Syphilis:
A growing concern

CE 1.5 CONTACT HOURS

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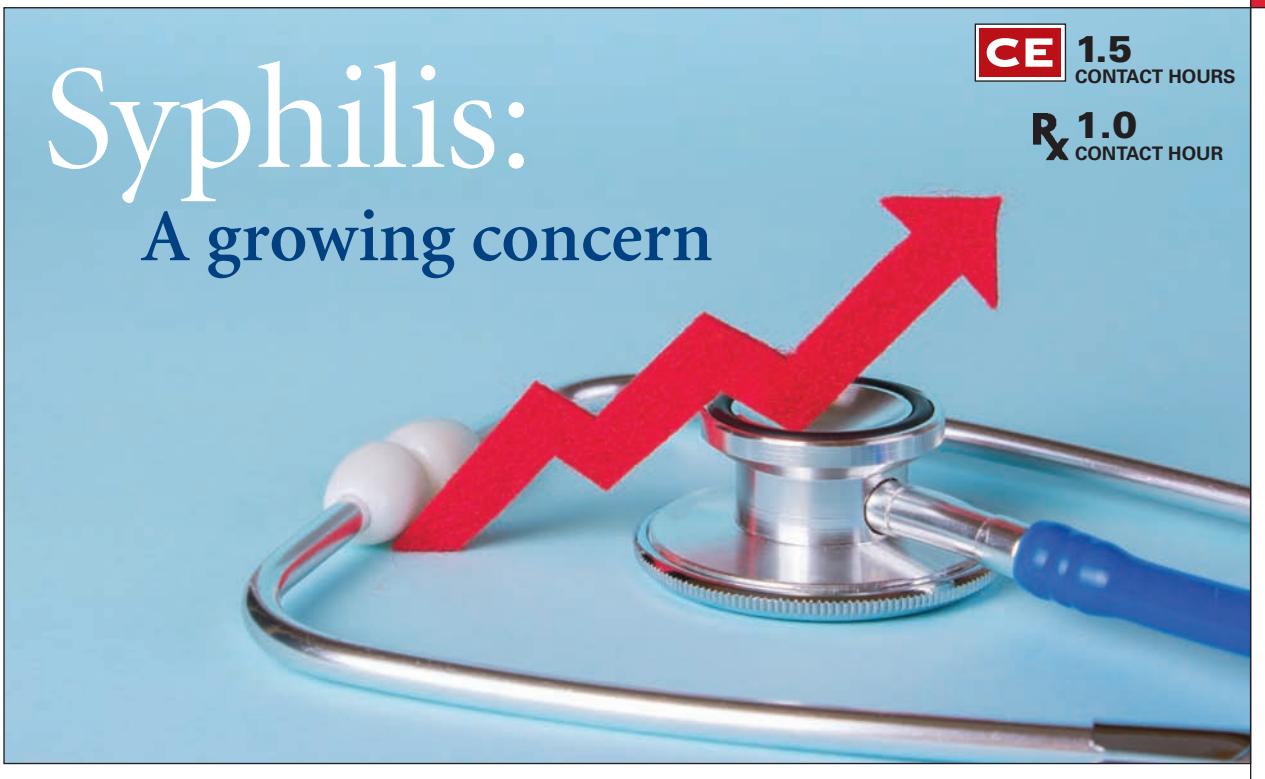

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Abstract: Since a brief low in 1998, reported cases of syphilis have continued to grow in the US. As primary care providers, NPs are at the forefront of the battle to eliminate syphilis. This article reviews the stages of this infection, diagnosis nuances, and treatment guidelines.

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Although syphilis may be considered a disease of antiquity, it remains a global health concern. In the mid-1990s, in the US, the number of cases of syphilis was reported to be at a historic low rate.[1] At that time, the CDC hoped that syphilis would be eliminated in the US. In 1999, the CDC's national goal was to reduce primary and secondary (P&S) syphilis cases to 1,000 or fewer by 2005.[2] Instead, this difficult-to-diagnose though easy-to-treat disease reversed course and almost immediately began to increase in prevalence.

By 2016, the CDC reported more than 27,000 cases, a 300% increase in P&S syphilis cases since 1998.[1] By 2017, the number of P&S syphilis cases had increased to 30,644.[3] This continued rise in prevalence reinforces the need for all healthcare providers to be knowledgeable about the history of, epidemiology of, causative agent of, clinical manifestations of, diagnostic testing for, and treatment protocol for syphilis.

History

Syphilis is a systemic disease caused by the bacterium *Treponema pallidum.*[3] This tightly coiled spirochete is one of several pathogenic *T. pallidum* subspecies and has the specific name of *T. pallidum (subsp. pallidum),* known more commonly by the shortened *T. pallidum.*[4] (See *Dark-field micrograph of T. pallidum.*) Syphilis is the only pathogenic human treponemal disease that is venereally transmitted. The stages of syphilis include primary, secondary, latent, and tertiary (late); with P&S syphilis being the most transmissible.[3]

Syphilis has long been present in medical history, with countries often blaming neighboring countries for bringing this disease to their borders.[5] Throughout the ages, syphilis spread worldwide without an effective treatment until the 20th century. In 1928, Alexander Fleming, Scottish bacteriologist, discovered penicillin, and the antibiotic has been used as the first-line treatment for syphilis since 1943.[5] Although antibiotics are

Keywords: chancre, dark-field microscopy, nontreponemal test, penicillin G benzathine, syphilis, treponemal test

an effective treatment for syphilis, numerous factors, including social barriers, lack of resources, and the disease's long incubation period and multiple stages, hinder the work of eliminating this disease entirely. In April 2017, the CDC issued an official call to action to end the growing prevalence of syphilis in the US.[6] This strong call endorses the need for providers to fully understand the scope of the problem and its diagnosis and treatment.

Epidemiology

The nadir of syphilis rates in 1998 was short-lived with a consistent increase thereafter.[3,6,7] In 2017, the CDC reported 30,644 new P&S syphilis cases and 101,567 new diagnoses of syphilis encompassing all stages of the disease.[3]

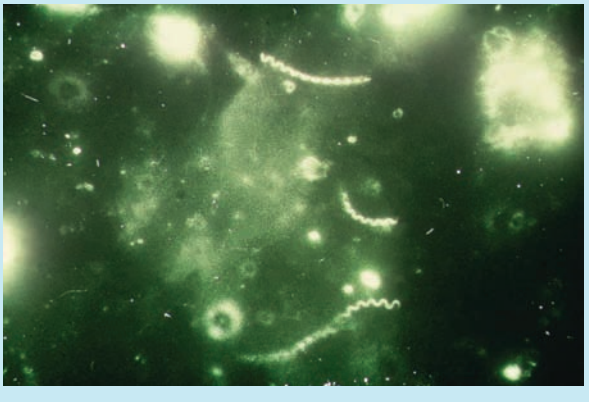
In 2016, of the 83% of all cases that provided documentation of their sexual partners, data indicated that 63% were men who have sex with men (MSM), 7% were MSM and men who have sex with women (MSMW), 17% identified as men who have sex with women only (MSW), and 13% were female.[1] Rates among women have increased as well, doubling from 2012 to 2016.[1] Likewise, congenital cases are on the rise as well, having increased by 88% to a total of 628 cases.[1]

Within the US, the reported cases of MSM P&S syphilis differ slightly by geographic region, though an increase in P&S cases occurs in every region of the country.[8] (See *Primary and secondary syphilis - rates of reported cases by region, US, 2008-2017.*)

Congenital syphilis is geographically focused, with three states encompassing 50% of all cases. According to Bernstein and colleagues, urbanization leads to increased population density and increased sexual network density, which may increase levels of disease.[1] The use of geosocial network phone applications and/or location-based applications for sex has been shown to increase the risk of sexually transmitted infections (STIs), as well as reduce the ability for partner notification because of anonymity.[9] As a result, fewer MSM partners are identified and treated.[10] Employment and income status influence the rate of both congenital syphilis and syphilis in MSM.[1] Poverty, unemployment, and low income levels result in higher rates of congenital syphilis and syphilis in MSM.[1] Racial divides are also noted, with the highest rates of syphilis (all stages) occurring among Black MSM.[1] In addition, in 2016, non-White mothers encompassed 75% of all reported cases of congenital syphilis.[1]

Dark-field micrograph of *T. pallidum*

This digitally colorized photomicrograph depicts what was viewed while examining this dark field preparation of a blood sample extracted from a patient with syphilis, which included these *T. pallidum* bacterial spirochetes.



Source: Courtesy of the Centers for Disease Control and Prevention/Susan Lindsley. https://phil.cdc.gov/Details.aspx?pid=1248. 1971.

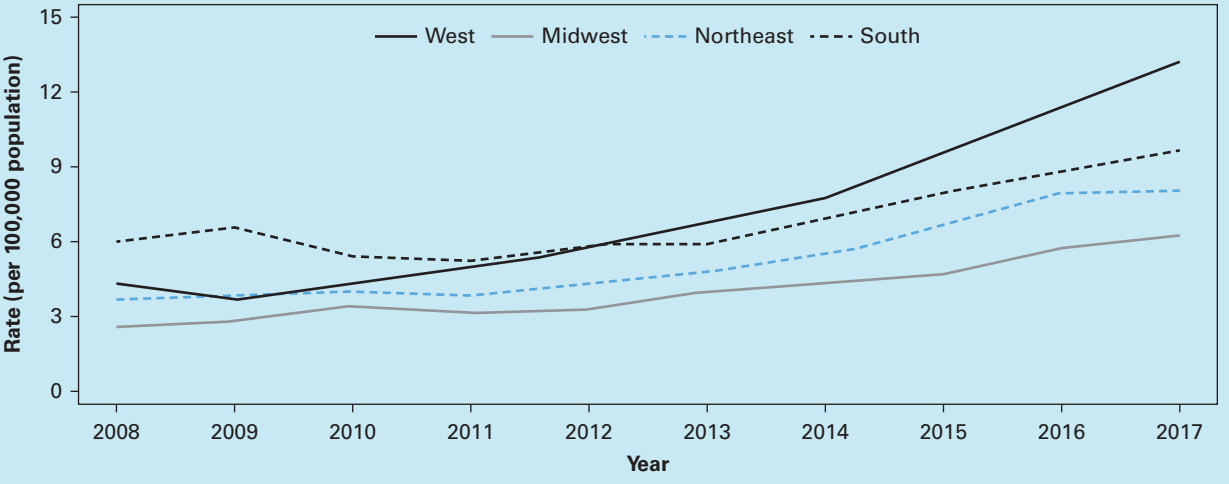
Causation

Most cases of syphilis are sexually transmitted, except for congenital syphilis. *T. pallidum* is transmitted by direct contact with a painless syphilitic sore, known as a chancre.[3] Chancres are usually located on the external genitalia of both sexes, but may be present on the mouth, hands, anus, or internal sites, such as the cervix and/or rectum.[3,7] The start of the first symptoms appear approximately 3 weeks after contact, with a range of 10 to 90 days.[3,7]

Transmission of syphilis through blood transfusion is rare in the US, with the last reported case in 1966.[11] Prevention of transfusion-transmitted syphilis (TTS) was a result of standard syphilis testing of blood donors as well as the fragility of *T. pallidum* when blood is stored in temperatures 68° F (20° C) for more than 72 hours. In countries without blood banks, where the needed blood may be obtained and transfused within hours, the risk for TTS is greater.[11]

Syphilis detection is hindered by many possible differential diagnoses that may be considered for the syphilitic symptoms, which is how syphilis earned its nicknames such as "The Great Mimicker," the "Great Pretender," and the "Great Imitator."[3,12,13] Each manifestation of syphilis depends on three independent factors: lesion locations, the infected patient's immune status, and time or duration of infection.[14]

Primary and secondary syphilis - rates of reported cases by region, US, 2008-2017.



Source: Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention. www.cdc.gov/std/stats17/figures/36.htm. 2018.

The location of the lesion sites, whether on the skin, mucous membranes, or internal, affects the patient's immune response to the bacterium as well as the transmission of the disease. Growth of *T.pallidum* is temperature-dependent, with the body's average internal temperature of 98.6° F (37° C) not optimal for growth.[14] This leads to differing immune responses for external surfaces compared with internal organs. The immune status indicates the ability of the infected patient's body to challenge the progression of the disease through its stages. In immunocompromised patients, the progression of the disease occurs more rapidly than in those without any immunosuppression.[14] Time or duration of infection correlates to the stages of syphilis within the individual patient. The manifestations of syphilis vary along a progression of different stages, with a broad, variable window of time for each stage. The stages are primary, secondary, latent, and tertiary (late).[3] The latent stage itself has been divided into early and late latent.

A further delineation of syphilis has been made using quantitative time, separating early and late syphilis. Early syphilis is defined as syphilis that has lasted for less than 1 year; this encompasses incubation period, and the primary, secondary, and early latent stages.[7] Late syphilis is defined as syphilis of greater than 1 year's duration, which includes late latent and tertiary stages.[7]

Stages of syphilis

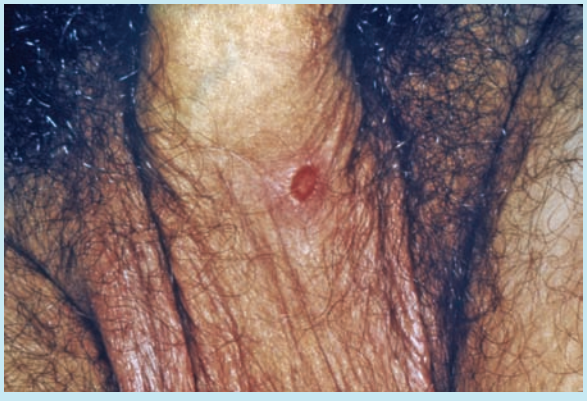
Primary stage. Primary syphilis is evidenced by a painless lesion, known as a chancre, that develops at the site of contact approximately 3 weeks after exposure, with a range of 1 to 12 weeks.[3,14] This postexposure window coincides with the incubation period during bacterial multiplication. The dissemination of *T. pallidum* systemically begins within a few hours of the inoculation.[14] The chancre begins as a macule, then papule, and rapidly develops into a painless erosion that is round or ovular in shape with sharp indurated margins. The size of the chancre ranges from 0.5 to 1.0 cm.[14] Along with the chancre, nontender regional lymphadenopathy will occur but may not be detected.[7] If untreated, the chancre will heal within 1 to 6 weeks.[3,7] (See *Primary syphilis chancres.*) However, if left untreated, syphilis will progress to the secondary stage.[3]

As indicated by the moniker, the Great Imitator, the syphilitic lesion must be evaluated for differential diagnoses. Not all primary chancres present as the "classic" chancre; comorbid infectious processes, such as HIV, other STIs, or bacterial infections, can confound the presentation.[14] Multiple chancres can occur as well, particularly in individuals with HIV.[14]

Secondary stage. The onset of the secondary stage of syphilis is variable and marked by the development of a nonpruritic rash. This rash may appear while the chancre is healing or occur up to 8 weeks after the chancre heals.[3,7] The rash associated with

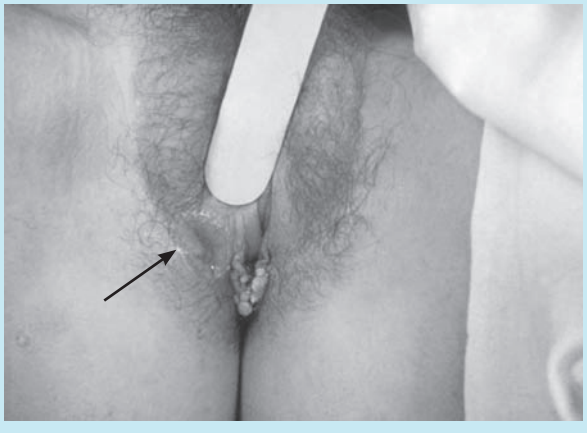
Primary syphilis chancres

Chancre on glans of penis.



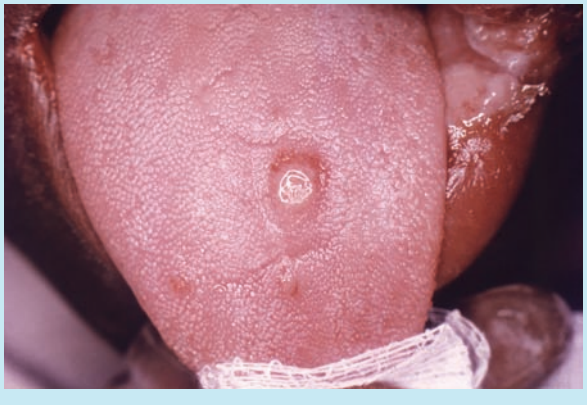
Source: Courtesy of the Centers for Disease Control and Prevention/Dr. N. J. Fiumara. https://phil.cdc.gov/Details.aspx?pid=6760. 1976.

Chancre on the vulvar surface (see arrow).



Source: Courtesy of the Centers for Disease Control/Susan Lindsley. https://phil.cdc.gov/Details.aspx?pid=2358. 1971.

Chancre on the surface of the tongue.



Source: Courtesy of the Centers for Disease Control and Prevention/Robert E. Sumpter. https://phil.cdc.gov/Details.aspx?pid=12623. 1967.

secondary syphilis is not standard for the disease and can present as papular, maculopapular, or pustular, though none of these rash presentations are capable of disease transmission.[3,7] The location of the rash is nonspecific, occurring in one or more areas of the body, often involving the palms and soles.[7] The rash may be so faint as to not be identified. (See *Secondary syphilis manifestations.*)

Groin, perianal, or vulva (condyloma lata), or oral lesions may coincide with symptoms of lymphadenopathy, fever, alopecia, myalgia, fatigue, and weight loss.[3,7] Headache, neck stiffness, and an increase in lymphocytes in the cerebrospinal fluid (CSF) can develop, caused by the systemic dissemination of the disease infiltrating the central nervous system.[7] The symptoms of secondary syphilis will resolve without treatment. The length of time for the secondary stage is dependent on the immunity status of the individual. However, if left untreated, secondary syphilis will progress to the latent stage and possibly the tertiary stage.[3]

Latent stage. The latent stage of syphilis occurs between the resolution of the secondary stage and onset of the tertiary stage. Although there is a lack of clinical manifestations during the latent stage, serologic testing will be positive.[7] The duration of the latent stage can vary, particularly between the immunocompetent and the immunosuppressed patient. Immunosuppressed individuals, particularly those with HIV coinfection, may have a brief few months of the latent stage, although immunocompetent patients can have up to 5 years free from overt manifestations of syphilis.[14]

The latent stage may be divided into early or late latent syphilis, determined by the duration of the asymptomatic period. The CDC considers the first year of the latent phase to be early latent.[15] Some individuals who had an undiscovered chancre and an absent or mild cutaneous eruption for the secondary stage of syphilis may be initially diagnosed with syphilis in this early latent stage during preventive care services. Late latent syphilis refers to the latter part of the latent phase, any period after 1 year.[7,15]

The division between the early and late latent stages of syphilis is based on its infectious nature the response to therapeutic intervention.[15] Early latent syphilis is considered infectious and responds to antibiotic therapy. Late latent syphilis is not judged contagious and does not respond well to treatment.[7] It requires a longer duration of antibiotic therapy. One exception to this is pregnant women, who may transmit congenital

syphilis to their fetuses during the late latent phase.[7] Syphilis, if left untreated in the latent phase, may progress to the tertiary stage.[3]

Tertiary stage. Tertiary, or late syphilis, is a systemic, multiorgan disease process. Tertiary syphilis occurs in about one in three untreated but infected individuals and may be fatal.[14] Appearance of symptoms vary greatly from months with immunocompromised individuals or 3 to 30 years for others.[3,14] The four most common presentations are neurologic, cardiovascular, ocular, and gummatous (skin) syphilis, with the skin being the most commonly affected region (70%).[7,14]

Neurosyphilis causes a broad range of symptoms from headache to paralysis, coordination and sensory deficits, and altered behavior to dementia. Cardiovascular syphilis causes an inflammation of the inner lining of the artery (endarteritis).[7] Sequelae include aortic aneurysms, aortic regurgitation, and inflammation of the cardiac arteries resulting in arterial stenosis.[7] Ocular syphilis can invade any eye structure with resulting conditions of variable visual acuity or possible blindness.[3] Gummatous syphilis refers to the formation of benign rubbery tumorous lesions, called gumma. These destructive disfiguring lesions may necrose and ulcerate.[14] (See *Tertiary syphilis lesion.*)

Congenital syphilis

Transmission of the *T. pallidum* happens in utero via the placenta vasculature. This transmission of syphilis can occur at any stage of the disease in the mother and at any gestational age.[16] If the mother is untreated, possible outcomes include fetal death, spontaneous abortion, poor fetal growth, or neonatal disease.[7] Untreated infected newborns are considered to be in the latent stage of syphilis.[7] Further physical deterioration stems from the tertiary stage multisystem disease processes, which can proceed to death.

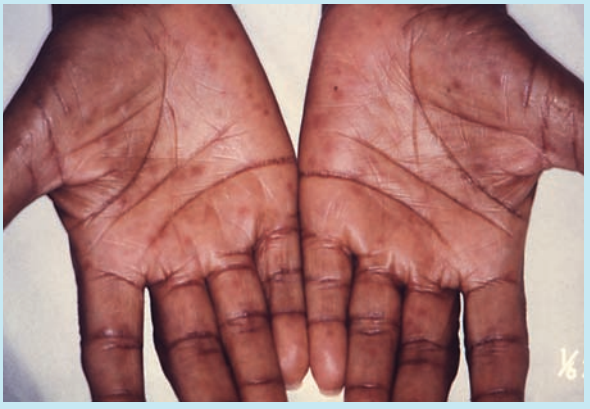
Diagnosis

Syphilis can be a challenge to diagnose. Classic tools used for organism recognition, such as cultivation on artificial media, direct microscopic observation, and Gram staining, are not available for use in the identification of *T. pallidum*.[7] Syphilis does not survive on routine lab media, is too slight of build to be seen under a microscope, and fails traditional Gram staining.

A technique known as dark-field microscopy (DFM) can be used to successfully view live treponomes and aid with diagnosing syphilis through determination of morphology and motility.[17] DFM only detects trepenomes from certain sites of moist lesions of patients in the P&S stage of syphilis. The primary difficulty with DFM diagnostic testing is the need for a high level of skill by the microscopist and a viable organism that remains motile.[17] This requires DFM examination within 30 minutes of collection, which is difficult to do in a primary care practice.[18]

Currently there is no single serologic test that can accurately diagnose all the stages of syphilis. Diagnosis relies on the use of two serologic tests that detect different types of antibodies, the nontreponemal test and the treponemal test.[7,17,19] Nontreponemal testing is an

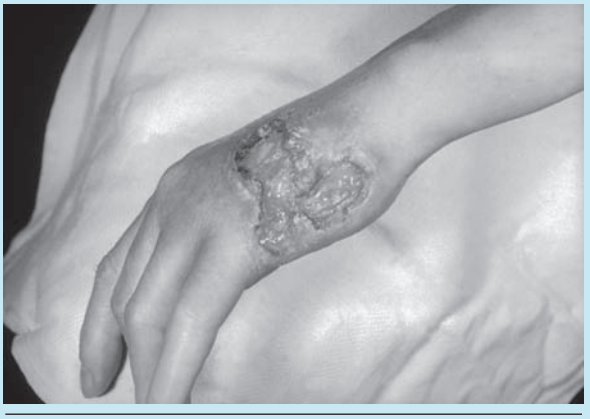
Secondary syphilis manifestations



Source: Courtesy of the Centers for Disease Control and Prevention/ Dr. M. F. Rein. https://phil.cdc.gov/Details.aspx?pid=3476. 1976.

Tertiary syphilis lesion

The left hand of patient with a gummatous lesion due to tertiary syphilis.



Source: Courtesy of the Centers for Disease Control and Prevention/Susan Lindsley. https://phil.cdc.gov/Details.aspx?pid=2381. 1971.

indirect method that detects antibodies to the cellular damage resulting from a treponemal infection.[7] Positive nontreponemal testing results are not definitive for syphilis but should rather be regarded as a screening tool. The most common nontreponemal tests are the Rapid Plasma Reagin (RPR) and the Venereal Disease Research Laboratory (VDRL) test.[7] The nontreponemal results vary significantly during the primary stage of syphilis. Positive results from nontreponemal testing are reported titers at dilutional rates (for example, 1:2, 1:4, 1:8), and are not considered specific for syphilis, requiring confirmation using a treponemal test.[17] Treponemal tests detect antibodies to the components of *T. pallidum.*[17] Treponemal test results are reported in qualitative terms: reactive or nonreactive. Fluorescent treponemal antibody-absorption (FTA-ABS) and the *T. pallidum* particle agglutination assay (TP-PA) are two common treponemal tests. A positive result from both the nontreponemal test followed by a positive treponemal test is considered confirmative for syphilis. The use of the two tests in sequence provides a sensitivity of 76% to 100% and a specificity of 97% to 99%, depending on the syphilis stage.[20]

The traditional sequence of syphilis screening recommended by the CDC begins with nontreponemal screening (such as RPR) followed by a treponemal test if needed.[7] Both treponemal and nontreponemal antibodies are detected within 1 week of inoculation of *T. pallidum*.[7] This traditional sequence of nontreponemal testing followed by treponemal testing has recently been challenged by some clinical labs that have reversed the testing order (treponemal followed by nontreponemal). One reason for the change is the hope of detecting the very early infected patient given that the treponemal antibodies appear before nontreponemal antibodies.[21] The CDC continues to recommend the traditional sequence of screening tests but has provided a recommended algorithm for reverse sequence syphilis screening as an alternative.[22]

Special considerations are needed for individuals with complex medical comorbidities. Serologic testing may be inconsistent for individuals with HIV.[15] The CDC recommends that a presumptive diagnosis of syphilis be given to HIV-positive individuals when clinical findings suggest that doing so may be appropriate regardless of the serologic testing results.[15] Treatment should be instituted and other options for diagnostic testing, such as a lumbar puncture, should be considered. Clinical signs of neurosyphilis in individuals warrant further testing, and the multiple presentations of neurosyphilis should be considered. CSF collection is needed and should follow the CDC's recommended algorithm for CSF analysis in combination with serologic testing.[15]

Treatment

Penicillin G benzathine is the standard for treatment of all stages of syphilis.[15] The dosage and duration of therapy are individualized according to the stage of the disease and special considerations (pregnancy, pediatric patients, HIV infection). The CDC recommendation for the treatment of P&S and early latent syphilis in nonpregnant, immunocompetent adults is penicillin G benzathine 2.4 million units I.M. in a single dose.[15] The CDC has clearly defined the treatment protocol for syphilis that also includes alternative antibiotics for those with penicillin allergy.[15] (See *Syphilis treatment guidelines and considerations for immunocompetent adults.*) It is important to note that this form of penicillin is specific and other forms of the drug must not be substituted for penicillin G benzathine. The CDC recommends that primary care providers consult infectious disease specialists regarding the care of patients with syphilis.[15] Prior to treatment, patients should be informed of the risks and benefits of antibiotic therapy, including the potential for rare drug-related adverse reactions, such as anaphylaxis or Jarisch-Herxheimer reaction. Jarisch-Herxheimer reaction symptomatology includes myalgia, fever, and headache within the first 24 hours of treatment; it is primarily observed when treating early syphilis.[15]

Although the focus of this article is on the treatment of adults with syphilis, it is important to note that children with syphilis should be referred to a pediatric specialist. In addition, there should be a consideration of child abuse with possible referral to a specialist in this field.

Follow-up

Nontreponemal test antibody titers are also collected after treatment. Following treatment, the nontreponemal test's reactivity should decline. Treponemal tests will remain reactive for life in most cases.[3,4,15] Syphilis is never considered cured because confirmation is indicated by the eradication of the infectious organism. The CDC guidelines state that confirmation of successful response to treatment is determined by a fourfold reduction in the nontreponemal titer at 1 year posttreatment of primary, secondary, and early latent syphilis, and 2 years posttreatment for late latent and

Syphilis treatment guidelines and considerations for immunocompetent adults[15]

Stage	Primary treatment	Alternative treatment	Other considerations	Follow-up
Adult Primary, secondary, or early latent (<1 yr)	Penicillin G benzathine 2.4 million units I.M. one single dose	Doxycycline 100 mg orally twice daily for 14 days OR Tetracycline 500 mg orally four times daily for 14 days	HIV testing should be completed. In areas of high prevalence, individuals with negative HIV test results should be retested in 3 months.	6- and 12-month clinical and serologic evaluations expected. If results are positive, evaluate and treat according to CDC follow-up guidelines.
Adult Late latent (>1 yr or unknown duration) and tertiary (gummas or cardiovascular)	Penicillin G benzathine 2.4 million units I.M. once a week for 3 weeks (total dose is 7.2 million units)	Doxycycline 100 mg orally twice daily for 28 days OR Tetracycline 500 mg orally four times daily for 28 days	If neurologic symptoms present, further testing may include CSF analysis, ophthalmic, and otologic examinations. HIV testing should be completed.	Per CDC, limited information exists on follow-up for tertiary syphilis.
Pregnancy	Penicillin treatment appropriate for stage. No alternatives are available if penicillin allergy present.		Considered high-risk pregnancy. For adequate treatment for fetus, penicillin must be given 30 days prior to delivery.	Serologic titers are obtained at 28-32 weeks gestation and at delivery, and more often if appropriate.

Adapted from CDC Sexually transmitted diseases treatment guidelines 2015.

tertiary syphilis.[15] Individuals who do not respond to treatment should be monitored and treated according to the CDC's follow-up section in the guidelines. The follow-up section of the guidelines should also be used for patients who are reinfected.[15]

Management of sex partners

The possible stage of syphilis, timing of notification, and serologic testing results determine the treatment of sex partners. The CDC recommendations for management of individuals whose sex partners have tested positive for syphilis are:

- Individuals whose sex partner has received a diagnosis of primary, secondary, or early latent syphilis within the past 90 days should be treated presumptively, regardless of the serologic testing results.
- Individuals whose sex partner's diagnosis of primary, secondary, or early latent syphilis was received more than 90 days prior should be treated for syphilis if the serologic testing is positive; no treatment is needed if results are negative. If no serologic test is immediately available, then the individual should be treated for syphilis.
- Partners of individuals with late latent syphilis should be evaluated serologically and be treated according to the findings.[15]

Screening

The US Preventive Services Task Force (USPSTF) recommends screening of adolescents and adults at high risk for syphilis infection. The individuals at greatest risk, according the USPSTF, include MSM and individuals with HIV. Other risk factors are dependent on prevalence and include history of incarceration, commercial sex work, and men under age 29.[23] Both the CDC and the USPSTF recommend screening all pregnant women for syphilis at their first prenatal visit.[15,23]

Conclusion

Patients infected with syphilis are often unaware of their condition. Their healthcare provider must have a solid knowledge base of the varying manifestations of the infection, a high suspicion for the infection, and familiarity with the appropriate diagnostic testing. NPs, so often on the forefront of primary care in rural and underserved areas, are instrumental in halting the spread of this debilitating STI. NP

REFERENCES

1. Bernstein KT, Grey J, Bolan G, Aral SO. Developing a topology of syphilis in the United States. *Sex Transm Dis.* 2018;45(9S suppl 1):S1-S6.
2. Centers for Disease Control and Prevention. The national plan to eliminate syphilis from the United States - executive summary. 1999. www.cdc.gov/stopsyphilis/exec.htm.

3. Centers for Disease Control and Prevention. Syphilis – CDC Fact Sheet (Detailed). 2017. www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm.
4. Radolf JD. Treponema. In: Baron S, ed. *Medical Microbiology.* 4th ed. Galveston, TX: University of Texas Medical Branch at Galveston; 1996.
5. Tampa M, Sarbu I, Matei C, Benea V, Georgescu SR. Brief history of syphilis. *J Med Life.* 2014;7(1):4-10.
6. Centers for Disease Control and Prevention. CDC Call to Action: let's work together to stem the tide of rising syphilis in the US. 2018. https://npin.cdc.gov/publication/cdc-call-action-lets-work-together-stem-tide-rising-syphilis-us.
7. Cohen SE, Klausner JD, Engelman J, Philip S. Syphilis in the modern era: an update for physicians. *Infect Dis Clin North Am.* 2013;27(4):705-722.
8. Centers for Disease Control and Prevention. Syphilis - Sexually Transmitted Diseases Surveillance 2017. 2017. www.cdc.gov/std/stats17/Syphilis.htm.
9. Beymer MR, Weiss RE, Bolan RK, et al. Sex on demand: geosocial networking phone apps and risk of sexually transmitted infections among a cross-sectional sample of men who have sex with men in Los Angeles County. *Sex Transm Infect.* 2014;90(7):567-572.
10. Philip SS, Bernstein KT. Syphilis is (still) here: how must sexually transmitted disease public health programs adapt? *Sex Transm Dis.* 2018;45(9S suppl 1):S63-S64.
11. Kaur G, Kaur P. Syphilis testing in blood donors: an update. *Blood Transfus.* 2015;13(2):197-204.
12. Peeling RW, Hook EW 3rd. The pathogenesis of syphilis: the Great Mimicker, revisited. *J Pathol.* 2006;208(2):224-232.
13. Barnett R. Syphilis. *Lancet.* 2018;391(10129):1471.
14. Carlson JA, Dabiri G, Cribier B, Sell S. The immunopathobiology of syphilis: the manifestations and course of syphilis are determined by the level of delayed-type hypersensitivity. *Am J Dermatopathol.* 2011;33(5):433-460.
15. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep.* 2015;64(RR-03):1-137.
16. Plotzker RE, Murphy RD, Stoltey JE. Congenital syphilis prevention: strategies, evidence, and future directions. *Sex Transm Dis.* 2018;45(9S suppl 1):S29-S37.
17. Pillay A. Centers for Disease Control and Prevention Syphilis Summit-Diagnostics and Laboratory Issues. *Sex Transm Dis.* 2018;45(9S suppl 1):S13-S16.
18. Association of Public Health Laboratories. Consultation on Laboratory Diagnosis of Syphilis Meeting Summary Report. 2018. www.aphl.org/aboutAPHL/publications/Documents/ID-2018Aug-Syphilis-Meeting-Report.pdf.
19. Marra CM, Ghanem KG. Centers for Disease Control and Prevention Syphilis Summit: difficult clinical and patient management issues. *Sex Transm Dis.* 2018;45(9S suppl 1):S10-S12.
20. Gayet-Ageron A, Lautenschlager S, Ninet B, Perneger TV, Combescure C. Sensitivity, specificity and likelihood ratios of PCR in the diagnosis of syphilis: a systematic review and meta-analysis. *Sex Transm Infect.* 2013;89(3):251-256.
21. Dunseth CD, Ford BA, Krasowski MD. Traditional versus reverse syphilis algorithms: a comparison at a large academic medical center. *Pract Lab Med.* 2017;8:52-59.
22. Centers for Disease Control and Prevention. Discordant results from reverse sequence syphilis screening--five laboratories, United States, 2006-2010. *MMWR.* 2011;60(5):133-137.
23. U.S. Preventive Services Task Force. *Information for health professionals.* 2018. www.uspreventiveservicestaskforce.org/Page/Name/tools-and-resources-for-better-preventive-care.

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