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Syphilis

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many as 70% of affected infants having been breastfed. Sex, race, and seasonality do not affect occurrence rates.

Infants who have botulism can present with a range of symptoms from mild constipation to respiratory difficulties leading to sudden death. Constipation is a typical early and often overlooked sign. Symmetric descending paralysis follows the onset of constipation within days, affecting cranial nerves and facial movements first. The infant may become apathetic and listless, feed poorly, have decreased head control, demonstrate a weak cry and suck, drool, have facial diplegia, and demonstrate hypotonia over days to weeks. Fever is conspicuously absent. Decreased movement of the extremities and loss of the deep tendon reflexes are late signs that are followed by flaccid paralysis and respiratory failure.

The diagnosis of infant botulism can be confirmed by detecting botulinum toxin in the stool or serum via the mouse neutralization assay or by isolating toxigenic clostridia in fecal material. Electromyography, immunoassays, and polymerase chain reaction testing are not used for diagnosis because of limited specificity and sensitivity or lack of laboratory standardization. The differential diagnosis includes sepsis, meningitis, and other causes of paralysis, such as Guillain-Barré syndrome, poliomyelitis, and myasthenia gravis.

The disease progresses for about 1 to 2 weeks, followed by gradually improving symptoms over 3 to 4 weeks. The prognosis is very good if appropriate nutritional and respiratory supportive care are provided; the case-fatality rate is less than 2%. A 5-year placebo-controlled, randomized clinical trial showed that a single intravenous dose of human-derived botulinum immunoglobin decreased the duration of hospital stay from 5.5 weeks to 2.6 weeks. The rate of intubations was reduced by two thirds for patients who received the antitoxin. To be most effective, human botulinum immunoglobin should be used as early as possible in the course of the illness. It can be obtained from the California Department of Health Services (24-hour telephone number 510/540-2646). Its use is restricted to infant botulism.

In Brief

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Author Disclosure

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Syphilis is an infection caused by the spirochete *Treponema pallidum* that affects children in two different forms: acquired syphilis, which is seen primarily among adolescents, and congenital syphilis. Acquired syphilis is transmitted almost exclusively by sexual contact, although transmission can occur from contaminated blood or contact with infected tissues. The prevalence of syphilis among adolescents in the United States is about 1.7 per 100,000 population in the 15- to 19-year-old age group; the predominance is slightly female. Overall, the rate of syphilis has been decreasing since an epidemic resurgence in the 1980s, but among young men between the ages of 20 and 24 years of age, it has risen recently, reflecting outbreaks affecting men who have sex with men. Syphilis remains more common among African-Americans (12.8 per 100,000) than among nonwhite Hispanic Americans (1.8) and nonHispanic Caucasian Americans (0.6).

Primary syphilis is characterized by a papule on the genitals, which develops into a painless ulcer called a chancre. Chancres, which are highly infectious and may be accompanied by localized lymphadenopathy, heal spontaneously within 4 to 6 weeks.

Secondary syphilis occurs in untreated patients 2 to 10 weeks after the chancre heals. Manifestations are systemic and related to spirochetes circu-

lating in the bloodstream. A hallmark is the typical nonpruritic, maculopapular rash involving the entire body, including palms and soles. Other features of secondary syphilis are condylomata lata (wartlike plaques around the anus and vagina), generalized lymphadenopathy, and a flulike illness characterized by fever, malaise, arthralgias, sore throat, and headache. Lesions of the skin and mucosal surfaces are highly contagious. Neurosyphilis, marked by cerebrospinal fluid (CSF) pleocytosis and an elevated protein concentration, may occur in as many as 30% of patients, although symptoms may be absent.

Within 1 to 2 months after the onset of the rash, secondary infection becomes latent. During the early latent period, which can last from 12 months to several years, relapses of secondary manifestations may occur. Eventually, patients either remain in clinical remission (late latent period) or develop the symptoms of tertiary syphilis. Now rare in the pediatric population, tertiary syphilis is characterized by granulomas (gummas) of the skin and musculoskeletal system caused by a delayed hypersensitivity reaction. There also may be neurologic sequelae (dementia, tabes dorsalis, seizures) and cardiovascular disease (aortitis).

Two types of serologic tests are used routinely to diagnose syphilis. Nontreponemal tests, such as the Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR), are not specific for syphilis and are used as screening tests. Because the quantitative results tend to correlate with disease activity, they can be used to monitor treatment success or failure or to detect reinfection. Autoimmune diseases can cause false-positive results, but this phenomenon is becoming less frequent with refinements in the tests. Neurosyphilis is diagnosed by a positive nontreponemal test on a CSF specimen.

Treponemal tests, which detect specific antibodies to *T pallidum*, include the fluorescent treponemal antibody absorption test (FTA-ABS) and the microhemagglutination assay for antibodies to *T pallidum* (MHA-TP). They are used as confirmatory tests after a positive nontreponemal screen. The titers become positive almost immediately after initial infection and remain positive for life, even with adequate therapy. Therefore, treponemal tests cannot be used to follow disease activity or detect reinfection.

Penicillin remains the drug of choice for all types of syphilis, with no evidence of resistant strains of *T pallidum*. For penicillin-allergic patients, desensitization followed by penicillin therapy is the preferred regimen, although other agents, such as doxycycline, are available. Primary and secondary syphilis can be treated with a single intramuscular dose (50,000 U/kg) of benzathine penicillin G. Patients who are at high risk (eg, those who are human immunodeficiency virus [HIV]-positive) or who have late latent infection may require three weekly doses. Neurosyphilis is treated with aqueous crystalline penicillin G administered intravenously for 10 to 14 days.

All sexually active adolescents should be tested for syphilis and counseled about appropriate sexually transmitted disease (STD) prevention. Any patient who has a positive syphilis screen should be tested for HIV and other STDs because of the high rate of coinfection.

Congenital syphilis is contracted by transplacental transmission of spirochetes, which can occur at any stage of pregnancy and is more common when mothers have primary and secondary infection rather than latent infection. Maternal risk factors particularly associated with congenital syphilis are lack of prenatal care and cocaine abuse, which is a marker for prostitution, unprotected sexual contact, trading of sex for drugs, and poor prenatal care.

Intrauterine infection can result in fetal death, stillbirth, and prematurity as well as clinical congenital disease. As with acquired syphilis, congenital infection has early and late manifestations. Analogous to the secondary stage of acquired syphilis, early congenital disease results from transplacental hematogenous spread of spirochetes and presents during the first 2 years after birth. However, only one third of infected infants are symptomatic at birth; most are identified by routine screening tests. In those who remain untreated, symptoms develop over weeks to months.

Almost any organ system may be affected in early congenital syphilis. Liver manifestations can include hepatosplenomegaly, jaundice, elevated liver enzymes, and bile stasis. Hematologic disease may involve lymphadenopathy, Coombs-negative hemolytic anemia, and thrombocytopenia from consumption of platelets by an enlarged spleen. Mucous membrane involvement may present as mucous patches, rhinitis (snuffles), and condylomatous lesions. Characteristic musculoskeletal disease includes osteochondritis, an extremely painful inflammation that may lead the child to resist moving the affected limb (pseudoparalysis of Parrot), and periostitis. Infants may have a mucocutaneous rash similar to that of secondary acquired syphilis, with resulting desquamation of hands and feet. Early congenital syphilis also can present with central nervous system (CNS) abnormalities, failure to thrive, chorioretinitis, pancreatitis, and renal disease.

The late manifestations of congenital syphilis, resulting from chronic inflammation of affected tissues (especially bone, teeth, and CNS), appear gradually during the first 2 decades of life. Bony changes result in the classic prominence of the forehead ("olympian brow"), anterior tibial bowing ("saber shins"), and scaphoid scapulae. Dental anomalies can range from Hutchinson teeth (peg-shaped upper central inci-

sors) to mulberry molars (abnormal first lower molars with an excessive number of cusps). Defects of the enamel commonly result in caries and tooth destruction.

Other late manifestations may include saddle nose (a depression of the nasal root with destruction of the adjacent bone and cartilage resulting from snuffles), rhagades (linear scars from previous mucocutaneous fissures), and neurologic abnormalities, more typically juvenile paresis than tabes dorsalis. Interstitial keratitis, which can lead to blindness as well as eighth nerve deafness and Clutton joint (a painless arthritis usually of the knee), probably represents hypersensitivity reactions.

The same tests used to diagnose acquired syphilis are used to detect congenital infection. All pregnant women should be screened for syphilis with nontreponemal tests and treated if results are positive and syphilis is confirmed, regardless of stage of pregnancy or disease. Every symptomatic infant should be evaluated for congenital syphilis. Any asymptomatic neonate whose mother had a positive screen for syphilis should be evaluated if maternal treatment was:

1) inadequate, unknown, or undocumented;
2) within 1 month of delivery;
3) with a nonpenicillin regimen;
4) not followed by at least a fourfold reduction in nontreponemal antibody titers.

The interpretation of neonatal serologic tests can be confounded by passively transmitted maternal immunoglobulin G antibodies. A neonate whose nontreponemal titer is not at least fourfold greater than the maternal titer is unlikely to be infected. Passively acquired antibody gradually declines, becoming undetectable by 3 to 6 months of age.

Congenital syphilis is treated similarly to acquired syphilis, except that all infants should be presumed to have CNS disease because the CSF may appear normal, including a negative VDRL, even when neurosyphilis is present. The standard regimen is aqueous crystalline penicillin G (100,000 to 150,000 U/kg per day) for 10 to 14 days. An alternative regimen that does not require intravenous access is procaine penicillin G (50,000 U/kg per day) administered intramuscularly for 10 to 14 days. Treated infants should be followed up serologically to confirm decreasing antibody titers.

Prenatal screening is the most effective intervention to prevent congenital syphilis. All pregnant women should be encouraged to seek early prenatal care, including routine testing for syphilis. Pregnant women at particular risk (or those in communities that have a high prevalence) should be tested several times throughout pregnancy, including at delivery. Maternal serologic status during the pregnancy should be documented before a newborn is allowed to leave the hospital. As always, prevention is the best medicine.

Comment: Rates of primary and secondary syphilis among women in the United States continue to fall, and as night follows day, so does the rate of congenital syphilis (CS). That's the good news. However, CS is a preventable disease that still takes a toll, particularly among infants of poor minority women. The Centers for Disease Control and Prevention recently reported that almost one third of infants who have CS are born to mothers who had received no prenatal care, and of mothers who had received care, fewer than 50% began care during the first trimester. Failure of practitioners to screen consistently and repeatedly also contributes to our failure to eliminate a disease we no longer should be seeing.

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Editor, In Brief

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