Congenital syphilis: Evaluation, management, and prevention

Author: Simon R Dobson, MD, FRCP(C)
Section Editors: Sheldon L Kaplan, MD, Leonard E Weisman, MD
Deputy Editor: Carrie Armsby, MD, MPH

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: Mar 2022. | **This topic last updated:** Mar 26, 2021.

INTRODUCTION

Congenital syphilis occurs when the spirochete *Treponema pallidum* is transmitted from a pregnant woman to her fetus. Infection can result in stillbirth, prematurity, or a wide spectrum of clinical manifestations; only severe cases are clinically apparent at birth [1].

The evaluation, management, and prevention of congenital syphilis will be discussed here. The clinical features and diagnosis of congenital syphilis are discussed separately. (See "Congenital syphilis: Clinical features and diagnosis".)

Syphilis in pregnancy and acquired syphilis also are discussed separately:

- (See "Syphilis in pregnancy".)
- (See "Syphilis: Epidemiology, pathophysiology, and clinical manifestations in patients without HIV".)
- (See "Syphilis: Epidemiology, pathophysiology, and clinical manifestations in patients without HIV", section on 'Clinical manifestations'.)
- (See "Syphilis: Treatment and monitoring".)
- (See "Neurosyphilis".)
- (See "Syphilis: Screening and diagnostic testing".)

EVALUATION AND MANAGEMENT OF INFANTS <1 MONTH OF AGE

The vagaries of the maternal history of syphilis and signs or lack of signs in the newborn in combination with the potential consequences of delayed or missed diagnosis of congenital syphilis demand a "safety first" approach to both diagnosis and treatment [2,3]. The United States Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics (AAP) Committee on Infectious Diseases provide guidelines for the evaluation and management of congenital syphilis (algorithm 1 and table 1) [4,5]. Similar guidelines are provided by the World Health Organization [6].

Initial evaluation — The diagnosis of congenital syphilis should be suspected in all infants whose mothers have reactive nontreponemal and treponemal tests for syphilis; the treponemal test is necessary to exclude a false-positive nontreponemal result. (See "Syphilis in pregnancy".)

The initial evaluation of infants born to mothers who have reactive nontreponemal and treponemal test results should include [4,5]:

- A quantitative nontreponemal test (Venereal Disease Research Laboratory test [VDRL] or rapid plasma reagin [RPR]) on infant serum; testing umbilical cord blood could yield a false positive result if the cord blood is contaminated with maternal blood. The nontreponemal test that is performed on the infant should be the same as that which was done on the mother so that the infant's titers can be compared with the mother's titers.

- Physical examination for evidence of congenital syphilis (table 2) and darkfield microscopic examination (picture 1) or direct fluorescent antibody (DFA) staining of suspicious lesions or body fluids (eg, nasal discharge). (See "Congenital syphilis: Clinical features and diagnosis", section on 'Early congenital syphilis' and "Congenital syphilis: Clinical features and diagnosis", section on 'Diagnostic tests'.)

- Pathologic examination of the placenta or umbilical cord with specific fluorescent antitreponemal antibody staining.

Additional evaluation depends upon the findings from the initial evaluation.

Subsequent evaluation and management — The subsequent evaluation depends upon clinical, serologic, and epidemiologic factors, including (algorithm 1 and table 1) [4,5]:

- The neonate's syphilis serology (nonreactive or reactive; and if reactive, whether the infant's titer is at least fourfold [two dilutions] higher than the corresponding maternal titer).

- The mother's risk factors for syphilis (see "Syphilis in pregnancy", section on 'Prevalence').

- The mother's syphilis serology (in relation to previous tests and/or treatment and in relation to the neonate's titers).
- If the mother has been treated for syphilis:
  - The timing of the treatment (before or during pregnancy; more or less than four weeks before delivery).
  - The adequacy of therapy (table 3).
  - The likelihood of failure of maternal therapy to prevent congenital disease (higher maternal titers and unknown duration of maternal syphilis are associated with failure of maternal therapy to prevent congenital disease) [7].

Proven or highly probable disease — Congenital syphilis is proven or highly probable if the infant has at least one of the following [4,5]:

- An abnormal physical examination that is consistent with congenital syphilis (table 2).
- A serum VDRL or RPR titer that is ≥fourfold the corresponding maternal titer (eg, neonate's titer 1:32 and maternal titer 1:8).
- A positive darkfield (picture 1) or fluorescent antibody test of body fluid(s), placenta, or umbilical cord.

Infants with proven or highly probable congenital syphilis should undergo the following evaluation (algorithm 1 and table 1):

- Cerebrospinal fluid (CSF) examination for cell count, protein, and VDRL.
- Complete blood count (CBC) with differential and platelet count.
- Additional tests as clinically indicated: long-bone radiographs (for lack of movement of extremity), chest radiograph (for signs of lower respiratory tract disease), liver function tests (for hepatomegaly, jaundice), cranial ultrasound (for neurologic manifestations), ophthalmologic examination, and auditory brainstem response (for concerns about hearing).

We recommend that infants with proven or highly probable congenital syphilis be treated with 10 days of parenteral penicillin G [4,5]. (See 'Ten-day regimens' below.)

To prevent long-term morbidity, central nervous system syphilis is presumed in neonates with clinical, radiographic, or laboratory abnormalities compatible with syphilis. Although CSF results

do not alter the treatment, examination of the CSF is necessary to determine the need for subsequent monitoring and to provide a baseline for monitoring the response to therapy. (See 'Cerebrospinal fluid evaluation' below.)

Possible congenital syphilis — For neonates who have a normal physical examination and reactive VDRL or RPR <fourfold the maternal titer, and whose mothers were not treated, were inadequately treated (table 3), or had evidence of reinfection or relapse, the CDC and AAP recommend the following evaluation (algorithm 1 and table 1) [4,5]:

- CSF VDRL, cell count, and protein
- CBC with differential and platelet count
- Other tests as clinically indicated (eg, chest radiographs, long-bone radiographs, eye examination, liver function tests, neuroimaging, and auditory brainstem response)

We recommend a full 10-day course of parenteral penicillin if any part of the evaluation is abnormal or not performed, or if the CSF examination cannot be interpreted because it is contaminated with blood [4,5]. (See 'Ten-day regimens' below.)

The neonate may be treated with a single dose of intramuscular (IM) penicillin G benzathine if all three tests are performed, the results are normal, and follow-up of the infant is assured [4,5] (see 'Single-dose regimen' below). Nonetheless, many experts prefer to treat such infants with a full 10-day course, particularly if the mother has secondary syphilis at delivery or seroconverted during the pregnancy [4,5] (see 'Ten-day regimens' below). Our preference is for the 10-day course. For infants who will be treated with a 10-day course of penicillin, complete evaluation is not necessary but may help to establish the diagnosis and need for long-term CSF follow-up [4,8,9]. (See 'Cerebrospinal fluid evaluation' below.)

Congenital syphilis less likely — No additional evaluation is necessary for the asymptomatic neonate with reactive serology whose mother was treated **during** pregnancy, provided that all of the following criteria are met (algorithm 1 and table 1):

- The infant has a normal physical examination.
- The infant's VDRL or RPR titer is reactive but less than fourfold the maternal titer.
- Mother received adequate therapy during pregnancy that was suitable for the stage of her infection and had an appropriate response (ie, VDRL or RPR titers decreased fourfold after therapy for early syphilis; VDRL or RPR remained stable and low [VDRL ≤1:2; RPR ≤1:4] for late syphilis).
- Mother was treated more than four weeks before delivery.

- Mother has no evidence of relapse or reinfection; relapse or reinfection are indicated by a ≥fourfold increase in titer.

In accord with the AAP and CDC, we suggest that neonates who meet the above criteria be treated with a single dose of IM penicillin G benzathine (algorithm 1) [4,5] (see 'Single-dose regimen' below). Infection of the fetus may occur despite appropriate maternal therapy during pregnancy. The reported failure rates of maternal treatment to prevent congenital infection range from 2 to 14 percent [7,10-12]; higher rates are more frequent in mothers with secondary syphilis. Treating the infant at birth may prevent the development of clinical disease if maternal therapy during pregnancy did not prevent fetal infection [13,14].

As an alternative, some specialists opt not to treat such infants, but to provide close (ie, monthly) serologic follow-up, and provide treatment if the infant's titers do not decline as expected for transplacentally acquired antibody. (See 'Nontreponemal tests' below.)

Congenital syphilis unlikely — No additional evaluation is necessary for the asymptomatic neonate whose mother was treated **before** pregnancy, provided that **all** of the following criteria are met [4]:

- The infant has a normal physical examination
- The infant's VDRL or RPR titer is <fourfold the maternal titer
- Mother was appropriately and adequately treated before pregnancy
- Mother's VDRL or RPR titer remained low and stable before and during pregnancy and at delivery (ie, VDRL <1:2; RPR <1:4)

In accordance with the AAP and CDC, we suggest that infants in this category do not require treatment with penicillin (algorithm 1 and table 1) [4,5]. However, some experts would provide a single dose of IM penicillin G benzathine if follow-up is uncertain (to protect the infant in the unlikely event that the mother was reinfected). (See 'Single-dose regimen' below.)

Infant VDRL or RPR nonreactive — The neonate who has a normal physical examination and nonreactive VDRL or RPR does not require additional evaluation (algorithm 1 and table 1).

Such infants require treatment if the mother was not treated, was inadequately/suboptimally treated (table 3), or has evidence of reinfection or relapse (indicated by ≥fourfold increase in titers after treatment) [5]. Some experts would also opt to treat such infants even if their mothers were adequately treated [2,4,15]. Our preference is to treat such infants whose mothers were adequately treated because a single dose of penicillin is relatively benign compared with the risk of missed disease. (See 'Single-dose regimen' below.)

Treatment for neonates with nonreactive VDRL or RPR and normal physical examination generally consists of a single dose of IM penicillin G benzathine. (See 'Single-dose regimen' below.)

EVALUATION AND MANAGEMENT OF CHILDREN >1 MONTH OF AGE

Children who are identified as having reactive serologic tests for syphilis after one month of age should have maternal serology and records reviewed to assess whether the child has congenital or acquired syphilis, although this distinction may be difficult [1,16].

The evaluation of such children may include [4,5]:

- Cerebrospinal fluid (CSF) analysis for Venereal Disease Research Laboratory test (VDRL), white blood cell count, and protein.
- Complete blood count (CBC) with differential and platelet count.
- Evaluation and testing for HIV infection.
- Other tests as clinically indicated (eg, long-bone radiographs, chest radiograph, liver function tests, abdominal ultrasonography, ophthalmologic examination, auditory brain stem response, and neuroimaging studies).

The distinction between congenital and acquired syphilis can be difficult and ultimately may rest upon maternal history and clinical judgment [1]. CSF and CBC abnormalities may occur in both congenital and acquired syphilis, but radiographic changes in the metaphysis and epiphysis are more suggestive of congenital syphilis. (See "Congenital syphilis: Clinical features and diagnosis", section on 'Long-bone radiographs'.)

In a young child, the possibility of sexual abuse should be considered as a cause of acquired syphilis. (See "Evaluation of sexual abuse in children and adolescents", section on 'Sexually transmitted infections'.)

Children who are diagnosed with congenital syphilis after one month of age (including those with previously untreated late congenital syphilis) require parenteral penicillin therapy [4,5]. (See '>1 month of age' below.)

EVALUATION OF SIBLINGS

Evaluation of the siblings of an index case of congenital syphilis may be warranted if such an evaluation did not occur previously [17].

PENICILLIN THERAPY

Parenteral penicillin is the drug of choice for the treatment of congenital syphilis [4,5]. Penicillin is the only drug with documented efficacy, and it has minimal toxicity. *T. pallidum* is extremely sensitive to penicillin, as demonstrated by experimental animal work [2]. The minimal inhibitory concentration (MIC) for penicillin is approximately 0.004 units (or 0.0025 mcg/mL). There is no evidence of increasing spirochete resistance to penicillin, but such evidence would come only from the recognition of therapeutic failures.

Effective treatment of syphilis requires maintenance of a MIC of 0.03 units/mL of penicillin in serum (or cerebrospinal fluid) for 7 to 10 days. Current regimens are designed to achieve and maintain several times the necessary MIC and to avoid penicillin-free intervals during therapy.

<1 month of age

Single-dose regimen — The single-dose regimen for treatment of congenital syphilis is as follows:

- Penicillin G benzathine (50,000 units/kg, intramuscularly [IM] as a single dose)

Two randomized trials have evaluated the efficacy of single-dose penicillin therapy in preventing/treating congenital syphilis in asymptomatic infants born to mothers with no treatment or inadequate/suboptimal treatment for syphilis during pregnancy (table 3) [13,14]. One compared single-dose penicillin G benzathine with no therapy in asymptomatic infants at high risk of congenital syphilis (untreated mothers with Venereal Disease Research Laboratory test [VDRL] ≥1:32) [13]. None of 11 infants in the treatment group developed congenital syphilis (defined by immunoglobulin M (IgM) Western blots and VDRL titers), compared with four of eight infants who were not treated [13]. In the second trial, treatment of asymptomatic infants (normal physical examination, normal cerebrospinal fluid [CSF] evaluation, normal long-bone radiographs, and no visceral abnormalities) with either single-dose penicillin G benzathine or 10 days of parenteral procaine penicillin G was effective in preventing clinical evidence of congenital syphilis and decreasing rapid plasma reagin (RPR) by at least fourfold [14].

Single-dose therapy is contraindicated for asymptomatic infants born to women with inadequate/suboptimal treatment (table 3) unless the infant has undergone appropriate

evaluation (CSF quantitative VDRL, cell count, and protein; complete blood count [CBC] with differential and platelet count; and long-bone radiographs) and has completely normal results [4,5]. The evaluation is necessary to exclude central nervous system (CNS) syphilis, which requires a full 10-day course of therapy. Treatment failures with single-dose therapy have been reported among infants who developed clinical findings of syphilis after incomplete evaluation [18,19]. The frequency of such treatment failures appears to be low but is unknown. (See 'Possible congenital syphilis' above.)

Ten-day regimens — There are two alternative 10-day penicillin regimens for the treatment of congenital syphilis [4,5]:

- Aqueous penicillin G 50,000 units/kg intravenously (IV) every 12 hours (for infants ≤7 days of age) and every 8 hours (for infants >7 days of age) for a total of 10 days, **or**
- Procaine penicillin G 50,000 units/kg intramuscularly (IM) as a single daily dose for 10 days

The levels of penicillin that are achieved in the CSF after IM procaine penicillin are lower than those with IV aqueous penicillin [20]. However, the clinical significance of this observation is unclear, since there have been no treatment failures reported after treatment with procaine penicillin [5].

A full 10-day course of penicillin should be administered, even if the infant initially received ampicillin for possible sepsis [4,5]. If more than one day of penicillin therapy is missed, the entire course should be restarted.

>1 month of age — Children who are diagnosed with congenital syphilis after one month of age (including those with late congenital syphilis) and children with acquired syphilis should be treated with aqueous penicillin G (50,000 units/kg IV every four to six hours for 10 days) [4,5]. In addition, for children with congenital syphilis or findings compatible with CNS involvement, some experts suggest that the 10-day course of aqueous penicillin be followed with a single dose of penicillin G benzathine (50,000 units/kg IM).

As an alternative for the child with positive syphilis serology, but no clinical manifestations of disease, and normal CSF studies, some experts would treat with three weekly doses of penicillin G benzathine (50,000 units/kg IM) [4,5].

Adverse effects

Jarisch-Herxheimer reaction — The Jarisch-Herxheimer reaction generally consists of fever 2 to 12 hours after initiation of therapy for active syphilis [21]. However, cardiovascular collapse, seizures, and death also have been reported [22]. The Jarisch-Herxheimer reaction is thought to

be produced by the release of endotoxin-like compounds during penicillin-mediated lysis of *T. pallidum*. It is rare in newborns but can occur in older infants and children.

Special circumstances

Missed doses — If more than one day of penicillin therapy is missed, the entire course should be restarted [4,5]. Effective treatment of syphilis requires maintenance of a minimal inhibitory concentration (MIC) of 0.03 units/mL of penicillin in serum (or CSF) for 7 to 10 days. (See 'Penicillin therapy' above.)

Penicillin allergy — Penicillin is the treatment of choice for congenital syphilis. There are insufficient data regarding the adequacy of treatment with agents other than penicillins (eg, ceftriaxone). For the infant/child who requires treatment for syphilis but has a penicillin allergy or develops an allergic reaction that is presumed to be due to penicillin, the United States Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics (AAP) recommend desensitization and then treatment with penicillin [4,5]. (See "Penicillin allergy: Immediate reactions", section on 'Desensitization'.) If a nonpenicillin agent is used, close serologic and CSF follow-up are necessary. (See 'Follow-up evaluations' below.)

Maternal coinfection with HIV — Infants born to mothers who are coinfected with syphilis and HIV should receive the same evaluation and treatment as those whose mothers do not have HIV infection [4]. There is insufficient evidence to determine whether such infants require different evaluation, treatment, or follow-up.

FOLLOW-UP EVALUATIONS

Infants and children who have reactive serologic tests for syphilis or were born to mothers who were seroreactive at delivery should be monitored for clinical or serologic manifestations of congenital syphilis; those who were treated should be monitored to assure adequate treatment response [4,5,15,23,24].

Examination — Infants who have reactive serologic tests for syphilis or were born to mothers who were seroreactive at delivery should undergo evaluation for manifestations of congenital syphilis during regularly scheduled well-child care visits during the first year and beyond (for manifestations of late congenital syphilis) (table 2 and table 4) [4,5]. Evaluation for hearing loss, ophthalmologic abnormalities, and neurodevelopmental problems should occur yearly [2]. (See "Hearing loss in children: Screening and evaluation" and "Vision screening and assessment in infants and children" and "Developmental-behavioral surveillance and screening in primary care".)

Serology — Reactive serology in the infant does not differentiate between the infant's antibody response to infection and transplacentally acquired maternal antibody. Serial monitoring of the infant's serology is necessary to ensure an appropriate treatment response or exclude congenital syphilis. In children diagnosed with congenital syphilis after infancy, serial monitoring of serology is necessary to ensure appropriate treatment response.

Nontreponemal tests — Quantitative Venereal Disease Research Laboratory test (VDRL) or rapid plasma reagin (RPR) should be performed every two to three months in infants born to mothers with syphilis, including infants who were seronegative at birth whose mothers acquired syphilis late in gestation (whether or not the infant was treated with penicillin), and in children treated for congenital syphilis after infancy. Serology should be repeated until the test becomes nonreactive or the titer has decreased fourfold (equivalent to two dilutions) [4,25,26].

The infant's VDRL or RPR titers should decline by three months of age and be nonreactive by six months of age if the infant was successfully treated or not infected (ie, if the reactive test was caused by passive transfer of maternal immunoglobulin G [IgG] antibody) [4,27,28]. The response may be slower in infants and children treated after one month of age.

Treatment failure — Treatment failure, or failure of maternal treatment to prevent congenital syphilis, is indicated by:

- Failure of the VDRL or RPR titers to decline, or
- Increase in the VDRL or RPR after 6 to 12 months of age (or treatment in children treated after the neonatal period)

In such circumstances, the infant/child should undergo a lumbar puncture to obtain cerebrospinal fluid (CSF) for VDRL, cell count, and protein, and be treated with 10 days of parenteral penicillin, even if he or she was treated previously [4,5]. (See 'Cerebrospinal fluid evaluation' below and 'Penicillin therapy' above.)

Treponemal tests — Treponemal tests (eg, fluorescent treponemal antibody absorption [FTA-ABS], *T. pallidum* particle agglutination [TP-PA], enzyme immunoassay [EIA], chemiluminescence immunoassay [CIA], microhemagglutination test for *T. pallidum* [MHA-TP]) should not be used to evaluate treatment response because they can remain positive despite effective treatment [4,29].

However, treponemal tests can be helpful in establishing a diagnosis of congenital syphilis. A treponemal test should be performed after 12 to 15 months of age in infants who had reactive serologic tests for syphilis or were born to mothers who were seroreactive at delivery [2,15]. If the treponemal test is reactive, it should be repeated at 18 and 24 months of age. A positive

treponemal test at ≥18 months of age (after the disappearance of passively acquired maternal antibody) confirms the diagnosis of congenital syphilis [2,26]. Children who have a positive treponemal test for syphilis at ≥18 months of age and did not previously receive treatment should undergo full evaluation and treatment. (See 'Evaluation and management of children >1 month of age' above.)

Cerebrospinal fluid evaluation — Serial CSF evaluation is necessary for infants and children whose initial CSF evaluation was abnormal (ie, reactive CSF VDRL or elevated CSF white blood cell count or protein without an alternative explanation) [4]. CSF should be evaluated every six months until the results are normal. A reactive CSF VDRL or abnormal CSF white blood cell count or protein that cannot be attributed to other ongoing illnesses requires retreatment for possible neurosyphilis with 10 days of parenteral penicillin therapy [4,5] (see 'Penicillin therapy' above). Neuroimaging studies may be warranted in children with persistently reactive CSF VDRL, elevated CSF cell count, and/or elevated CSF protein [5].

OUTCOME

In the United States, the case fatality rate for congenital syphilis is between 6 and 8 percent [30,31]. Approximately 90 percent of fatal cases are associated with lack of prenatal care or inadequate prenatal care.

Appropriate treatment of early congenital syphilis within the first three months of life prevents some, but not all, of the late manifestations of congenital syphilis [28,32,33]. Interstitial keratitis (picture 2) and anterior tibial bowing ("saber shins") (picture 3) may occur or progress despite appropriate therapy [34].

Syphilis infection may persist for life. Treponemes appear to persist in extracellular loci with little or no inflammatory response elicited. A history of syphilis or treatment for syphilis provides relatively minor and unreliable protection against subsequent infection [35]. Active disease after reinfection is common, regardless of nontreponemal antibody reactivity.

PREVENTION

Measures to prevent congenital syphilis include screening of pregnant women and international adoptees, contact tracing, contact precautions, and monitoring of close contacts of infectious patients for clinical or serologic evidence of disease.

In 2007, the World Health Organization (WHO) launched an initiative to eliminate congenital syphilis that set targets of at least 90 percent of pregnant women being tested for syphilis and at least 90 percent of seropositive pregnant women receiving adequate treatment by 2015 [36]. Considerable progress has been made toward these goals, particularly with regards to [37]:

- Increasing access to maternal and newborn services
- Screening and treating pregnant women and their partners
- Establishing surveillance, monitoring, and evaluation systems
- Ensuring advocacy and sustained political commitment

Linking the efforts for global elimination of congenital syphilis to an integrated strategy of eliminating mother-to-child HIV transmission affords the opportunity of synergistic benefits. In a 2015 report the included data from 58 countries, the median proportion of pregnant women receiving at least one antenatal care visit was 90 percent, and there were notable successes in declaring some countries free of mother-to-child transmission of syphilis [38].

Prevention of acquired syphilis is discussed in greater detail separately. (See "Syphilis: Treatment and monitoring", section on 'Treatment after an exposure' and "Syphilis: Epidemiology, pathophysiology, and clinical manifestations in patients without HIV", section on 'Epidemiology'.)

Screening — Most cases of congenital syphilis are preventable with routine prenatal care, screening of pregnant women for syphilis, penicillin treatment of infected women and their sexual partners, and appropriate monitoring and interpretation of treatment response [7,39-44]. Screening and treatment of syphilis during pregnancy are discussed separately. (See "Syphilis in pregnancy" and "Syphilis in pregnancy", section on 'Maternal screening'.)

However, current screening practices have limitations. Lack of prenatal care is the most important. Among the 431 cases of congenital syphilis reported to the United States Centers for Disease Control and Prevention (CDC) in 2008, approximately one-third were born to mothers who did not receive prenatal care [30]. Although the CDC and the American Academy of Pediatrics (AAP) recommend that newborn infants remain hospitalized until there is documentation of the mother's syphilis serology (at least once during pregnancy and ideally again at delivery), adherence to this recommendation may be difficult, particularly when an early discharge is planned [4,5,45].

The possibility of false negative results of nontreponemal serology is another important limitation (see "Syphilis: Screening and diagnostic testing", section on 'Negative nontreponemal test in early syphilis'). A negative maternal nontreponemal test at delivery does not exclude incubating syphilis or primary syphilis if it is too early for maternal antibodies to have reached

detectable concentrations [46,47]. Infants born in such circumstances continue to escape detection until they become symptomatic, typically at 3 to 14 weeks of age [2]. Repeat maternal screening at the first postpartum visit may be warranted for mothers who engage in high-risk behaviors or reside in areas with high prevalence of syphilis.

International adoptees — Syphilis testing is recommended as part of the evaluation of internationally adopted children, even if they are reported to have received evaluation and treatment in their home country [21]. Congenital syphilis may be undiagnosed or inadequately treated in developing countries [48]. (See "International adoption: Infectious disease aspects", section on 'Syphilis'.)

Isolation precautions — Standard precautions are recommended for infants with suspected or proven congenital syphilis [5]. (See "Infection prevention: Precautions for preventing transmission of infection", section on 'Standard precautions'.) In addition, gloves should be worn when caring for infants with skin or mucous membrane lesions until 24 hours of treatment have been completed [49]. Moist open lesions, secretions, and body fluids (eg, cerebrospinal fluid, blood) contain spirochetes and are infectious [15].

Close contacts — Persons, including hospital personnel, who had close unprotected contact with a child with early congenital syphilis before the child was diagnosed or during the first 24 hours of treatment should be examined for syphilitic lesions (ie, chancre) two to three weeks after contact [5]. Serologic testing should be performed and repeated three months after exposure, or sooner if symptoms develop. Immediate treatment (penicillin G benzathine 50,000 units/kg intramuscularly as a single dose; maximum dose 2.4 million units) may be warranted if the degree of exposure was substantial.

REPORTING REQUIREMENTS

In the United States, congenital syphilis is a national notifiable disease [50]. However, reporting requirements vary by state. Reporting to the US Centers for Disease Control and Prevention by the states is voluntary. For reporting purposes, congenital syphilis includes stillbirths due to syphilis, cases of congenital syphilis detected in newborns, and cases of congenitally acquired syphilis in infants and children [1]. Reporting of syphilis to state or local health departments permits contact investigation, appropriate follow-up, and identification of populations at increased risk.

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Congenital syphilis (The Basics)")

SUMMARY AND RECOMMENDATIONS

- The United States Centers for Disease Control and Prevention and the American Academy of Pediatrics Committee on Infectious Diseases provide guidelines for the evaluation and management of congenital syphilis (algorithm 1 and table 1). (See 'Evaluation and management of infants <1 month of age' above.)

- The diagnosis of congenital syphilis should be suspected in all infants born to women who have reactive nontreponemal and treponemal tests for syphilis and infants/children with clinical findings compatible with congenital syphilis (table 2). The initial evaluation of infants <1 month of age should include (see 'Initial evaluation' above):

  - Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) titers (the same test that was performed on the mother)

  - Physical examination for evidence of congenital syphilis with darkfield microscopic examination or direct fluorescent antibody (DFA) staining of suspicious lesions or body fluids (eg, nasal discharge); **and**

  - Pathologic examination of the placenta and umbilical cord with specific fluorescent antitreponemal antibody staining (if possible)

  Additional evaluation depends upon the findings from the initial evaluation (table 1). (See 'Subsequent evaluation and management' above.)

- Congenital syphilis is proven or highly probable if the infant has examination findings compatible with congenital syphilis (table 2); VDRL or RPR titer that is ≥fourfold the corresponding maternal titer; or a positive darkfield (picture 1) or fluorescent antibody test of body fluid(s), placenta, or umbilical cord. Such infants should be evaluated with cerebrospinal fluid (CSF) VDRL, cell count, and protein; complete blood count with differential and platelet count; and additional tests as clinically indicated (table 1). (See 'Proven or highly probable disease' above.)

- For infants with proven or highly probable congenital syphilis, we recommend treatment with 10 days of parenteral penicillin (**Grade 1A**). (See 'Ten-day regimens' above.)

- Infants born to women with syphilis or a history of syphilis remain at risk for syphilis even if the infant has a normal physical examination and VDRL or RPR that is nonreactive or less than fourfold the maternal titer. The evaluation and treatment of at-risk neonates varies depending upon the mother's history of syphilis and syphilis treatment and the treatment plan for the infant (algorithm 1 and table 1). (See 'Possible congenital syphilis' above and 'Congenital syphilis less likely' above.)

- For infants who are at risk for congenital syphilis, we recommend treatment with parenteral penicillin (**Grade 1A**). The regimen varies depending upon the clinical circumstances (table 1). (See 'Penicillin therapy' above.)

- Infants and children who have reactive serologic tests for syphilis or were born to mothers who were seroreactive at delivery should undergo monitoring for clinical manifestations of congenital syphilis at well-child care visits throughout childhood. VDRL or RPR should be repeated every two to three months until the test becomes nonreactive or the titer has decreased fourfold. Serial CSF evaluation is necessary for infants and children whose initial CSF evaluation was abnormal without an alternative explanation. (See 'Follow-up evaluations' above.)

- Measures to prevent congenital syphilis include screening of pregnant women and international adoptees, contact tracing, contact precautions, and monitoring of close contacts of infectious patients for clinical or serologic evidence of disease. (See 'Prevention' above.)

REFERENCES

1. Centers for Disease Control and Prevention. Syphilis (Treponema pallidum) 2018 Case Definition. https://ndc.services.cdc.gov/case-definitions/syphilis-2018/ (Accessed on June 17, 2021).
2. Dobson SR, Sanchez PJ. Syphilis. In: Feigin and Cherry's Textbook of Pediatric Infectious Diseases, 8th Ed, Cherry JD, Harrison GJ, Kaplan SL, Steinbach, WJ, Hotez, PJ (Eds), Elsevier, Philadelphia, PA 2019. p.1268.
3. Kimball A, Torrone E, Miele K, et al. Missed Opportunities for Prevention of Congenital Syphilis - United States, 2018. MMWR Morb Mortal Wkly Rep 2020; 69:661.
4. Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015; 64:1.
5. American Academy of Pediatrics. Syphilis. In: Red Book: 2021-2024 Report of the Committee on Infectious Diseases, 32nd ed, Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH (Eds), American Academy of Pediatrics, Itasca, IL 2021. p.729.
6. WHO guidelines for the treatment of Treponema pallidum (syphilis). 2016. Available at: http://apps.who.int/iris/bitstream/10665/249572/1/9789241549806-eng.pdf?ua=1 (Accessed on September 15, 2016).
7. McFarlin BL, Bottoms SF, Dock BS, Isada NB. Epidemic syphilis: maternal factors associated with congenital infection. Am J Obstet Gynecol 1994; 170:535.
8. Beeram MR, Chopde N, Dawood Y, et al. Lumbar puncture in the evaluation of possible asymptomatic congenital syphilis in neonates. J Pediatr 1996; 128:125.
9. Moyer VA, Schneider V, Yetman R, et al. Contribution of long-bone radiographs to the management of congenital syphilis in the newborn infant. Arch Pediatr Adolesc Med 1998; 152:353.
10. Alexander JM, Sheffield JS, Sanchez PJ, et al. Efficacy of treatment for syphilis in pregnancy. Obstet Gynecol 1999; 93:5.
11. Conover CS, Rend CA, Miller GB Jr, Schmid GP. Congenital syphilis after treatment of maternal syphilis with a penicillin regimen exceeding CDC guidelines. Infect Dis Obstet Gynecol 1998; 6:134.
12. Sheffield JS, Sánchez PJ, Morris G, et al. Congenital syphilis after maternal treatment for syphilis during pregnancy. Am J Obstet Gynecol 2002; 186:569.
13. Radcliffe M, Meyer M, Roditi D, Malan A. Single-dose benzathine penicillin in infants at risk of congenital syphilis--results of a randomised study. S Afr Med J 1997; 87:62.
14. Paryani SG, Vaughn AJ, Crosby M, Lawrence S. Treatment of asymptomatic congenital syphilis: benzathine versus procaine penicillin G therapy. J Pediatr 1994; 125:471.

15. Kollmann TR, Dobson S. Syphilis. In: Infectious Diseases of the Fetus and Newborn Infant, 7 th, Remington JS, Klein JO, Wilson CB, et al (Eds), Elsevier Saunders, Philadelphia 2011. p.52 4.
16. Christian CW, Lavelle J, Bell LM. Preschoolers with syphilis. Pediatrics 1999; 103:E4.
17. Chakraborty R, Luck S. Syphilis is on the increase: the implications for child health. Arch Dis Child 2008; 93:105.
18. Beck-Sague C, Alexander ER. Failure of benzathine penicillin G treatment in early congenital syphilis. Pediatr Infect Dis J 1987; 6:1061.
19. Woolf A, Wilfert CM, Kelsey DB. Childhood syphilis in North Carolina. N C Med J 1980; 41:443.
20. Azimi PH, Janner D, Berne P, et al. Concentrations of procaine and aqueous penicillin in the cerebrospinal fluid of infants treated for congenital syphilis. J Pediatr 1994; 124:649.
21. Woods CR. Syphilis in children: congenital and acquired. Semin Pediatr Infect Dis 2005; 16:245.
22. HOLZEL A. Jarisch-Herxheimer reaction following penicillin treatment of early congenital syphilis. Br J Vener Dis 1956; 32:175.
23. Ikeda MK, Jenson HB. Evaluation and treatment of congenital syphilis. J Pediatr 1990; 117:843.
24. Rathbun KC. Congenital syphilis: a proposal for improved surveillance, diagnosis, and treatment. Sex Transm Dis 1983; 10:102.
25. Hardy JB, Hardy PH, Oppenheimer EH, et al. Failure of penicillin in a newborn with congenital syphilis. JAMA 1970; 212:1345.
26. Rawstron SA, Mehta S, Marcellino L, et al. Congenital syphilis and fluorescent treponemal antibody test reactivity after the age of 1 year. Sex Transm Dis 2001; 28:412.
27. Chang SN, Chung KY, Lee MG, Lee JB. Seroreversion of the serological tests for syphilis in the newborns born to treated syphilitic mothers. Genitourin Med 1995; 71:68.
28. Lago EG, Vaccari A, Fiori RM. Clinical features and follow-up of congenital syphilis. Sex Transm Dis 2013; 40:85.
29. Singh AE, Guenette T, Gratrix J, et al. Seroreversion of treponemal tests in infants meeting canadian surveillance criteria for confirmed early congenital syphilis. Pediatr Infect Dis J 2013; 32:199.
30. Centers for Disease Control and Prevention (CDC). Congenital syphilis - United States, 2003-2008. MMWR Morb Mortal Wkly Rep 2010; 59:413.

31. Gust DA, Levine WC, St Louis ME, et al. Mortality associated with congenital syphilis in the United States, 1992-1998. Pediatrics 2002; 109:E79.
32. PUTKONEN T. Does early treatment prevent dental changes in congenital syphilis? Acta Derm Venereol 1963; 43:240.
33. Stamos JK, Rowley AH. Timely diagnosis of congenital infections. Pediatr Clin North Am 1994; 41:1017.
34. OKSALA A. Interstitial keratitis after adequate penicillin therapy; a case report. Br J Vener Dis 1957; 33:113.
35. Pavithran K. Acquired syphilis in a patient with late congenital syphilis. Sex Transm Dis 1987; 14:119.
36. The World Health Organization. The global elimination of congenital syphillis: Rationale an d strategy for action. http://www.who.int/reproductivehealth/publications/rtis/9789241595858/en/ (Accessed on December 20, 2016).
37. The World Health Organization. Elimination of mother-to-child transmission (EMTCT) of HIV and syphilis: Global guidance on criteria and processes for validation. http://www.who.int/reproductivehealth/publications/rtis/9789241505888/en/ (Accessed on December 20, 2016).
38. Kiarie J, Mishra CK, Temmerman M, Newman L. Accelerating the dual elimination of mother-to-child transmission of syphilis and HIV: Why now? Int J Gynaecol Obstet 2015; 130 Suppl 1:S1.
39. Coles FB, Hipp SS, Silberstein GS, Chen JH. Congenital syphilis surveillance in upstate New York, 1989-1992: implications for prevention and clinical management. J Infect Dis 1995; 171:732.
40. Mascola L, Pelosi R, Blount JH, et al. Congenital syphilis. Why is it still occurring? JAMA 1984; 252:1719.
41. Desenclos JC, Scaggs M, Wroten JE. Characteristics of mothers of live infants with congenital syphilis in Florida, 1987-1989. Am J Epidemiol 1992; 136:657.
42. Webber MP, Lambert G, Bateman DA, Hauser WA. Maternal risk factors for congenital syphilis: a case-control study. Am J Epidemiol 1993; 137:415.
43. Southwick KL, Guidry HM, Weldon MM, et al. An epidemic of congenital syphilis in Jefferson County, Texas, 1994-1995: inadequate prenatal syphilis testing after an outbreak in adults. Am J Public Health 1999; 89:557.
44. Warner L, Rochat RW, Fichtner RR, et al. Missed opportunities for congenital syphilis prevention in an urban southeastern hospital. Sex Transm Dis 2001; 28:92.

45. Martin D, Bertrand J, McKegney C, et al. Congenital syphilis surveillance and newborn evaluation in a low-incidence state. Arch Pediatr Adolesc Med 2001; 155:140.

46. Dorfman DH, Glaser JH. Congenital syphilis presenting in infants after the newborn period. N Engl J Med 1990; 323:1299.

47. Sánchez PJ, Wendel GD, Norgard MV. Congenital syphilis associated with negative results of maternal serologic tests at delivery. Am J Dis Child 1991; 145:967.

48. Staat MA. Infectious disease issues in internationally adopted children. Pediatr Infect Dis J 2002; 21:257.

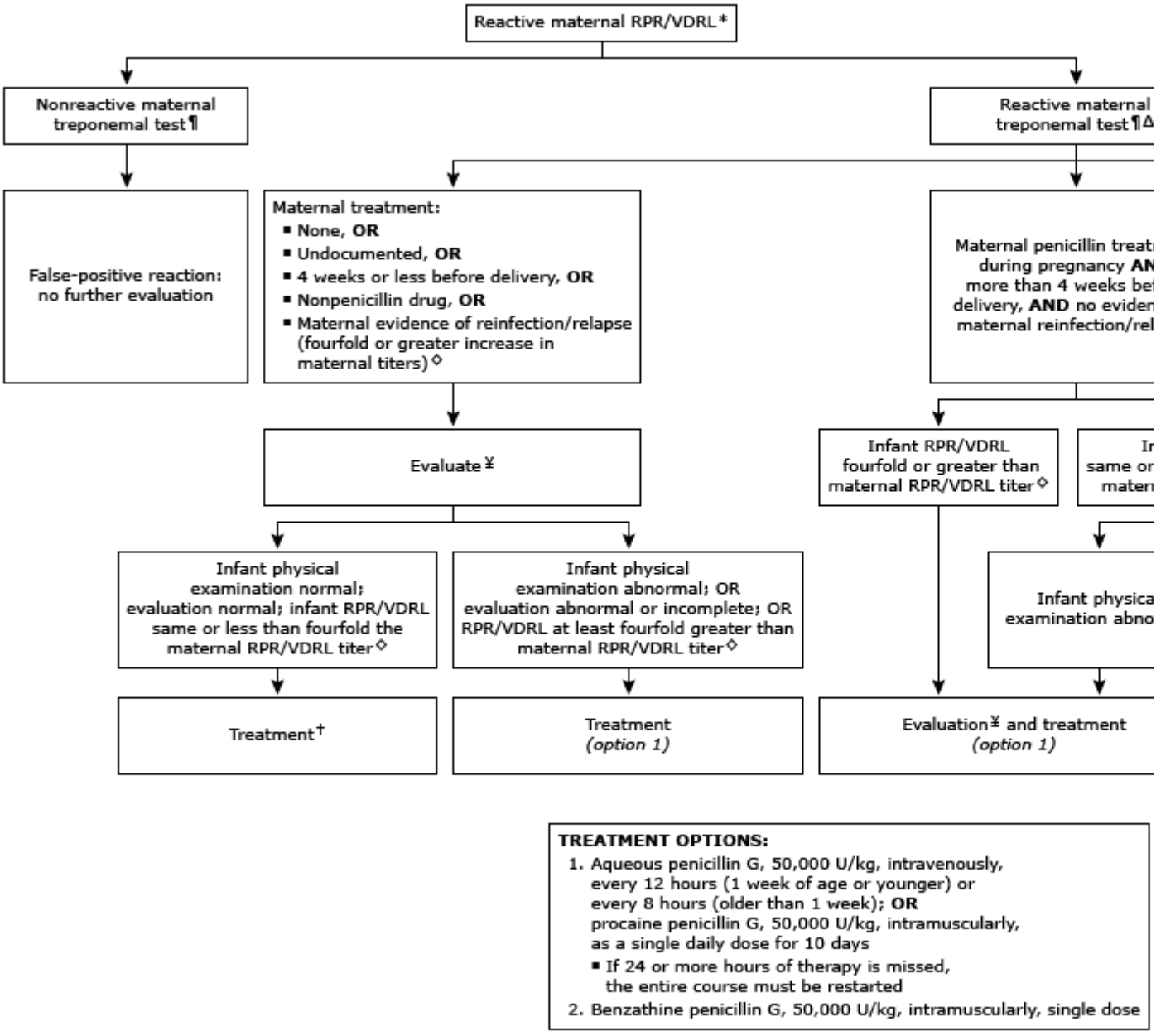
49. TUCKER HA, ROBINSON RC. Disappearance time of Treponema pallidum from lesions of early syphilis following administration of crystalline penicillin G. Bull Johns Hopkins Hosp 1947; 80:169.

50. Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System. http://www.cdc.gov/osels/ph_surveillance/nndss/phs/infdis.htm (Accessed on August 12, 2011).

Topic 15400 Version 30.0

GRAPHICS

Congenital syphilis: Evaluation and management



RPR: rapid plasma reagin; VDRL: Venereal Disease Research Laboratory; TP-PA: *Treponema pallidum* particle a antibody absorption; TP-EIA: *T. pallidum* enzyme immunoassay; MHA-TP: microhemagglutination test for an

* This algorithm does not apply if maternal samples are screened in reverse order (ie, treponemal test is pe of interpretation of reverse sequence testing, please refer to the UpToDate topic on diagnosis of syphilis.

¶ TP-PA, FTA-ABS, TP-EIA, or MHA-TP.

Δ Test for HIV antibody. Infants of HIV-infected mothers do not require different evaluation or treatment.

◇ A fourfold change in titer is the same as a change of 2 dilutions. For example, a titer of 1:64 is fourfold gre fourfold lower than a titer of 1:16.

§ Women who maintain a VDRL titer 1:2 or less or an RPR 1:4 or less beyond 1 year after successful treatme

¥ Complete blood cell and platelet count; CSF examination for cell count, protein, and quantitative VDRL; oth radiographs, long-bone radiographs, eye examination, liver function tests, neuroimaging, and auditory brai

‡ Some experts would consider a single intramuscular injection of benzathine penicillin (treatment option 2)

† Treatment (option 1 or option 2, above) with many experts recommending treatment option 1. If a single d infant must be fully evaluated, full evaluation must be normal, and follow-up must be certain. If any part of performed, or if the CSF analysis is rendered uninterpretable, then a 10-day course of penicillin is required.

From: American Academy of Pediatrics. Syphilis. In: Red Book: 2012 Report of the Committee on Infectious Diseases, 29th ed, Pickering Village, IL 2012. Copyright © 2012 American Academy of Pediatrics. Used with permission. The contents of this figure remain unchan Infectious Diseases, 31st ed.

Graphic 51559 Version 19.0

Evaluation and management of neonates (<1 month) born to women with syphilis or history of syphilis*

Initial neonatal evaluation		Maternal treatment		Subsequent neonatal evaluation	Treatment of neonate
Neonate VDRL/RPR	**Neonate evaluation**	**Timing**	**Type**		
Any result	**Examination compatible with congenital syphilis or visualization of spirochete in clinical specimen**¶	Any	Any or none	▪ CSF VDRL, cell count, protein ▪ CBC with differential and platelet count ▪ Additional tests as clinically indicated$^{\Delta}$	10 days of parenteral penicillin$^{\diamond}$
≥ Fourfold maternal titer	Any	Any	Any	▪ CSF VDRL, cell count, protein ▪ CBC with differential and platelet count ▪ Additional tests as clinically indicated$^{\Delta}$	10 days of parenteral penicillin$^{\diamond}$
< Fourfold maternal titer	Normal physical examination	During pregnancy	None, inadequate, suboptimal‡	▪ CSF VDRL, cell count, protein ▪ CBC with differential and platelet count ▪ Additional tests as clinically indicated$^{\Delta}$	If the entire evaluation is performed and normal†: Single dose IM benzathine penicillin$^{¥}$; some experts would treat with 10 days of parenteral penicillin$^{\diamond}$

					If any portion of the evaluation is abnormal, not performed, or not interpretable: 10 days of parenteral penicillin◇
< Fourfold maternal titer	Normal physical examination	Before pregnancy	Evidence of reinfection or relapse (≥ fourfold increase in post-treatment titer)	▪ CSF VDRL, cell count, protein ▪ CBC with differential and platelet count ▪ Additional tests as clinically indicated[Δ]	If the entire evaluation is performed and normal: Single dose IM benzathine penicillin[¥] If any portion of the evaluation is abnormal, not performed, or not interpretable: 10 days of parenteral penicillin◇
< Fourfold maternal titer	Normal physical examination	During pregnancy	Adequate[§]	None	Single dose IM benzathine penicillin[¥]; some experts would not treat but provide close serologic follow-up
< Fourfold maternal titer	Normal physical examination	Before pregnancy	Adequate[§]	None	None; some experts would treat with a single dose of IM benzathine penicillin[¥]
Nonreactive	Normal physical	During pregnancy	None, inadequate,	None	Single dose IM benzathine

	examination		suboptimal‡		penicillin¥
Nonreactive	Normal physical examination	During pregnancy	Adequate§	None	None; some experts would treat with a single dose of IM benzathine penicillin¥

Neonate characteristics in **bold text** indicate proven or highly probable congenital syphilis disease in the infant.

VDRL: Venereal Disease Research Laboratory serologic test for syphilis; RPR: rapid plasma reagin serologic test for syphilis; CSF: cerebrospinal fluid; CBC: complete blood count; IM: intramuscular; IV: intravenous.

* Mother with reactive nontreponemal (VDRL or RPR) and treponemal (microhemagglutination test for *T. pallidum* [MHA-TP] or fluorescent treponemal antibody absorption [FTA-ABS]) serologic tests for syphilis. All such infants require clinical and serologic follow-up (see text for details).

¶ Examination findings compatible with early congenital syphilis may include (but are not limited to) hepatomegaly/hepatosplenomegaly; rash; condyloma lata; snuffles; jaundice; pseudoparalysis; anemia; and edema.

Δ Additional tests may include: Long-bone radiographs, chest radiograph, liver function tests, cranial ultrasonography, ophthalmologic examination, and auditory brainstem response.

◇ There are two alternate regimens: Aqueous penicillin G (50,000 units/kg IV every 12 hours [for infants ≤7 days of age] and every 8 hours [>7 days of age] for a total of 10 days); or procaine penicillin G 50,000 units/kg IM as a single daily dose for 10 days.

§ Adequate therapy encompasses treatment with penicillin more than four weeks before delivery; appropriate dose for the stage of disease; documentation of treatment response (fourfold decline in titer for early syphilis and titer remained stable or low [VDRL ≤1:2; RPR ≤1:4] for late syphilis); no evidence of reinfection or relapse (fourfold increase in titer after treatment).

¥ Benzathine penicillin G (50,000 units/kg intramuscularly as a single dose).

‡ Inadequate or suboptimal maternal therapy encompasses: Treatment with a nonpenicillin antibiotic; treatment less than four weeks before delivery; inappropriate dose for the stage of disease; no documentation of maternal therapy; maternal titers did not decline at least fourfold after treatment for early syphilis or did not remain stable and low [VDRL ≤1:2; RPR ≤1:4] for late syphilis; or maternal titers increased by fourfold after treatment (suggesting reinfection or relapse).

† Normal CSF is generally defined by nonreactive VDRL, CSF WBC <25 cells/microL, and CSF protein <150 mg/dL for term infants and <170 mg/dL for preterm infants; however, some experts define normal CSF WBC as <5 cells/microL and normal CSF protein as <40 mg/dL.

References:

1. Workowski KA, Bolan GA. Sexually Transmitted Diseases Treatment Guidelines, 2015. MMWR Recomm Rep 2015; 64:1.

2. *American Academy of Pediatrics. Syphilis. In: Red Book: 2018 Report of the Committee on Infectious Diseases, 31st ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics, Itasca, IL 2018. p.773.*
3. *Dobson SR, Sanchez PJ. Syphilis. In: Feigin and Cherry's Textbook of Pediatric Infectious Diseases, 8th ed, Cherry JD, Harrison GJ, Kaplan SL, et al (Eds), Elsevier Saunders, Philadelphia 2019. p.1268.*
4. *Kollmann TR, Dobson SD. Syphilis. In: Infectious Diseases of the Fetus and Newborn infant, 7th edition, Remington JS, Klein JO, Wilson CB, et al (Eds), Elsevier Saunders, Philadelphia 2011. p.524.*

Graphic 80812 Version 14.0

Clinical manifestations of early congenital syphilis*

Gestational/perinatal	
Stillbirth	
Prematurity	
Birth weight <2500 g	
Nonimmune hydrops fetalis	
Placenta	Large, thick, pale (send for pathologic/histologic evaluation)
Umbilical cord	Inflamed with abscess-like foci of necrosis within Wharton's jelly, centered around the umbilical vessels (necrotizing funisitis); barber-pole appearance (send for pathologic/histologic evaluation)
Systemic	
Fever	May be more prominent in infants born to mothers who are affected late in pregnancy and whose serology is negative at delivery
Hepatomegaly	Splenomegaly occurs in approximately one-half of patients with hepatomegaly—isolated splenomegaly does not occur
Generalized lymphadenopathy	May be as large as 1 cm; generally nontender and firm
Failure to thrive	
Edema	Due to anemia/hydrops fetalis, nephrotic syndrome, malnutrition
Mucocutaneous	
Syphilitic rhinitis ("snuffles")	Can be an early feature, developing after the first week of life; **contains spirochetes and is infectious (use contact precautions)**
Maculopapular rash	Usually appears one to two weeks after rhinitis. Oval lesions, initially red or pink and then coppery brown; may be associated with superficial desquamation or scaling, particularly on the palms or soles; more common on the buttocks, back, posterior thighs, and soles; **contains spirochetes and is infectious (use contact precautions)**.
Vesicular rash (pemphigus syphiliticus)	May be present at birth, most often develops in first four weeks; widely disseminated; vesicular fluid **contains spirochetes and is infectious (use contact precautions)**
Condylomata lata	Single or multiple, flat, wartlike, moist lesions around the

	mouth, nares, and anus and other areas of the skin where there is moisture or friction; **lesions contain spirochetes and are infectious (use contact precautions)**; frequently present without other signs of infection
Jaundice	Hyperbilirubinemia secondary to syphilitic hepatitis and/or hemolysis
Hematologic	
Anemia	Newborn period: Hemolytic (Coomb's test [direct antiglobulin test] negative); may persist after effective treatment After one month of age: May be chronic and nonhemolytic
Thrombocytopenia	May be associated with bleeding or petechiae; can be the only manifestation of congenital infection
Leukopenia	
Leukocytosis	
Musculoskeletal	
Pseudoparalysis of Parrot	Lack of movement of an extremity because of pain associated with bone lesion; affects upper extremities more often than lower; usually unilateral; rarely present at birth; poorly correlated with radiographic abnormalities
Radiographic abnormalities:	Most frequent abnormality in untreated early congenital syphilis; not usually clinically discernible; typically multiple and symmetric
Periostitis	Irregular periosteal thickening; usually present at birth, but may appear in the first few weeks of life
Wegner sign	Metaphyseal serration or "sawtooth metaphysis"
Wimberger sign	Demineralization and osseous destruction of the upper medial tibial
Neurologic	
CSF abnormalities	Reactive CSF VDRL; elevated CSF white blood cell count; elevated CSF protein
Acute syphilitic leptomeningitis	Onset during the first year of life, usually between 3 and 6 months; presentation similar to bacterial meningitis but CSF findings more consistent with aseptic meningitis (mononuclear predominance); responds to penicillin therapy
Chronic meningovascular syphilis	Onset toward the end of the first year; hydrocephalus; cranial nerve palsies; intellectual/neurodevelopmental

	deterioration; cerebral infarction; protracted course
Miscellaneous	
Pneumonia/pneumonitis/respiratory distress	Complete opacification of both lung fields on chest radiograph
Nephrotic syndrome	Usually occurs at two to three months of age and manifests with generalized edema and ascites

CSF: cerebrospinal fluid; VDRL: Venereal Disease Research Laboratory test.

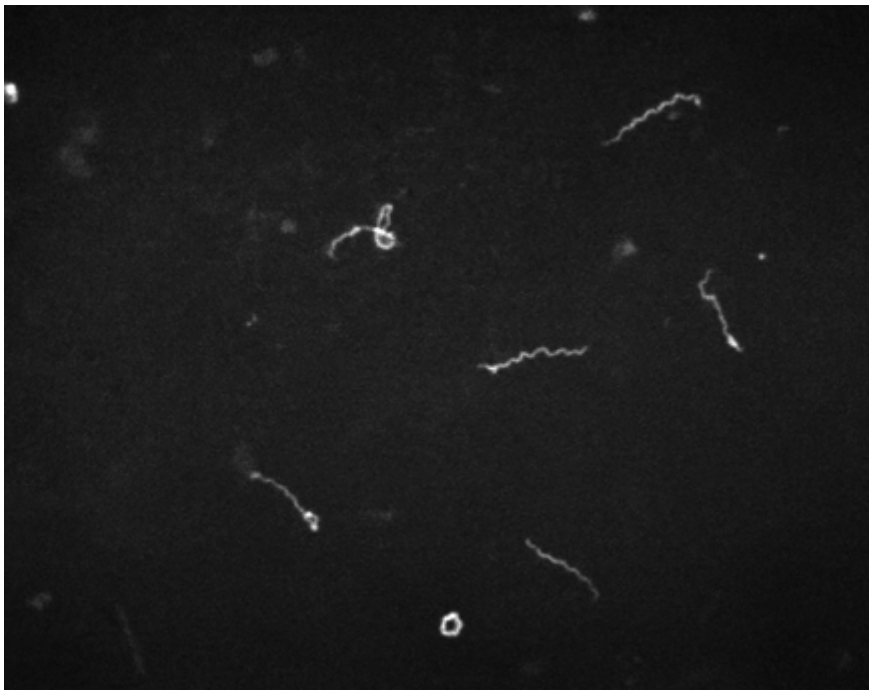
* All of these findings may occur in other congenital infections; none is specific for congenital syphilis.

Data from:

1. *Ingall D, Sanchez PJ, Baker CH. Syphilis. In: Infectious Diseases of the Fetus and Newborn infant, 6th edition, Remington JS, Klein JO, Wilson CB, Baker CJ (Eds), Elsevier Saunders, Philadelphia 2006. p.545.*
2. *Dobson SR, Sanchez PJ. Syphilis. In: Feigin and Cherry's Textbook of Pediatric Infectious Diseases, 7th, Cherry JD, Harrison GJ, Kaplan SL, et al. (Eds), Elsevier Saunders, Philadelphia 2014. p.1761.*
3. *Woods CR. Syphilis in children: congenital and acquired. Semin Pediatr Infect Dis 2005; 16:245.*
4. *Saloojee H, Velaphi S, Goga Y, et al. The prevention and management of congenital syphilis: an overview and recommendations. Bull World Health Organ 2004; 82:424.*
5. *Chakraborty R, Luck S. Syphilis is on the increase: the implications for child health. Arch Dis Child 2008; 93:105.*
6. *Rawstron SA. Treponema pallidum (Syphilis). In: Principles and Practice of Pediatric Infectious Diseases, 3rd edition, Long SS, Pickering LK, Prober CG (Eds), Churchill Livingstone Elsevier, Philadelphia 2008. p.930.*

Graphic 67809 Version 8.0

Treponema pallidum spirochetes depicted with darkfield microscopy



Using a darkfield microscopy technique, this photomicrograph revealed the presence of *Treponema pallidum* spirochetes, which are the bacterial agents that cause syphilis.

Courtesy of the Centers for Disease Control and Prevention/Schwartz WF.

Graphic 72322 Version 5.0

Inadequate or suboptimal treatment of maternal syphilis

Inadequate therapy
Treatment with a nonpenicillin antibiotic
Treatment less than four weeks before delivery (including treatment with penicillin)
Inappropriate dose for stage of disease
Inadequate documentation of maternal treatment
Lack of performance of serial non-treponemal* antibody titers after maternal treatment
Maternal therapy was not documented
Inadequate response to therapy
Maternal non-treponemal antibody titers did not decline at least fourfold (two dilutions) after treatment
Maternal non-treponemal antibody titers suggest reinfection or relapse (ie, fourfold increase)

* Non-treponemal test: Rapid plasma reagin (RPR) test or Venereal Disease Research Laboratory (VDRL) test.

References:

1. *Centers for Disease Control and Prevention. Syphilis (Treponema pallidum) 2018 Case Definition. https://ndc.services.cdc.gov/case-definitions/syphilis-2018/ (Accessed on June 17, 2021).*
2. *American Academy of Pediatrics. Syphilis. In: Red Book: 2021-2024 Report of the Committee on Infectious Diseases, 32nd ed, Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH (Eds), American Academy of Pediatrics, Itasca, IL 2021. p.729.*
3. *Workowski KA, Bolan GA. Sexually Transmitted Diseases Treatment Guidelines, 2015. MMWR Recomm Rep 2015; 64:1.*

Graphic 73418 Version 7.0

Stigmata of late congenital syphilis

Facial features	Frontal bossing, saddle nose, short maxilla, protuberant mandible
Ophthalmologic	Interstitial keratitis, chorioretinitis, secondary glaucoma, corneal scarring, optic atrophy
Ears	Sensorineural hearing loss
Oropharynx	Hutchinson teeth, mulberry molars, perforation of hard palate
Cutaneous	Rhagades, gummas
Central nervous system	Intellectual disability, arrested hydrocephalus, seizures, optic atrophy, juvenile general paresis
Skeletal	Saber shins (anterior bowing of the tibia), Higoumenakis sign (enlargement of the sternoclavicular portion of the clavicle), Clutton joints (painless arthritis), scaphoid scapula

Data from:

1. *Ingall D, Sanchez PJ, Baker CH. Syphilis. In: Infectious Diseases of the Fetus and Newborn infant, 6th edition, Remington JS, Klein JO, Wilson CB, Baker CJ (Eds), Elsevier Saunders, Philadelphia 2006. p.545.*
2. *Dobson SR, Sanchez PJ. Syphilis. In: Feigin and Cherry's Textbook of Pediatric Infectious Diseases, 7th, Cherry JD, Harrison GJ, Kaplan SL, et al. (Eds), Elsevier Saunders, Philadelphia 2014. p.1761.*
3. *Woods CR. Syphilis in children: congenital and acquired. Semin Pediatr Infect Dis 2005; 16:245.*
4. *Chakraborty R, Luck S. Syphilis is on the increase: the implications for child health. Arch Dis Child 2008; 93:105.*

Graphic 81529 Version 3.0

Congenital syphilis: Interstitial keratitis

This photograph shows a stromal haze in both eyes of this child due to interstitial keratitis, a manifestation of late congenital syphilis. Interstitial keratitis is an inflammation of the connective tissue structure of the cornea. It usually is bilateral.

Reproduced from: the Public Health Image Library, Centers for Disease Control and Prevention. Photo by Susan Lindsley.

Graphic 52740 Version 2.0

Congenital syphilis: Saber shins

Reproduced with permission from: Sweet RL, Gibbs RS. Atlas of Infectious Diseases of the Female Genital Tract. Lippincott Williams & Wilkins, Philadelphia 2005. Copyright © 2005 Lippincott Williams & Wilkins.

Graphic 81604 Version 2.0

Contributor Disclosures

Simon R Dobson, MD, FRCP(C) No relevant financial relationship(s) with ineligible companies to disclose. **Sheldon L Kaplan, MD** Grant/Research/Clinical Trial Support: Pfizer [Streptococcus pneumoniae]; Merck [Staphylococcus aureus]; MeMed Diagnostics [Bacterial and viral infections]; Allergan [Staphylococcus aureus]. Consultant/Advisory Boards: MeMed Advisory Board [Diagnostics bacterial and viral infections]. Other Financial Interest: Pfizer [PCV13, linezolid]; Elsevier [Pediatric infectious diseases]. All of the relevant financial relationships listed have been mitigated. **Leonard E Weisman, MD** Equity Ownership/Stock Options: Vax-Immune [Ureaplasma diagnosis, vaccines, antibodies, other medical diagnostics and pre-analytical devices]. Patent Holder: Baylor College of Medicine [Ureaplasma diagnosis, vaccines, antibodies, process for preparing biological samples]. All of the relevant financial relationships listed have been mitigated. **Carrie Armsby, MD, MPH** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→