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ADVANCES IN PEDIATRICS

Resurgence of Syphilis

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Keywords

• Syphilis • HIV+ • PrEP • MSM • Women • Penicillin

Key points

- Since 2013, syphilis rates have been increasing for all age groups and races.
- Currently, men who have sex with men (MSM), and in particular MSM who are HIV+, have the highest rates of syphilis infection.
- As rates of syphilis increase in women, the number of infants being born with congenital syphilis has increased.

INTRODUCTION

Syphilis is a sexually transmitted infection (STI) caused by the spirochete bacterium *Treponema pallidum*. Syphilis has 4 stages: primary, secondary, latent (hidden), and tertiary (late). Primary syphilis is characterized by a painless sore called a chancre. The chancre is the site where the bacteria entered the body and usually appears within 3 weeks of contact but can take as long as 90 days. The chancre can take up to 6 weeks to heal and usually requires no treatment. The person is highly contagious during primary syphilis and continues to be contagious after the sore heals [1].

Two to six weeks after the appearance of the chancre a reddish brown, small, flat, or raised rash develops over the body including the palms of the hands and soles of the feet. This rash characterizes secondary syphilis and can last up to 2 months. As the bacteria spreads through the body, the person is still contagious and can experience fever; sore throat; fatigue; weight loss; lymphadenopathy; patchy hair loss of the eyebrows, eyelashes, or scalp hair; and neurologic symptoms including headache, neck stiffness, irregular pupils,

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and unequal reflexes. Small open sores can also develop on mucous membranes. These sores may contain pus or can have a moist wartlike appearance (condyloma lata) [1].

If a person with these symptoms is untreated, all symptoms will resolve and the infection will become hidden. This is the latent phase and the infection can remain hidden for up to 20 years. During latency, the person may continue to be contagious. It is also common to experience a relapse of secondary syphilis several times during latency. During the latent stage a woman can pass syphilis to her fetus causing a miscarriage, stillbirth, or birth to an infant infected with congenital syphilis [1].

Tertiary syphilis can develop anytime 1 year after initial infection. Tertiary syphilis is associated with the most morbidity of any stage of syphilis and can consist of any of the following: large internal or superficial sores known as gummata, cardiovascular symptoms, and neurologic symptoms. Neurosyphilis, often seen in tertiary syphilis, can occur during any stage of the infection, especially in immunocompromised patients [1].

HISTORY AND EPIDEMIOLOGY

Numerous theories have attempted to explain the origins of syphilis. The pre-Columbian hypothesis and the Unitarian hypothesis propose that syphilis has been infecting humans since 3000 BC after the spirochete experienced numerous mutations from those that cause pinta (*Treponema carateum*), Yaws (*Treponema pertenue*), and endemic syphilis (*Treponema Pallidum endemicum*). The mutations were in response to geographic and climate changes and interactions with different populations. However, the Columbian theory proposes that syphilis was brought to Europe by Columbus when he returned from the New World in 1493 [2–5].

The first descriptions of syphilis were transcribed in a poem, Syphilis sive morbus gallicus, by Girolamo Fracastoro in 1530. It euphemizes the shepherd Syphilis who is cursed with illness by the all-powerful Greek god, Apollo [4].

For centuries to follow, all sexually transmitted infections (STIs) were considered one malady. It was not until the nineteenth century that syphilis was determined to be a unique infectious agent after Ricord in 1831 determined that patients with syphilis only got syphilis after being in contact with other patients with syphilis and patients only got gonorrhea when in contact with others with gonorrhea [2,6].

In 1905 the etiologic agent for syphilis was discovered by Schaudinn, and Hoffman named the bacterium *T pallidum.* In 1906, dark-field microscopy was introduced by Landsteiner to detect spirochetes. In 1910, the first serologic test for syphilis was introduced by Wasserman [6]. In 1949, the first test to specifically diagnosis *T pallidum* infection was developed by Nelson and Mayer. This test was able to diagnosis syphilis and monitor treatment response in asymptomatic patients [6].

The treatment for syphilis has been very diverse and has involved inflicting significant pain on patients and serious adverse reactions. The earliest treatment was derived from a plant brought back to Europe from the New World called *Guaiacum Officinale*, commonly known as the guaiac tree. It was a very effective purgative agent and was thought to be a "blood Cleanser." By the mid-1500s oral or injected mercury was used to treat syphilis. Mercury is a potent diuretic and it was thought that syphilis could be removed from the body through excessive sweating and diuresis. By the late 1880s, bismuth became the preferred heavy metal used to treat syphilis, because it was less toxic than mercury and had a stronger bactericidal effect. By the early 1900s, arsenic compounds such salvarsan and neosalvarsan were the mainstay of syphilis treatment, and they were replaced in the early 1940s with penicillin [2,7]. Penicillin continues to be an effective first-line treatment for syphilis, and it was once thought that it would eradicate the bacterium [8].

A large autopsy study published by Yale University in 1947 concluded that approximately 10% of the US population was afflicted with syphilis [9]. Although penicillin was discovered in 1929, the first use of penicillin to treat syphilis was described by John Mahoney of the United Stated Public Health Service (USPHS) in 1943 [5,10,11]. The USPHS conducted the infamous "Tuskegee Study of the Untreated Syphilis in Negro Male" [5,11], an observational study of the natural history of syphilis. The subjects included 412 African-American men with syphilis and 192 without syphilis in rural Alabama. Both study groups were followed until 1973 or until autopsy results were available, and all received free meals, medical examinations, and burial insurance. However, infected subjects with positive serologies were not informed that they had syphilis and were not treated [11]. It was not until 1997 that the US government apologized for its role in the study.

Syphilis is an infection that does not discriminate. Over the years, all levels of society have been affected by syphilis, varying by social circumstances of the time [2]. In the United States, after World War I (WWI) rates of syphilis dropped dramatically after diagnostic tests and acceptable treatments with arsenic compounds became available. The number of syphilis cases increased following the return of soldiers from WWII, but with the discovery of penicillin in the 1940s, the increase quickly plateaued and throughout the 1950s new diagnoses decreased [8,12,13]. With the advent of the sexual revolution in the 1960s syphilis cases began to increase again and continued to increase through the 1970s, with significant spread among men who have sex with men (MSM). Then the human immunodeficiency virus (HIV) and AIDS epidemic began. During the 1980s and early 1990s, AIDS induced changes in sexual behaviors, and syphilis rates in the United States significantly dropped, especially among MSM. However, during this same period, syphilis rates increased among minority heterosexual populations in urban centers. The increase in syphilis rates paralleled the crack cocaine epidemic in these urban populations [12,13]. During this time intense public health measures reduced the number of new cases of syphilis and this trend continued throughout the 1990s. The decline was so significant that by 2000 the incidence was lower than in 1941. This continuous decline in syphilis cases and the concentration of new cases in small urban geographic areas led many to believe that syphilis could be eradicated. The Centers for Disease Control (CDC) developed a National Plan to eradicate syphilis in 1999, which was revised in 2006 [13,14].

From 2001 to 2005 the rates began to increase again, predominantly among MSM. Between 2004 and 2005 the incidence of new cases increased by 11.1%, and in 2004 and 2005, for the first time since the middle 1990s, the incidence began to increase among woman (0.8–0.9 cases per 100,000 population). From the mid-1990s through 2005 the rate of congenital syphilis decreased yearly at a rate of 14.1% [13–15].

From 2013 to 2017 the incidence of primary and secondary syphilis increased by 72.2% (Fig. 1). In 2017 alone it increased by 10.5% (9% in men and 21.2% in women). The increase in women is particularly problematic because it is accompanied by a concomitant increase in congenital syphilis [14,15]. The incidence has also increased significantly in men who have sex with women. The incidence varies by geographic location, with rates in 2017 of 13, 10.2, 8, and 6.2 cases per 100,000 in the west, south, northeast, and midwest regions of the United States, respectively [15] (Fig. 2).

In 2017, the incidence of primary and secondary syphilis increased in all age groups over 15 years. In men, the highest rate of primary and secondary syphilis was in the 25 to 29 year age group (51.9 per 100,000 men), whereas in women the highest rate was in the 20 to 24 year age group (7.8 per 100,000 women) (Fig. 3). From 2016 to 2017, the rates of primary and secondary syphilis infection increased 9.8%, 7.8%, 10.7%, 14.3%, 17.8%, 6.5%, 4.3% 11.8%, and 16.7% for those aged 15 to 19, 20 to 24, 30 to 34, 35 to 39, 45 to 54, 55 to 64, and 65 years or greater, respectively [15,16].

Blacks had the highest rates of primary and secondary syphilis in 2017, with 24.7 cases per 100,000 population–a rate 4.5 times higher than that for whites

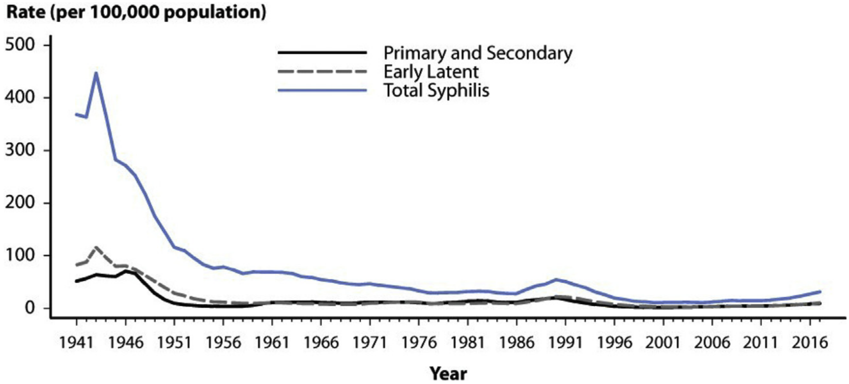

Fig. 1. Syphilis—rates of reported cases by stage of infection, United States, 1941 to 2017. (*From* Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2017. Atlanta: U.S. Department of Health and Human Services; 2018. https://www.cdc.gov/std/stats17/syphilis.htm.)

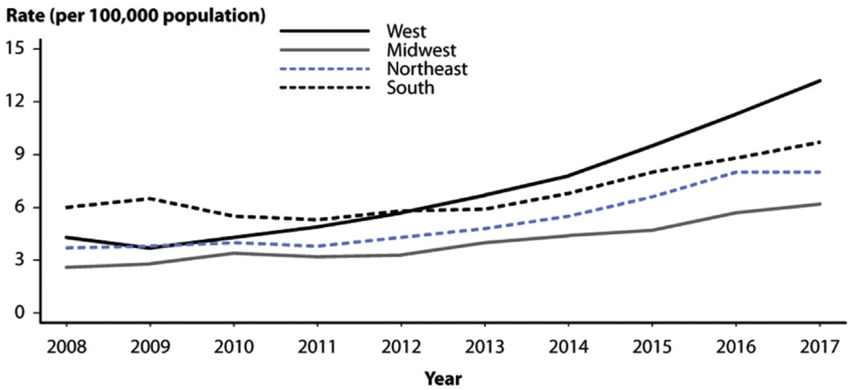

Fig. 2. Primary and secondary syphilis—rates of reported cases by region, United States, 2008 to 2017. (*Data from* Centers for Disease Control and Prevention Sexually Transmitted Disease Surveillance 2017. Atlanta (GA): US Department of Health and Human Services; 2018 https://www.cdc.gov/std/stats.)

(5.4 per 100,000 population). Asians had the lowest rate (4.4 cases per 100,000 population), whereas native Hawaiians and other Pacific Islanders, Hispanics, and American Indian/Native Alaskans had rates of 13.9, 11.8, and 11.1 cases per 100,000 population, respectively [16].

Syphilis continues to have high coinfection rates in persons living with HIV disease. The rates of coinfection are highest in MSM with 45.5% of primary and secondary syphilis cases and lowest in women with 4.5% [16] (Fig. 4).

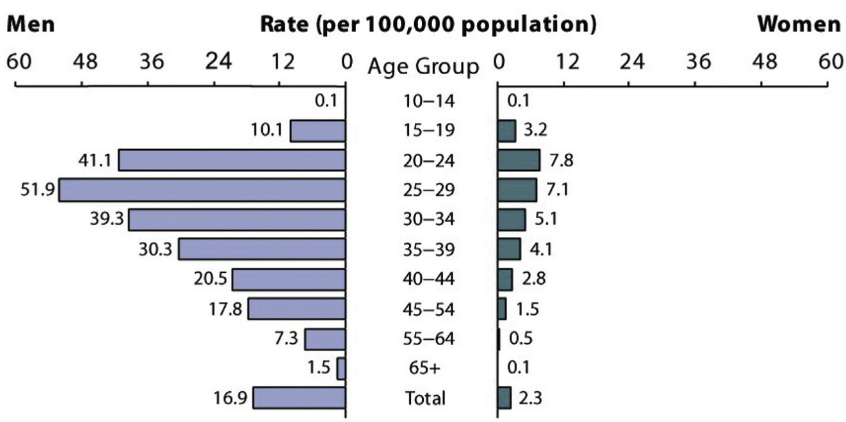

Fig. 3. Primary and secondary syphilis—rates of reported cases by age group and sex, United States, 2017. (*From* Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2017. Atlanta: U.S. Department of Health and Human Services; 2018. https://www.cdc.gov/std/stats17/syphilis.htm.)

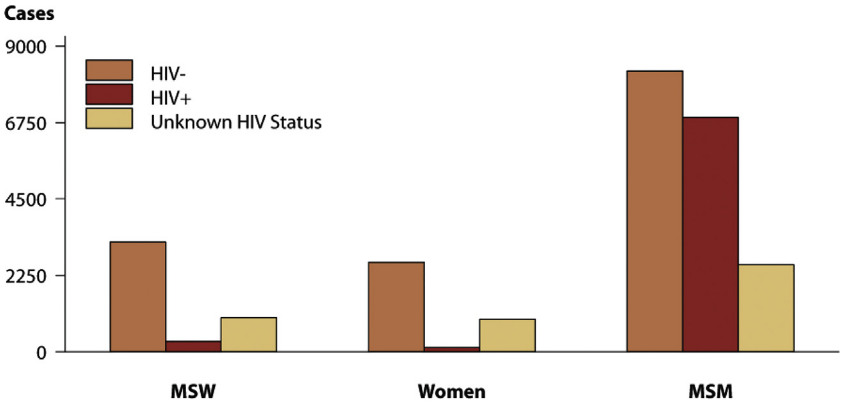

Fig. 4. Primary and secondary syphilis—reported cases by sex, sexual behavior, and HIV, United States, 2017. (*From* Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2017. Atlanta: U.S. Department of Health and Human Services; 2018. https://www.cdc.gov/std/stats17/syphilis.htm.)

The reasons for the dramatic increase in the incidence of primary and secondary syphilis over the last 5 years continue to be debated. It has been hypothesized that the introduction of HIV preexposure prophylaxis (PrEP) is contributing to the increase among MSM. HIV PrEP is a daily combination pill of the antiretroviral drugs tenofovir and emtricitabine. When taken as directed, PrEP significantly reduces the number of new HIV cases [17]. It is theorized that some MSMs are taking HIV PrEP in place of instead of in addition to the use of condoms, particularly those who engage in receptive anal sex. Volk and colleagues [18] found a 41% decrease in self-reported use of condoms in a cohort of PrEP users. This is an example of "risk compensation." However, other studies have shown no risk compensation in PrEP users [19]. The use of condoms is only partially protective because syphilis only requires direct contact to cause infection, and chancres may be present on many different parts of the body. The increase in primary and secondary syphilis incidence amongst MSMs, including PrEP users, may be partially attributable to increased testing, because continued use of the medication requires an HIV test every 3 months. Frequent interactions with a health care provider bolster opportunities for screening and treatment of other STIs, including syphilis.

Although the burden of disease is disproportionately shared by younger minority male populations, particularly MSMs, the incidence of primary and secondary syphilis cases in the United States is increasing in nearly every demographic, indicating that PrEP use is not the primary reason for the increase. However, in 2017, all races and ethnicities have the highest number of cases of syphilis in the MSM population (Fig. 5).

Rates are increasing in other vulnerable populations. Congenital infections have increased in the United States since 2013, increasing 48.3% to 23.3 cases per 100,000 live births from 2016 to 2017, and resulting in 918 congenital infections

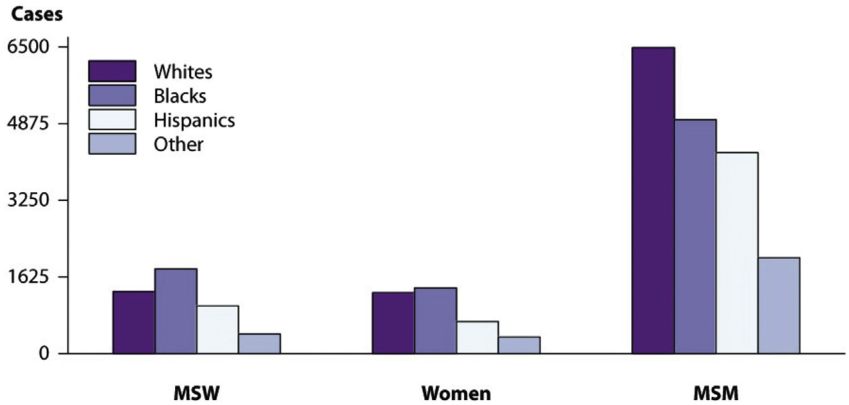

Fig. 5. Primary and Secondary Syphilis — Reported Cases* by Sex, Sexual Behavior, Race, and Hispanic Ethnicity, United States, 2017.

* Of all reported cases of primary and secondary syphilis, 15.0% were among men without data on sex of sex partners, and 0.1% were cases with unknown sex; 5.7% of all cases had missing or unknown race/Hispanic ethnicity. Cases with missing or unknown race/Hispanic ethnicity are included in the ''Other'' category.

with 64 syphilitic stillbirths and 13 infant deaths. The increase in congenital infections is consistent with the increase in primary and secondary infections in all women (see Fig. 5). The rates of congenital syphilis vary by geographic location, with the highest rate in 2017 being in the West and lowest in the Northeast (37 and 5.7 cases per 100,000 per live births, respectively) [16] (Fig. 6).

The rates of all stages of syphilis have been increasing throughout the twenty-first century, with 2017 having the highest rates since the early 1990s. Early latent syphilis in 2017 increased 17.6%, whereas late latent syphilis increased 17.3%. Neurosyphilis, which can occur at any stage, has remained relatively low with a prevalence of 0.84% between 2009 and 2015. The highest prevalence of neurosyphilis is in those diagnosed with HIV [20].

Although the rates for most STIs have increased since 2013, the increasing rates of primary and secondary syphilis are of particular concern due to the significant morbidity associated with untreated syphilis and the increased risk of congenital syphilis. In 2016 the CDC issued a call to action for health care providers and specific high-risk populations to work together to curb the alarming yearly increase in new syphilis cases [21].

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) CALL TO ACTION

Fortunately, *T pallidum* remains sensitive to penicillin. Patients allergic to penicillin have had limited options for treatment, with penicillin desensitization being the recommended course of action. However, the resurgence of syphilis intensifies the need for timely diagnosis and treatment, and alternative

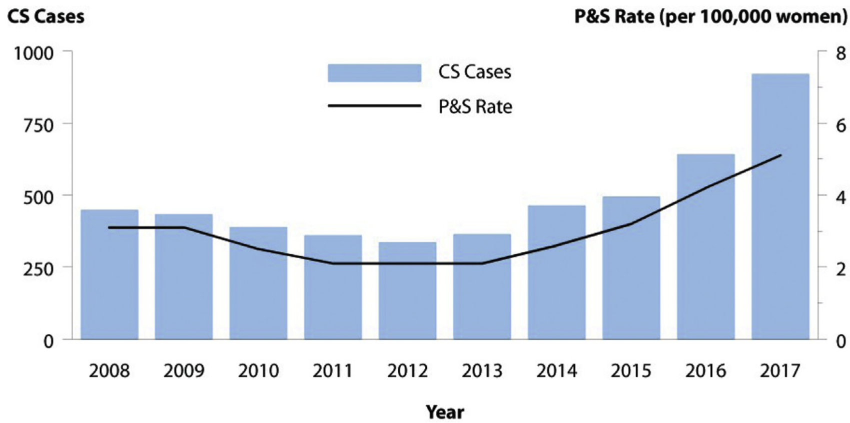

Fig. 6. Prevalence of primary and secondary syphilis and the number of cases of congenital syphilis. CS, congenital syphilis; P&S, primary and secondary syphilis. (*From* Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2017. Atlanta: U.S. Department of Health and Human Services; 2018. https://www.cdc.gov/std/stats17/syphilis.htm.)

antibiotics are being investigated. Tetracycline and doxycycline have been endorsed as alternative therapies despite a paucity of efficacy data [22]. Doxycycline regimens are preferred due to better compliance with less frequent dosing and fewer gastrointestinal side effects. In more recent studies, doxycycline has been shown to be an effective alternative to penicillin, with 100% effectiveness for early syphilis and 92.4% for all stages at 12 months after treatment [23].

Azithromycin, 2 gm, in a single dose has been used, but *T pallidum* chromosomal mutation associated with azithromycin and other macrolide-resistant drugs and treatment failures have been documented in the United States. Azithromycin should be used with caution and only when treatment with penicillin or doxycycline is not feasible. The CDC states that azithromycin should not be used in MSM, persons with HIV, or pregnant women due to the possibility of an azithromycin-resistant strain of syphilis in these populations. Ceftriaxone can also be used as an alternative therapy to penicillin but should be avoided in patients with severe penicillin allergy. It is essential that all patients treated with alternative therapies have careful clinical and serologic follow-up [24]. However, penicillin is the only treatment used in pregnant women diagnosed with syphilis. Doxycycline is contraindicated for use in pregnancy; therefore, if a pregnant woman is penicillin allergic, penicillin desensitization and treatment with penicillin is recommended [24] (Table 1).

The resurgence in syphilis has also focused attention on improving its diagnosis. Currently, there are 2 main techniques for detecting spirochetes associated with syphilis. Direct detection testing methods include dark-field microscopy, nucleic acid amplification methods, direct fluorescent antibody

Table 1
2015 CDC STI treatment guidelines for syphilis

	Infants (>1 mo age) & children	Adults	Alternative nonpregnant adult treatment
Primary and secondary syphilis	Benzathine penicillin G, 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose	Benzathine penicillin G, 2.4 million units IM in a single dose	Doxycycline, 100 mg, twice daily for 14 d, tetracycline, 500 mg, 4 times daily for 14 d. Ceftriaxone, 1–2 gm, daily IM or IV for 10–14 d
Early latent syphilis	Benzathine penicillin G, 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose	Benzathine penicillin G, 2.4 million units IM in a single dose	Doxycycline, 100 mg, twice daily for 14 d, tetracycline, 500 mg, 4 times daily for 14 d. Ceftriaxone, 1–2 gm, daily IM or IV for 10–14 d
Late latent syphilis OR latent syphilis of unknown duration	Benzathine penicillin G, 50,000 units/kg IM, up to the adult dose of 2.4 million units, administered as 3 doses at 1-wk interval (total 150,000 units/kg up to the adult total dose of 7.2 million units)	Benzathine penicillin G, 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-wk interval	Doxycycline, 100 mg, twice daily or tetracycline, 500 mg, 4 times daily for 28 d.
Tertiary with normal CSF *Examination*		Benzathine penicillin G, 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-wk interval	If allergic to penicillin consult an infectious disease expert
Neurosyphilis and ocular syphilis	Aqueous crystalline penicillin G, 200,000–300,000 units/kg/d IV, administered as 50,000 units/kg every 4–6 h for 10 d	Aqueous crystalline penicillin G, 18–24 million units/d, administered as 3–4 million units IV every 4 h or continuous infusion for 10–14 d	Procaine penicillin G 2.4 million units IM once daily PLUS probenecid, 500 mg, orally 4 times a day, both for 10–14, ceftriaxone, 2 gm, daily either by IM or by IV for 10–14 d

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Table 1
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	Infants (>1 mo age) & children	Adults	Alternative nonpregnant adult treatment
Special note on pregnancy	Pregnant women should be treated with the penicillin regimen appropriate for their stage of infection. Pregnant women who report penicillin allergy should be desensitized and treated with penicillin.		
Special note on persons with HIV	Early latent syphilis = Benzathine penicillin G, 2.4 million units IM in a single dose Late latent syphilis = Benzathine penicillin G, at weekly doses of 2.4 million units for 3 wk Efficacy of alternative regimens in person with HIV infection has not been well studied.		
Special note on infants and children	Birth and maternal records need to be reviewed to assess for congenital vs acquired syphilis. Recommend management by a pediatric infectious disease specialist and evaluation for sexual abuse through consultation with child protection services. In late latent syphilis CSF examination need to rule out neurosyphilis.		
Special note on neurosyphilis and ocular syphilis	Above mentioned treatment is shorter than those used for latent syphilis. Therefore, benzathine penicillin 2.4 million units IM once per week for up to 3 wk can be considered after completion of these neurosyphilis treatment regimens to provide comparable total duration of therapy. In pencillin-allergic patient, ceftriaxone, 2 gm, daily either by IM or by IV for 10–14 d can be used as an alternative or consider penicillin desensitization in consultation with a specialist.		

Abbreviations: IM, intramuscular; IV, intravenous.

Data from Centers for Disease Control and Prevention Sexually Transmitted Disease Treatment Guidelines, 2015. In. Atlanta (GA): US Department of Health and Human Services; 2015.

testing, and histopathologic examination of infected tissues. Direct methods are advantageous because they can detect infection in some patients before they have mounted the measurable antibody response that is required for serologic testing methods. However, access to direct methods, especially dark-field microscopy, is limited in many clinical settings. Although demonstration of *T pallidum* is the definitive method of diagnosis, successful testing with dark-field microscopy has limited sensitivity, thus failure to detect *T pallidum* by this method does not rule out syphilis [25].

Direct fluorescent antibody testing for *T pallidum* is easier to perform than dark-field microscopy but is no longer available in the United States. Detection of *T pallidum* DNA through nucleic acid amplification is also commercially available; however, such testing is not yet approved by Food and Drug Administration [26]. Specimens for testing by this method include CSF, whole blood, serum, or swabs from genital lesions. Preliminary studies have shown *T pallidum* PCR testing has a high degree of accuracy and better sensitivity and specificity than dark-field microscopy; however, more studies are needed to confirm this finding [27].

Indirect serologic testing, the other method used for syphilis diagnosis, is based on the detection of antibodies produced in response to infection. These antibodies fall into 2 categories: nontreponemal test for screening and treponemal test for confirmation [25]. Presumptive diagnosis requires the use of both nontreponemal and treponemal serologic testing.

All nontreponemal tests measure IgG and IgM antiphospholipid antibodies formed by the host in response to lipoid material released by damaged host cells early in the infection and to lipid from the cell surface of the treponeme. The most commonly used nontreponemal tests used in the United States are the Venereal Disease Research Laboratory (VDRL) slide test and the rapid plasma reagin test (RPR). Both tests are inexpensive, can be performed rapidly, and provide semiquantitative results through serial 2-fold dilutions. However, for diagnosis of acute infection the testing must be confirmed by one of the specific treponemal tests to exclude a false-positive result [25]. False-negative results can occur in patients with early primary syphilis (before the development of a host antibody response), latent acquired syphilis of long duration, and late congenital syphilis. Occasionally, in cases where high antibody titers are present, nontreponemal testing may show only a weakly positive or false-negative result, known as the prozone phenomenon. Diluting the serum will subsequently result in a positive result [28]. False-positive results for nontreponemal testing can also occur due to advanced age, certain viral infections (eg, Epstein-Barr, hepatitis, varicella, mumps, and measles), lymphoma, tuberculosis, malaria, endocarditis, autoimmune and inflammatory diseases (eg, rheumatoid arthritis, lupus, vasculitis and thyroiditis, ulcerative colitis), pregnancy, abuse of intravenous drugs, laboratory or technical error, and Wharton jelly contamination when umbilical cord blood specimens are used [25].

Both the RPR and VDRL provide semiquantitative results through serial 2-fold dilutions. These titers can be used to both define disease activity and monitor response to therapy. RPR and VDRL titers differ, with RPR titers generally being higher than VRDL titers. Therefore, the same test must be used to monitor follow-up response to therapy. A sustained 4-fold or greater decrease in titer (equivalent to a change of 2 dilutions, eg, 1:32–1:8) demonstrates adequate treatment. A sustained 4-fold increase after treatment suggests reinfection or relapse. Nontreponemal titers usually decrease 4-fold within 6 to 12 months after therapy for primary or secondary syphilis, and if treated during early primary or secondary syphilis they usually become nonreactive within a year after successful therapy. Patients treated for latent or tertiary syphilis may continue to have low stable titers despite effective therapy [25].

Treponemal tests detect antibody to *T pallidum* proteins: commonly used tests are enzyme immunoassays (TP-EIA), chemiluminescence assay (TP-CIA), and fluorescent treponemal antibody absorption test (FTA-ABS). Treponemal tests are technically more difficult to perform and more expensive than nontreponemal tests. Patients may remain reactive for years regardless of treatment, and titers correlate poorly with disease activity. For this reason, these tests are traditionally used to confirm infection following a positive nontreponemal test and should not be used to evaluate response to therapy, relapse, or reinfection in previous treated patients [25].

The "conventional diagnostic approach" for syphilis serologic testing starts with a nontreponemal test such as the RPR or VRDL and if positive a confirmatory test is performed using one of the treponemal tests such as the TP-PA or FTA-ABS. With early syphilis nontreponemal tests may be positive before the treponemal test is positive. To automate the testing process and reduce costs, some laboratories screen with a treponemal test such as TP-PA or TP-EIA first. With this reverse algorithm or "reverse-sequence screening" a positive treponemal test result is confirmed with a quantitative nontreponemal test (RPR or VDRL). If the results are discordant, a second treponemal test targeting a different *T. pallidum* antigen is performed to confirm the original test. If the second treponemal test is negative and the person is at low risk for syphilis, the original treponemal test result likely will be false positive [26].

None of these current testing methods allow for on-the-spot diagnosis, which delays treatment and increases the likelihood of losing the patient to follow-up. These limitations pose an urgent need for modernizing the testing capabilities such as those that are available for rapid HIV detection.

Additional items in the CDC's Call to Action include the development of electronic health records that include sexual history taking, STI screening, and treatment support documentation that can be easily integrated with public health departments; exploration of all options for the development of a syphilis vaccine; and expanded screening, particularly among the most at-risk populations including pregnant women and MSM, particularly those with HIV.

SUMMARY

Since the start of the twenty-first century rates of syphilis have been gradually increasing and now it is affecting a broader range of age groups, races, ethnicities, and geographic regions of the country. The CDC issued a Call to Action in 2017 to health care providers, researchers, and at-risk populations to work together to curb this resurgence. Syphilis is preventable and curable, and the CDC is calling for a twenty-first century approach to supplement control measures in use since the end of WWII. The Call to Action includes the development of improved electronic health records, modernized blood testing for detection and staging of the infection, expanded treatment options for those for whom penicillin is contraindicated and for whom penicillin is not effective in treating complications of syphilis, and development of a syphilis vaccine. Finally, the CDC is calling on all health care workers to expand screening for syphilis especially among the most at-risk populations including pregnant women and MSM, including those with HIV.

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