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# GUIDELINES FOR THE PREVENTION AND CONTROL OF CONGENITAL SYPHILIS

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# GUIDELINES FOR THE PREVENTION AND CONTROL OF CONGENITAL SYPHILIS

## 1. Introduction

Congenital syphilis causes fetal or perinatal death in 40% of the infants affected. The condition was well described in the 15th century and has long been recognized as a distinct syndrome in which the source is an infected adult. Several theories have been advanced to explain how the infection is transmitted, including transmission from a father infected with syphilis and transmission from an infant's nursing an infected wet nurse. Transplacental transmission from an asymptomatic infected mother was first described in 1906.

The availability of penicillin treatment for syphilis in pregnancy has not eradicated congenital syphilis. Since 1970, the incidence of congenital syphilis has closely reflected the incidence of primary and secondary syphilis in women. In 1986, more cases of congenital syphilis (365) were reported to the Division of Sexually Transmitted Diseases, Center for Prevention Services, CDC, than for any of the previous 15 years. That year almost one of every 10,000 live-born infants in the United States had congenital syphilis. The proportion of stillbirths caused by syphilis is unknown.

In July 1987, CDC invited 10 consultants* to discuss the problem of congenital syphilis and to determine possible ways to solve the problem. This supplement to the *Morbidity and Mortality Weekly Report* (*MMWR*) presents guidelines that were developed from discussions with these consultants. Efforts were made to balance the ideal with the feasible, promoting a focused and coordinated source of guidance for health care providers. Although some aspects of the guidelines are based on limited data, the information provided here represents the best judgment of experts.

## 2. Surveillance

Congenital syphilis surveillance should be conducted at the local, state, and national levels. The provisional case definition includes every infant (person <12 months of age) with one of the following: 1) a reactive nontreponemal serologic test for syphilis confirmed by a reactive treponemal test, 2) a positive darkfield microscopic examination on a non-oral mucous membrane, or 3) a positive fluorescent antibody examination for *Treponema pallidum* on any lesion.

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Physicians, clinics, and hospitals should report all cases that meet the provisional definition to the local public health authority. Laboratories should report indicative findings to the same authority. All areas that have five or more women with early infectious syphilis (infection of <1 year's duration) per 100,000 population should establish an active surveillance system for congenital syphilis at key hospitals. At a minimum, hospitals in areas with a high incidence of syphilis or that serve patient populations known to be at increased risk for syphilis should perform routine serologic tests for syphilis (STS) using blood samples from the umbilical cord.

All cases that are classified as "confirmed" or "compatible" or that require additional information to be classified should be reported to the state public health authority (see definitions of case classifications below). These initial reports identify problem areas and ensure appropriate follow-up at the state level. Later, a Congenital Syphilis Follow-up Form, CDC 73.126, should be completed and forwarded through the local and state public health authorities to the Division of Sexually Transmitted Diseases, CDC, for all infants (including stillborns) who have not been classified as "unlikely." Cases that cannot be classified with reasonable assurance (e.g., they are lost to follow-up) should also be described as fully as possible on the form CDC 73.126. The surveillance information documented on the form is used to determine why the particular case occurred and to identify trends. Completion of these forms enables investigators to measure the occurrence of congenital syphilis.

All forms CDC 73.126 should be completed by the time an infant reaches 8 months of age, including forms for cases lost to follow-up. For surveillance purposes, stillbirths also should be evaluated for syphilis, and those with a diagnosis consistent with congenital syphilis should be documented on the form CDC 73.126 through local and state public health authorities in the same manner as live births.

## Diagnostic Classifications of Congenital Syphilis

**Confirmed case**

- identification of *T. pallidum* by darkfield microscopy, fluorescent antibody, or other specific stains in specimens from lesions, autopsy material, placenta, or umbilical cord

**Compatible (formerly, "probable" or "possible") case**

- a reactive STS in a stillborn

**OR**

- a reactive STS in an infant whose mother had syphilis during pregnancy and was not adequately treated, regardless of symptoms in the infant

**OR**

- a reactive Venereal Disease Research Laboratory (VDRL) test of cerebrospinal fluid

**OR**

- a reactive STS in an infant with any of the following signs: snuffles, condyloma lata, osteitis, periostitis or osteochondritis, ascites, skin and mucous membrane lesions, hepatitis, hepatomegaly, splenomegaly, nephrosis, nephritis, or hemolytic anemia

**OR**

- fourfold or greater rise in titers* or nontreponemal tests (VDRL or rapid plasma reagin [RPR] and a confirmed fluorescent treponemal antibody absorption (FTA-ABS) or microhemagglutination assay for antibody to *T. pallidum* (MHA-TP) over a 3-month period

**OR**

- a reactive treponemal test or nontreponemal test that does not revert to nonreactive in 6 months

**Unlikely case**

- no reactive STS

**OR**

- treponemal tests revert to nonreactive within 6 months

**OR**

- no symptoms in live-born infant whose mother, treated for syphilis during pregnancy, had a fourfold or greater fall in titer **and** the infant's STS is also fourfold or lower than the maternal titer was at the time of treatment

Two other aspects of surveillance for congenital syphilis warrant emphasis. First, a sensitive system is needed by which state and local sexually transmitted diseases (STD) control programs are made aware of reactive STS. The programs should evaluate and follow individual reactive serologic test reports and should monitor the reporting patterns of laboratories and diagnosticians. Furthermore, a quality assurance system is needed to confirm that all medical laboratories performing tests for STD are complying with official reporting regulations. Compliance should be checked by letter, telephone, or personal visit at least every 6 months.

Second, state health departments should maintain a central registry of patients who receive treatment for syphilis. Each patient's record should include specific information about the stage of disease, the type(s) and amount(s) of medication administered, the types and results of laboratory tests, and, if the patient is pregnant, the trimester during which she is treated. This information is essential for the proper medical management of pregnant women, their fetuses, and their infants. Strict confidentiality and data security procedures must be established, periodically reviewed, and independently tested to ensure that registry information is neither misused nor unintentionally revealed to unauthorized persons.

## 3. Control

The control of early infectious syphilis is essential for the control of congenital syphilis. When the prevalence of infectious syphilis substantially increases among reproductive-age women, cases of congenital syphilis very likely will follow. Increased prevalence has been observed in several areas of the United States in recent years. To prevent future cases of congenital syphilis, STD control programs need to place more emphasis on early syphilis control, especially in areas with a high incidence.

### *3.1 Disease Intervention Activities for Early Infectious Syphilis*

The traditional "tools" of early syphilis control in the United States include an original

*"Fourfold rise in titer," "fourfold fall in titer," and other similar phrases are used throughout this document. They refer to changes (up or down) in serum titers of at least two dilutions (two "tubes"), e.g., from 1:2 to 1:8 (and the reverse), or from 1:4 to 1:16 (and the reverse), or from 1:32 to 1:8 (and the reverse).

interview of the patient to elicit information on sex partners, rapid notification of partners, selective reinterviews, and selected "clustering" around the patient and his/her examined sex partners to obtain information on other persons who may be at risk of infection. Recommended techniques, methods, and procedures are discussed in the disease intervention courses sponsored by the Division of Sexually Transmitted Diseases.

### *3.2 Specific Activities for State and Local STD Control Programs for the Prevention of Congenital Syphilis*

- Ensure that official public health statutes and/or regulations mandate STS on all pregnant women at the time of the initial prenatal visit and early in the third trimester.
- Monitor public and private laboratories regularly to ensure the prompt and thorough reporting of reactive STS.
- Assess the pregnancy status of women with diagnosed syphilis and of women who are the sex partners of men with diagnosed syphilis.
- Ask early infectious syphilis patients or their unexamined sex partners who reside in neighborhoods with a high incidence of syphilis to identify women in the area who may be pregnant. Refer all identified women for serologic testing and prenatal care.
- Inform every woman of reproductive age who is seen in an STD clinic (for any reason) about the need for prenatal care and STS in future pregnancies.
- Encourage prenatal screening for syphilis wherever pregnant women are seen for health care, including women, infants, and children (WIC) programs, methadone maintenance clinics, detention facilities, and prenatal care facilities; whenever possible, review existing clinic protocols and suggest specific amendments to the clinic medical director.
- Conduct selective serologic screening of women of childbearing age in groups with an increased risk of infection, e.g., women residing in neighborhoods that have a particularly high incidence of syphilis.
- Deliver educational messages to the medical community about laboratory tests, diagnostic criteria, treatment, and follow-up of patients who are at risk of infection and who may be pregnant.
- Develop and disseminate public service educational messages to women who share demographic characteristics with the women most often diagnosed with early syphilis. In many areas of the United States, these women are young, single, members of a minority group, and residents of a central city neighborhood. Brief, well-targeted radio announcements in the language and vernacular of the audience may be particularly effective.

### *3.3 STD Program Priorities*

Although no published studies have evaluated the benefit-to-cost ratio in controlling early syphilis by using the traditional method (see section 3.1) versus less laborious and time-consuming methods, the former has been a mainstay of most STD control programs in the United States for many years. The traditional syphilis-intervention process requires time, commitment, and human resources, and — like other public health strategies — it should be periodically assessed by state and local STD programs for its benefits and costs. In an era of increasing demands for public health resources, the relative effectiveness of the traditional process should be compared with that of less vigorous methods in areas of both high and low syphilis incidence.

A thorough initial interview that includes obtaining information on the patient's sex partners (names and addresses) usually takes at least 45 minutes. In areas with an increased incidence of syphilis, clinic procedures and flow patterns may need to be restructured to accommodate this essential time requirement.

### *3.4 Other Considerations*

The interrelationship of syphilis and human immunodeficiency virus (HIV) infection should be explored in areas with a high incidence of syphilis. HIV infection may influence the manifestation of syphilis or its response to therapy. The role, if any, of the genital ulcers of syphilis in increasing the risk of HIV transmission also needs study in U.S. population groups. State and local STD programs need to coordinate control resources for both syphilis and HIV, offer STS to all women requesting HIV tests, and perform periodic syphilis tests on all persons known to be HIV-antibody positive.

## 4. Prenatal Care

Comprehensive prenatal care started early in pregnancy is essential in preventing congenital syphilis. Unfortunately, many obstacles make it difficult for women, particularly some poor and some minority women, to obtain needed care. These obstacles include financial barriers, the limited availability of health care providers who are willing to serve these populations, provider difficulty in communicating with patients who are poor or from different ethnic backgrounds, organizational arrangements that minimize accessibility and acceptability of treatment, poor coordination of services, and patients' inadequate understanding of the need for care. Any modifications of the present system that would reduce these obstacles would also improve the opportunities for women with syphilis to receive care.

Additional specific strategies are needed to encourage the use of prenatal care by women who may be at increased risk of transmitting syphilis to their fetus, to ensure that these women are adequately screened, and to maintain follow-up. These strategies include targeted outreach efforts, coordination of activities among service providers, and special prenatal care components.

### *4.1 STD Control Programs*

STD control programs should institute special prenatal outreach programs for patients who are at risk for syphilis. All women of childbearing age who come to STD clinics should be asked the date of their last menstrual period. If they have not had a period in the previous 6 weeks, and if their periods are usually regular, they should be tested for pregnancy as soon as possible, preferably on site. If on-site pregnancy testing is not available, STD clinic personnel should make an appointment for the patient at a facility that can do the testing with minimum delay. An RPR card test should be performed routinely on all patients at STD clinics; the laboratory forms of pregnant patients should be "flagged" for priority processing. All pregnant patients, regardless of the results of the RPR, should be referred for prenatal care. If the RPR test is reactive, however, arrangements should be made **immediately** to institute appropriate treatment, sex partner referral, and prenatal care. State and local STD programs should arrange with prenatal care providers to treat women with reactive syphilis tests as medical emergencies. Such women should be given the highest priority for prenatal care, particularly at clinics with waiting lists. If the woman reports normal menses, or the pregnancy

test is negative, she should be informed about the availability of family planning services and about the potential hazards to a fetus caused by STD, cigarette smoking, alcohol, and drugs.

Patients with early infectious syphilis should be interviewed to identify their recent sexual partners. Women who are so identified should receive the highest priority for referral for treatment and, if pregnant, for enrollment in effective prenatal care. Patients with early infectious syphilis who live in high-incidence neighborhoods should also be asked to identify friends, associates, and family members who might be pregnant (see section 3.2). Outreach workers should contact these women, explain to them that syphilis is a potential problem in their community, offer them a test for syphilis, and assist them in enrolling in a prenatal care facility. Pregnant women with a reactive STS should receive the highest priority for treatment and prenatal care. STD program managers need to develop management systems that track and measure the outreach activities focused on pregnant patients and their prenatal care.

### *4.2 Drug Addiction Programs*

All women of childbearing age who come to clinics for drug addiction should also be asked the date of their last menstrual period, and the same procedures should be followed as those described for STD clinics, including on-site pregnancy testing. If the test is positive, an on-site RPR should be performed and referral made for prenatal care. Patients should also be informed about the availability of family planning services and potential fetal damage caused by STD, cigarette smoking, alcohol, and drugs.

### *4.3 Pregnancy Testing Sites*

All sites that provide pregnancy testing should be alerted to their responsibility for preventing congenital syphilis. If a woman has a positive pregnancy test, an RPR card test should be done immediately and on site. If the RPR is reactive, the same procedures should be followed as those described for STD clinics. Special attention should be paid to obtaining accurate addresses for use by the local STD intervention specialist. All sites that provide pregnancy testing should follow these procedures, including family planning clinics, school-based clinics, adolescent health clinics, hospital emergency rooms and outpatient clinics, and detention facilities.

### *4.4 Prenatal Care Sites*

Women must often wait several weeks for their first prenatal appointment because of overcrowded schedules and delays in determining Medicaid eligibility. Since a delay may reduce the likelihood of successful treatment if syphilis is identified, efforts should be made to test women early in pregnancy, possibly during a visit for laboratory tests. If syphilis is diagnosed, treatment and counseling should be started before the regularly scheduled prenatal care visit.

### *4.5 Content of Care*

Prenatal care providers are responsible for ensuring that their pregnant patients are tested for syphilis and for coordinating their activities with those of the local STD program so that infected women will receive treatment promptly. Recommended activities for prenatal care providers include:

- Obtaining maternal blood for serologic testing at the first visit unless the results of a previous test during the current pregnancy are available. A second STS should be

performed at the beginning of the third trimester (28 weeks).

- Providing each patient with a card identifying what test was performed, the date it was done, the result, what treatment (if any) was given, and the clinic's name and telephone number.
- Maintaining a list, arranged by date of test and patient's name, of the results of the STS. Entries should be maintained for 1 year after the pregnancy is terminated. Prenatal care providers are responsible for determining the serologic status of their patients. Providers either should obtain the specimen or should document that a nonreactive test was obtained earlier in the pregnancy. The patient-borne record of STS and reactive results will assist in this documentation.
- Identifying specimens from pregnant women by clearly labeling the laboratory slips "prenatal." Reactive tests should be followed by the STD program as part of an ongoing surveillance activity (see section 2).
- "Flagging" the charts of clients whose serologic tests are reactive. Charts should remain flagged until the patient returns to the clinic. If the patient does not return or respond to routine notification, the local health department should be informed and referral services requested.
- Instructing pregnant patients who may not be involved in mutually monogamous relationships to insist that their sex partners use condoms during the full term of the pregnancy.
- Providing monthly quantitative nontreponemal serologic tests for the remainder of the current pregnancy of women who have been treated for early syphilis. Women who show a fourfold rise in titer should be retreated. Treated women who do **not** show a fourfold decrease in titer within 3 months should be retreated. After delivery, follow-up should be conducted as outlined for nonpregnant patients.
- Testing all patients for syphilis (RPR or VDRL) 1 month after they have completed treatment for any other STD diagnosed during pregnancy.

### *4.6 Monitoring Performance*

The responsibility for monitoring the system of services for preventing congenital syphilis should rest with the state or local STD control program. Since personnel and priorities of the multiple programs involved in preventing congenital syphilis will change over time, a tracking system to monitor performance and the changes in service delivery should be established and maintained.

## 5. Laboratory Tests

The usefulness of laboratory tests in the diagnosis of syphilis depends upon the selection of appropriate standard tests, listed below. The quality of such tests depends upon the use of quality reagents by well-trained personnel. Laboratories and the staff performing laboratory tests should be under strict quality control procedures and should participate regularly in performance evaluation and quality assurance programs.

### Laboratory Tests for Syphilis

**Standard Tests**

- Antibody screening tests (nontreponemal)
  — Rapid plasma reagin (RPR)

- — Venereal Disease Research Laboratory (VDRL)
- — Unheated serum reagin (USR)
- — Reagin screen test (RST)

• Antibody confirmatory tests (treponemal)
- — Fluorescent treponemal antibody absorption (FTA-ABS)
- — Fluorescent treponemal antibody absorption double staining (FTA-ABS DS)
- — Microhemagglutination assay for antibody to *T. pallidum* (MHA-TP)
- — Hemagglutination treponemal test for syphilis (HATTS)
- — Bio-enzaBead Test (ELISA)

• Direct examination of lesion or tissue
- — Darkfield microscopy
- — Direct fluorescent antibody test for *T. pallidum* (DFA-TP)
- — Silver stains (modified Steiner)
- — Hematoxylin and eosin (H & E) stains

**Experimental Tests**

• FTA-ABS immunoglobulin (IgM)
• FTA-ABS 19S IgM
• IgM capture ELISA

## 6. Syphilis in Pregnancy

### *6.1 Maternal Serologies*

An STS should be performed at the beginning of prenatal care and at delivery. Intermediate testing at the beginning of the third trimester (28 weeks) should also be routine for high-risk populations. Seroreactive women must be evaluated promptly. This evaluation should include a history and physical examination, a quantitative nontreponemal test, and a confirmatory test.

Despite possible false-positive results in nontreponemal and treponemal tests, expectant mothers should be treated if 1) they have a reactive STS and 2) a prompt and thorough evaluation of the cause of the seroreactivity cannot be ensured. Special tests that include deoxyribonucleic acid (DNA) and Reiter absorptions for the fluorescent treponemal antibody (FTA) test eliminate most of the false-positive results. These tests can be performed by the Sexually Transmitted Diseases Laboratory Program, Center for Infectious Diseases, CDC, upon request from a reference laboratory. Delay in the presumptive treatment of a seroreactive pregnant woman, however, should never be allowed to exceed 4 weeks.

If a patient has a reactive nontreponemal test (e.g., VDRL), a nonreactive treponemal test (e.g., microhemagglutination assay for antibody to *T. pallidum* [MHA-TP]), and no clinical or epidemiologic evidence of syphilis, no treatment is necessary. Both the quantitative nontreponemal test and the confirmatory test should be repeated within 4 weeks. If clinical or serologic evidence of syphilis is found, or if the diagnosis of syphilis cannot be excluded with reasonable certainty, the patient should be treated as outlined below (section 6.2.3). In pregnancy, nontreponemal test titers tend to increase nonspecifically. This tendency causes difficulty in distinguishing between antibodies due to reinfection and antibodies remaining from an earlier treated infection.

Patients who have been adequately treated for syphilis in the past and who have documentation of their treatment need not be retreated unless clinical, serologic, or epidemiologic evidence of reinfection exists, e.g., darkfield-positive lesions, a sustained (for ≥2 weeks) fourfold titer rise in a quantitative nontreponemal test, or a history of recent sexual exposure to a person with early infectious syphilis.

## *6.2 Treatment in Pregnancy*

### *6.2.1 Data Limitations*

In the past 20 years, no major clinical trials have involved the currently recommended treatments for syphilis in pregnant patients. Thus, public health personnel cannot determine whether a decrease in therapeutic efficacy has occurred with these treatment regimens. However, individual failures of treatment (i.e., the occurrence of congenital syphilis in an infant whose mother was treated) have been reported. Although denominator data would be necessary for failure rates to be calculated, the reports nonetheless suggest the need to modify treatment strategies for pregnant women who have syphilis. For instance, the available data suggest that treatment with the currently recommended erythromycin regimen is associated with an unacceptably high failure rate.

The treatment efficacy with any regimen varies with the stage of maternal infection and with the stage of pregnancy. Available data indicate that the rate of treatment failure may be significantly higher among women with secondary syphilis and among women treated in the last trimester of pregnancy. The physiologic variables associated with pregnancy or placental transfer mechanisms may be quantitatively more important during the last trimester of pregnancy, and the organism load may be higher during the secondary stage of syphilis.

### *6.2.2 Treatment of Choice for Syphilis in Pregnancy*

REGARDLESS OF THE STAGE OF PREGNANCY, PATIENTS WHO ARE NOT ALLERGIC TO PENICILLIN SHOULD BE TREATED WITH PENICILLIN ACCORDING TO THE DOSAGE SCHEDULES APPROPRIATE FOR THE STAGE OF SYPHILIS AS RECOMMENDED FOR NONPREGNANT PATIENTS.

Suspected failures of penicillin treatment should be completely evaluated and reported.

### *6.2.3 Penicillin-Allergic Patients*

Penicillin may be given to pregnant women with syphilis even if they have a history of penicillin allergy provided 1) their skin-test reactions to the major and minor penicillin determinants are negative or 2) their skin tests are positive but they are then desensitized to penicillin. Patients can be desensitized and then given standard dosages of this antibiotic.

Penicillin desensitization can be accomplished by giving the patient gradually increasing oral* or intravenous penicillin doses over a period of 3-4 hours until full tolerance occurs. The intravenous desensitizing route has an advantage in that the penicillin can be stopped immediately if an allergic reaction develops; reactions, however, occur more frequently during intravenous desensitization. Desensitization should be done in consultation with an expert and only in facilities where emergency procedures are available, such as in a hospital.

*One oral desensitizing regimen given to pregnant patients used penicillin V. The starting dose was 100 units and was increased every 15 minutes. The final cumulative dose was 1,296,700 units given over a period of 3-4 hours. These patients were hospitalized and an intravenous line was established, but no premedications were used. A contingency plan, which was not needed, was to repeat the last dose or abandon the procedure if a serious reaction developed (N Engl J Med 1985;312:1229-32).

Tetracycline is not recommended for pregnant women because of potential adverse effects on the fetus. Erythromycin treatment of syphilis during pregnancy is generally discouraged. It should be considered only for patients who have documented evidence of penicillin allergy (skin test or anaphylaxis history) and who are not candidates for penicillin desensitization. Clinicians choosing erythromycin treatment have a weighty responsibility for close clinical follow-up of both the mother and fetus to assess the possibilities of treatment failure.

#### *6.2.4 Maternal Treatment Follow-up*

- Pregnant women who have been treated for early syphilis should have monthly quantitative nontreponemal serologic tests for the remainder of their pregnancy.
- Women who show a fourfold rise in titer should be retreated.
- Treated women who do not show a fourfold decrease in titer in a 3-month period should be retreated.
- After delivery, follow-up is the same as for nonpregnant patients.

#### *6.2.5 Needed Studies*

Well-designed studies on the treatment of pregnant women who have syphilis are clearly needed. The more urgent topics include:

- the transplacental pharmacokinetics of penicillin and other antibiotics;
- treatment efficacy and a continuing analysis of treatment-failure cases with currently recommended regimens;
- the efficacy of a treatment regimen consisting of benzathine penicillin G followed by amoxicillin/ampicillin and probenecid, or high-dose amoxicillin/ampicillin and probenecid for syphilis during pregnancy, especially for secondary syphilis encountered in the last trimester;
- probenecid as an adjunct to current penicillin treatment regimens to augment their efficacy, particularly for secondary syphilis in late pregnancy; and
- the role of infection with HIV in cases of prenatal syphilis treatment failure.

## 7. Syphilis in the Fetus and Neonate

### *7.1 Diagnostic Evaluation*

#### *7.1.1 Neonatal Serologic Tests for Syphilis*

Serum from the infant is preferred for both nontreponemal and confirmatory tests, since umbilical cord blood may produce false-positive results. After delivery and/or treatment, serial specimens are used to follow efficacy of treatment or degradation of transplacentally acquired maternal antibody.

When laboratory methods become generally available for fetal/neonatal specific immune globulin (IgM) treponemal determinations, serum will be the specimen of choice. Carefully controlled field trials will need to be conducted to provide guidance for their use in clinical practice.

#### *7.1.2 Microscopic Evaluation*

The placenta and the umbilical cord may serve as excellent sites for the collection of specimens that can be examined by darkfield microscopy, immunofluorescence, H & E stains,

or silver stains. Specimens from the placenta and umbilical cord should be microscopically examined for those infants born to mothers with reactive serologic results, when no histories are available, or when the placenta is hydropic. Additionally, all neonatal lesions should be examined for treponemes.

Treponemes seen in lesion material or in autopsy or biopsy sections by silver stain or darkfield, although considered definitive, may be confused in endemic areas with the *Borrelia* of Lyme disease. **Maternal nontreponemal serology may be used to differentiate Lyme disease from syphilis.** The VDRL is uniformly nonreactive in Lyme disease.

An effort should be made to diagnose congenital syphilis in a stillborn whenever clinical findings or a maternal history suggests the possibility of untreated syphilis. Direct and histologic microscopic examinations of placenta, organs, and umbilical cord, as well as radiographic examinations of long bones, are helpful in postmortem diagnosis. The MHA-TP test can be used on the blood of a stillborn; blood can be obtained by direct cardiac puncture.

#### *7.1.3 Radiography*

All infants delivered of women with a reactive STS who were not treated before pregnancy or before 20 weeks' gestation should be fully evaluated. The evaluation should include an examination of the long bones for osteochondritis, osteitis, and periostitis.

#### *7.1.4 Cerebrospinal Fluid Analysis*

Infants delivered of women with a reactive STS should have a cerebrospinal fluid (CSF) evaluation in any of the following circumstances:

- the infant shows any signs compatible with congenital syphilis

**OR**

- maternal therapy was inadequate, unknown, or it occurred late (≥ 20 weeks) in pregnancy

**OR**

- maternal therapy did not include penicillin

**OR**

- adequate follow-up cannot be ensured

Other living infants with a diagnosis of confirmed or compatible (see definitions in section 2) congenital syphilis should have a CSF examination before treatment to provide a baseline for follow-up examination. Although the importance of the CSF examination is debated, a quantitative VDRL CSF test can be meaningful if it is done in conjunction with tests for elevated total protein and lymphocyte count. The RPR card test **should not** be used for CSF evaluation.

Regardless of CSF results, however, all children with a diagnosis of confirmed or compatible congenital syphilis should be treated with a regimen effective for neurosyphilis.

### *7.2 Neonatal Treatment*

Although no recent comprehensive and comparative data on the treatment of neonates are available, several case reports of apparent treatment failure in infants treated with benzathine penicillin have been published. Available data clearly identify an obligation to evaluate neonates adequately to determine whether they have occult active infection. The most appropriate approach to active infection requires the use of a 10-day regimen of crystalline or procaine penicillin rather than benzathine penicillin.

## Recommended Regimens for Symptomatic or Asymptomatic Infants

Aqueous crystalline penicillin G 50,000 units/kg IM or IV daily in two divided doses for a minimum of 10 days

**OR**

Aqueous procaine penicillin G 50,000 units/kg IM daily for a minimum of 10 days.

For asymptomatic infants whose mothers were treated adequately with a penicillin regimen during pregnancy, treatment is not necessary if follow-up can be ensured.

For asymptomatic infants whose mothers were treated adequately with a penicillin regimen during pregnancy but whose follow-up **cannot** be ensured, many consultants recommend treatment with benzathine penicillin 50,000 units/kg IM in a single dose. Data on the efficacy of this regimen in congenital neurosyphilis are lacking; therefore, if neurosyphilis cannot be excluded, the 10-day regimens of aqueous crystalline penicillin or procaine penicillin are recommended. **Only** penicillin regimens are recommended for neonatal congenital syphilis.

### *7.3 Neonatal Follow-up*

In accordance with the guidelines of the American Academy of Pediatrics, follow-up for all infants should be incorporated into routine newborn care at 1, 2, 4, 6, and 12 months. Serologic tests should be performed until they become nonreactive. Patients with persistent, stable, low titers should be considered candidates for retreatment. Treated infants should be similarly followed, with a CSF examination at 6-month intervals until the examination becomes nonreactive. A reactive CSF VDRL at 6 months is an indication for retreatment.

## 8. Long-term Follow-up and Retreatment

Penicillin dosages for congenital syphilis after the neonatal period remain the same as those recommended for neonatal congenital syphilis. For larger children, the total amount of penicillin given should not exceed the dosage used in adult syphilis of more than 1 year's duration. After the neonatal period, the dosage of tetracycline for congenital syphilis in patients who are allergic to penicillin should be individualized, but these dosages need not exceed those used in adult syphilis of more than 1 year's duration. Tetracycline should not be given to children $<8$ years of age.

A thorough developmental evaluation should be done during the third year of life (age 2) on all children treated in infancy who were symptomatic at birth or had active congenital infection.

All patients with early syphilis or congenital syphilis should be encouraged to return for repeat quantitative nontreponemal tests at least 3, 6, and 12 months after treatment. In these patients, quantitative nontreponemal test titers will decline to nonreactive or low titer reactive within a year following successful treatment with penicillin. Serologic test results decline more slowly in patients treated for disease of longer duration. Patients with syphilis of more than 1 year's duration should also have a repeat serologic test 24 months after treatment. Careful follow-up serologic testing is particularly important for patients treated with antibiotics other than penicillin. Examination of CSF should be planned as part of the last follow-up visit after treatment with alternative antibiotics.

All patients with neurosyphilis must be carefully monitored with periodic serologic testing, clinical evaluation at 6-month intervals, and repeat CSF examinations for at least 3 years.

The possibility of reinfection should always be considered when patients with early syphilis are being retreated. A CSF examination should be performed before retreatment unless reinfection and a diagnosis of early syphilis can be established.

Retreatment should be considered when:

- clinical signs or symptoms of syphilis persist or recur

**OR**

- a sustained fourfold increase occurs in the titer of a nontreponemal test

**OR**

- an initially high-titer nontreponemal test fails to decrease fourfold within a year

Patients should be retreated with the regimens recommended for syphilis of more than 1 year's duration.

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