglutination (TP-PA) tests. Growing numbers of clinical laboratories have adopted a "reverse sequence" screening algorithm that begins with a treponemal assay, such as an enzyme immunoassay (EIA) or a chemiluminescence immunoassay (CIA).[18] The reverse sequence algorithm detects early primary syphilis and treated infections that may be missed with traditional screening (**Figure 3**). If the traditional algorithm is used and the initial non-treponemal test is nonreactive, patients with suspected primary syphilis should be treated and then retested after several weeks.[17]

For the diagnosis of neurosyphilis, a lumbar puncture should be performed with cerebral spinal fluid analysis (CSF) including white blood cell (WBC) count, protein concentration, and a VDRL test. A diagnosis of neurosyphilis is based on a reactive CSF-VDRL or a WBC-CSF of more than five microliters.[19] A CSF VDRL is highly specific, but not sensitive (i.e. a negative result does not rule out neurosyphilis).

Penicillin continues to be the most effective treatment for all stages of syphilis.[20] The recommended treatment of primary, secondary, and latent syphilis of less than one year duration is Benzathine penicillin G 2.4 million units intramuscular (IM) in a single dose. This is distinct from regular formulations of penicillin G, which are shorter-acting. Treatment of syphilis infection of more than one year includes parenteral Benzathine penicillin G weekly for three weeks. Other antibiotics that are generally effective for early or late syphilis include tetracycline, doxycycline, and ceftriaxone. The treatment of neurosyphilis is aqueous crystalline penicillin G 18 to 24 million intravenous (IV) or Procaine penicillin G 2.4 million units intramuscularly plus probenecid. Intramuscular doses of penicillin do not achieve high enough levels in the CSF to effectively treat neurosyphilis.[20]

ADDRESSING SYPHILIS IN RHODE ISLAND

Addressing syphilis requires awareness among PCPs and practitioners across multiple medical subspecialties. Socioeconomic status, low awareness, stigma, and access to healthcare may limit STD testing.[2,4,21] Providers should be familiar with taking a sexual history and delivering prevention messages as needed, especially among MSM who are at higher risk for acquiring syphilis. A survey of MSM conducted by the RI Department of Health (RIDOH) found that approximately 33% of MSM are not "out" to their doctors (i.e., have not disclosed their sexual behaviors). In response, RIDOH developed an educational website (www.health.ri.gov) entitled "Sexual Health Information for Gay Men" that provides information to MSM on how to talk to providers about sexual health, where to access free condoms, and advice on syphilis testing. In addition, RIDOH offers partner notification services (PNS) to all primary, secondary, and early latent syphilis diagnoses based on current CDC recommendations.[21,22] PNS is effective in promoting HIV/STD testing among sexual partners to facilitate diagnosis and treatment and to prevent further transmission. Syphilis screening is also a routine part of prenatal care in RI.[15,16]

To address increasing syphilis cases, the CDC recommends condoms, routine testing, and prompt treatment once diagnosed, as well as treatment of sexual partners. PCPs should be the primary site for clinical care. There are also several safety-net options for testing and treatment in RI which include the RI STD Clinic at The Miriam Hospital and urgent care centers.[6] Other safety-net clinics located in areas with high rates of Hispanic/Latino populations, such

as Clinica Esperanza and RI Free Clinic, facilitate access for these populations.

With rising rates of syphilis, RIDOH has invested in efforts promoting safer sex behaviors and STD screening among high-risk groups. Public education STD prevention messages have been viewed approximately 1.5 million times on various social media sites such as Facebook, Instagram, and YouTube. Throughout RI, there are eighty-five community settings that distributed 500,000 free condoms in 2017. Of the 142 cases of infectious syphilis reported to the RIDOH in 2017, 106 (75%) were interviewed by RIDOH for the purposes of partner services. In 2017 The Miriam Hospital STD Clinic, with support from the RIDOH, provided 2,582 syphilis tests and identified 60 new cases of infectious syphilis. In the fall 2018, the RIDOH launched the RIght Time sexual health app, which contains local resource information for sexually active individuals to access condoms, HIV/STD and family planning services.

The RIDOH also has a robust STD surveillance system across the state. This system is based on case reports submitted by diagnosing health care providers and clinical laboratories. Cases must be reported within four days of diagnosis using a confidential care report form (http://health.ri.gov/forms/reporting/cases/SexuallyTransmittedDiseases.pdf). A report will trigger partner services by RIDOH staff. The most recent RI HIV/STD Surveillance Report is available online (http://health.ri.gov/publications/surveillance/2016/HIVSTD.pdf). Additional resources are also available online as needed (http://www.health.ri.gov/publications/resourceguides/HIVSTDViralHepatitisProgramClinicalResources.pdf). The RIDOH also maintains a registry of all syphilis laboratory results and treatment histories which may be needed to accurately assess and treat, and can be accessed by calling RIDOH at 401-222-2577.

CONCLUSIONS

Syphilis has significantly increased in the US over the last decade, including in RI. Greater awareness is needed among medical providers, especially those that care for unserved populations including MSM. There are many barriers to effective care which disproportionately impact these populations in RI.[2] Focused research and public health initiatives directed at understanding and eliminating barriers to care are needed in order to improve syphilis prevention, early diagnosis, and treatment.[3] PCPs have a unique opportunity, together with other providers, to lead the public health effort to eliminate syphilis transmission in RI.

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