In Brief

Syphilis

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Author Disclosure
Dr Butterfield has disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

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Treponema pallidum is a motile spirochete and the causative microorganism of syphilis. *T pallidum* is transmitted through direct sexual contact with infectious lesions, transplacentally from infected mother to fetus, or via blood transfusion. The most common mode of transmission is sexual. Transmission occurs when the host's highly infectious skin lesions make direct contact with the partner, and the spirochete is able to enter the body through mucous membranes. Transmission via oral sex is possible if the infected individual has active lesions on the oral mucosa. *T pallidum* crosses the placenta and can infect a fetus at any gestational age. There is an inverse relationship between the severity of infection and gestational age at time of infection. Placental transmission can also occur at any clinical stage of syphilis, although mothers are more likely to transmit the infection while in the early stages of the disease. Blood transfusion transmission, although possible, is unlikely today given the universal screening of donors.

The clinical manifestations of syphilis are variable, depending on the stage of the illness. Primary syphilis is characterized by the development of a painless papule at the site of inoculation. This papule ulcerates to produce the classic chancre of primary syphilis, a 1- to 2-cm ulcer with a nonexudative base and raised borders. Chancres spontaneously heal after 3 to 6 weeks even in the absence of treatment, and because of their painless nature, many patients are unaware of their presence. Secondary syphilis symptoms occur weeks to months later and have characteristic systemic signs, including a polymorphic rash, classically described as a maculopapular rash that involves the trunk, extremities, palms, and soles; condyloma lata, which are large gray or white lesions distributed around mucous membranes; and constitutional symptoms, such as lymphadenopathy, malaise, and myalgias. Latent syphilis is defined as the lengthy period (sometimes decades) of asymptomatic indolence before the eruption of tertiary syphilis. Clinical manifestations of tertiary syphilis include dementia, aortic aneurysms and regurgitation, and granulomas, known as gummas, which can occur on the skin, bones, or internal organs.

The symptoms of congenital syphilis are divided into those that are apparent before age 2 years, termed early congenital syphilis, and those manifest after age 2 years and older, termed late congenital syphilis. Most infected infants are asymptomatic at birth. Symptoms of early congenital syphilis include diffuse rash, especially of the palms and often associated with exfoliation; rhinitis, known as snuffles; thrombocytopenia; and hepatomegaly and chorioretinitis. Late congenital syphilis primarily manifests with intellectual disability and cranial nerve palsies, as well as bone and teeth abnormalities, including granulomatous destruction of the nasal septum known as saddle nose, widely spaced and centrally notched incisors known as Hutchinson teeth, interstitial keratitis, sensorineural hearing loss, and arthritis. The possibility of acquired syphilis through sexual abuse must be considered in any child who presents with the disease.

Diagnosis of syphilis is complicated by the inability to culture *T pallidum* in vitro. Nontreponemal serologic tests are used as first-line screens. Nontreponemal tests include the VDRL test, the rapid plasma reagin test, and the automated reagin test. These tests are sensitive but nonspecific and are useful as primary screens given their ease and low cost. There is the potential for false-positive results, however, because of conditions, including pregnancy, autoimmune disease, rickettsial infection, and nonsyphilis treponemal infection.

Therefore, a reactive nontreponemal test result must be confirmed with a specific treponemal test, including the fluorescent treponemal antibody absorption and the *T pallidus* particle agglutination test. Congenital syphilis should be suspected in all newborns whose mothers have reactive nontreponemal and treponemal serologic test results, as well as any child with pertinent signs and symptoms. These children should undergo nontreponemal serologic tests, and children with probable or highly probable disease should undergo lumbar puncture to examine the cerebrospinal fluid cell counts, which would be elevated, and the VDRL test, which would have a positive result. Approximately 40% of newborns with syphilis have asymptomatic seeding of the cerebrospinal fluid.

Treatment of primary, secondary, and early latent syphilis remains a single dose of benzathine penicillin G, and no resistance has been reported. Three doses of benzathine penicillin G are recommended for late latent or tertiary syphilis. All patients who have a positive treponemal test result should be offered human immunodeficiency testing. Congenital syphilis should be treated with 10 to 14 days of aqueous penicillin G or procaine penicillin, in consultation with a pediatric infectious disease specialist. The US Preventive Services Task Force and the Centers for Disease Control and Prevention recommend universal syphilis screening for all pregnant women in the first trimester, again during the third trimester, and at delivery for women at high risk for syphilis.

Comments: While I usually have to check the *Red Book* to review screening and testing for syphilis because of its complexity, I found Dr Butterfield's presentation clear and understandable. Primary syphilis can often be missed because the lesions are painless and may be overlooked. Congenital syphilis transmission can occur at any stage of pregnancy or at birth. Nontreponemal tests that provide quantitative results and level of disease are needed to help define activity and monitor therapy. However, there may be false-positive results with other illnesses, such as Epstein-Barr virus, hepatitis, varicella, measles, lymphoma, tuberculosis, malaria, and connective tissue diseases, along with substance abuse of injection drugs. The nontreponemal test needs to be paired with a treponemal test, which is more specific for syphilis and reactive for life. The combination of these tests reinforces that the patient is truly infected, and the nontreponemal quantitative results allow monitoring of therapy. Specific follow-up is required for infants with congenital syphilis, and nontreponemal tests should be performed again at 2 to 4 months, 6 months, and 12 months until the results become nonreactive or the titer has decreased by 4-fold. Clinicians should always consider consulting with an infectious disease specialist if in doubt, and the *Red Book* is incredibly helpful in determining testing and treatment.

Janet Serwint, MD
Consulting Editor, In Brief

Parent Resources from the AAP at HealthyChildren.org

- http://www.healthychildren.org/English/health-issues/conditions/sexually-transmitted/Pages/Syphilis.aspx
- Spanish: http://www.healthychildren.org/spanish/health-issues/conditions/sexually-transmitted/paginas/syphilis.aspx

Answer Key for May 2014 Issue:
Cleft Lip and Palate: 1. E; 2. A; 3. D; 4. D; 5. E.
Infectious Diseases in Early Education and Child Care Programs: 1. B; 2. C; 3. A; 4. E; 5. D.
Cystic Fibrosis: 1. C; 2. E; 3. C; 4. A; 5. D.

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