

PRIMARY SYPHILIS

<u>Symptoms/Signs</u>	<u>Diagnostic Criteria</u>	<u>Management</u>
<p>Painless ulcer (chancre) with an indurated border and relatively smooth base, at a site of sexual exposure, e.g., genitals, anus, mouth.</p> <p>Ulcer is usually singular, but there may be more than one.</p> <p>Localized firm, nontender, enlarged lymph nodes.</p>	<p>1. Identification of <u>T. pallidum</u> on darkfield microscopic or DFA (direct fluorescent anti-body) exam of serum from a lesion.</p> <p style="text-align: center;">OR</p> <p>2. Typical ulcer</p> <p style="text-align: center;">AND</p> <p>a. Newly reactive RPR or VDRL,</p> <p style="text-align: center;">OR</p> <p>b. Four-fold or more increase over the last known titer in a person with a history of previous syphilis.</p> <p>Typical ulcer(s) and exposure to a known case of early syphilis in the previous 10-90 days is suggestive of primary syphilis.</p>	<p>A. <u>Treatment</u></p> <p><u>If not HIV-infected:</u></p> <ol style="list-style-type: none"> 1. Benzathine penicillin G, 2.4 mu IM, once, <p style="text-align: center;">OR</p> <ol style="list-style-type: none"> 2. If allergic to penicillin and not pregnant: Doxycycline 100 mg PO, b.i.d. for 14 days. <p style="text-align: center;">OR</p> <ol style="list-style-type: none"> 3. If cannot take penicillin <u>or</u> doxycycline: Erythromycin 500 mg PO, q.i.d. for 14 days. <p>NOTE: If pregnant, this is an interim measure only. See page 22.</p> <p><u>If HIV-infected, and neurosyphilis is ruled out:</u> Benzathine Penicillin G, 2.4 mu IM.</p> <p>B. <u>Counseling/Referral</u></p> <ol style="list-style-type: none"> 1. Explain the possible occurrence of the Herxheimer reaction and how to handle it. 2. Encourage HIV antibody testing. 3. Refer to a Communicable Disease Specialist for an interview. <p>C. <u>Follow-up</u></p> <ol style="list-style-type: none"> 1. Monitor compliance if taking oral medication. 2. Unless HIV-infected or pregnant and more frequent follow up is indicated, examine and repeat RPR/VDRL at 6 and 12 months. 3. For signs/symptoms of possible treatment failure, follow the latest CDC STD Treatment Guidelines. <p>D. <u>Sex Partners</u></p> <p>Examine and treat, with one of the above regimens, all partners exposed within 3 months of onset, or since onset, of symptoms.</p>
17	4/98	

SECONDARY SYPHILIS

<u>Symptoms/Signs</u>	<u>Diagnostic Criteria</u>	<u>Management</u>
<p>One or more may be present:</p> <p>Bilaterally symmetrical macular or papular, non-pruritic rash on body/extremities. May only be on palms and soles.</p> <p>Condyloma lata (moist papules) usually in the anogenital region or mouth.</p> <p>Patchy hair loss on scalp or eyebrows and eyelashes.</p> <p>Generalized enlarged lymph nodes.</p> <p>Mucous patches in mouth or on cervix.</p> <p>Fever and malaise.</p> <p>Splenomegaly.</p> <p>Iritis.</p>	<ol style="list-style-type: none">1. Identification of <u>T. pallidum</u> on darkfield microscopic or DFA (direct fluorescent anti-body) exam of serum from a lesion. OR2. Typical signs AND<ol style="list-style-type: none">a. Newly reactive RPR or VDRL, titer $\geq 1:8$ ORb. Four-fold or more increase over the last known titer in a person with a history of previous syphilis. <p>Typical lesions and exposure to a known case of early syphilis in the previous six months is suggestive of secondary syphilis.</p>	<ol style="list-style-type: none">A. <u>Treatment</u> <u>If not HIV-infected:</u><ol style="list-style-type: none">1. Benzathine penicillin G, 2.4 mu IM, once, OR2. If allergic to penicillin and not pregnant: Doxycycline 100 mg PO, b.i.d. for 14 days. OR3. If cannot take penicillin OR doxycycline: Erythromycin 500 mg PO, q.i.d. for 14 days. NOTE: If pregnant, this is an interim measure only. See page 22. <u>If HIV-infected, and neurosyphilis is ruled out:</u> Benzathine Penicillin G, 2.4 mu IM, once.B. <u>Counseling/Referral</u><ol style="list-style-type: none">1. Explain the possible occurrence of the Herxheimer reaction and how to handle it.2. Encourage HIV antibody testing.3. Refer to a Communicable Disease Specialist for an interview.C. <u>Follow-up</u><ol style="list-style-type: none">1. Monitor compliance if taking oral medication.2. Unless HIV-infected or pregnant and monthly followup is indicated, examine and repeat RPR/VDRL at 3 and 6 months.3. For signs/symptoms of possible treatment failure, follow according to the latest CDC STD Treatment Guidelines.D. <u>Sex Partners</u><ol style="list-style-type: none">1. Routine <u>examination</u> of all exposed within 6 months of onset, or since onset, of symptoms.2. <u>Treatment</u> (as above) of all exposed within the preceding 3 months, and those exposed more than 3 months ago if serologic test results are not immediately available and followup is uncertain.

EARLY LATENT SYPHILIS

<u>Symptoms/Signs</u>	<u>Diagnostic Criteria</u>	<u>Management</u>
<p>NONE.</p> <p>May have a history of prior genital lesion, rash, or other symptom of primary or secondary syphilis.</p>	<p>No clinical symptoms or signs,</p> <p style="text-align: center;">AND</p> <p>Reactive RPR/VDRL,</p> <p style="text-align: center;">AND</p> <p>Reactive EIA/FTA-ABS/MHA-TP</p> <p style="text-align: center;">AND</p> <p>Has had, within the past year:</p> <p>a. A nonreactive serologic test,</p> <p style="text-align: center;">OR</p> <p>b. Symptoms highly suggestive of primary or secondary syphilis,</p> <p style="text-align: center;">OR</p> <p>c. A four-fold increase in titer on serial RPR or VDRL tests.</p> <p>A reactive RPR or VDRL and sexual exposure to a known case of early</p>	<p>A. <u>Treatment</u></p> <p><u>If not HIV-infected:</u></p> <ol style="list-style-type: none"> 1. Benzathine penicillin G, 2.4 mu IM, once, <p style="text-align: center;">OR</p> <ol style="list-style-type: none"> 2. If allergic to penicillin and not pregnant: Doxycycline 100 mg PO, b.i.d. for 14 days. If pregnant, as an <u>interim measure only</u>: Erythromycin 500 mg PO, q.i.d. for up to 14 days. (See page 22.) <p><u>If HIV-infected, and neurosyphilis is ruled out:</u> Benzathine Penicillin G, 2.4 mu IM, once.</p> <p>B. <u>Counseling/Referral</u></p> <ol style="list-style-type: none"> 1. Explain the possible occurrence of the Herxheimer reaction and how to handle it. 2. Encourage HIV antibody testing. 3. Refer to a Communicable Disease Specialist. <p>C. <u>Follow-up</u></p> <ol style="list-style-type: none"> 1. Monitor compliance if taking oral medication. 2. Unless HIV-infected or pregnant and monthly followup is indicated, repeat RPR/VDRL at least at 6 and 12 months. 3. For signs/symptoms of possible treatment failure, follow according to the latest CDC STD Treatment Guidelines. <p>D. <u>Sex Partners</u></p> <ol style="list-style-type: none"> 1. Routine <u>examination</u> of all exposed within

<p>19</p> <p>4/98</p>	<p>syphilis within the past year is <u>suggestive</u> of early latent syphilis.</p>	<p>the previous year.</p> <p>2. <u>Treatment</u> (as above) of all exposed within the preceding 3 months, and those exposed more than 3 months ago if serologic test results are not immediately available and followup is uncertain.</p>
-----------------------	---	---

<p>LATE LATENT SYPHILIS</p>		
<p><u>Symptoms/Signs</u></p>	<p><u>Diagnostic Criteria</u></p>	<p><u>Management</u></p>
<p>None.</p>	<p>No clinical symptoms or signs,</p> <p style="text-align: center;">AND</p> <p>Reactive RPR/VDRL,</p> <p style="text-align: center;">AND</p> <p>Reactive EIA/FTA-ABS/MHA-TP</p> <p style="text-align: center;">AND</p> <p>Does not meet the other criteria for <u>early latent syphilis</u>.</p> <p>NOTE: A cerebrospinal fluid (CSF) exam to rule out neurosyphilis should be done in the following instances: --Neurologic signs or symptoms;</p>	<p>A. <u>Treatment</u></p> <p><u>If not HIV-infected:</u></p> <p>1. Benzathine penicillin G, 2.4 mu IM, weekly for 3 doses (7.2 mu total),</p> <p style="text-align: center;">OR</p> <p>2. If allergic to penicillin and not pregnant: Doxycycline 100 mg PO, b.i.d. for 28 days.</p> <p>3. If allergic to penicillin and pregnant: See page 22.</p> <p><u>If HIV-infected, and neurosyphilis is ruled out:</u> Benzathine Penicillin G, 2.4 mu IM, weekly for 3 doses (total of 7.2 mu).</p> <p>B. <u>Follow-up</u></p> <p>1. Monitor compliance if taking oral medication. 2. Unless HIV-infected or pregnant and monthly followup is indicated, repeat RPR/VDRL at 6, 12 and 24 months to establish stable titer level.</p> <p>C. <u>Sex Partners</u></p>

<p>20</p> <p>4/98</p>	<p>--Apparent treatment failure; --HIV infection; --Non-penicillin therapy planned; --RPR <u>≥</u>1:32.</p>	<ol style="list-style-type: none">1. Examine steady (e.g., marital) sex partners.2. Children of infected women may also need an examination, since the fetus may be infected if the mother had untreated syphilis, for even a few years' duration, when pregnant.
-----------------------	---	--

OTHER SYPHILIS

A. Neurosyphilis

Neurosyphilis may occur as a late manifestation, as a complication in early syphilis or in congenital syphilis. When symptomatic, it is manifested by a variety of neurologic symptoms/signs, depending on the actual site of involvement. Diagnosis is made from a Venereal Disease Research Laboratory test (VDRL) and cellular examination of cerebrospinal fluid (CSF). Suggested drug regimens are described in the CDC Guidelines.

B. Response to Treatment and Need for Retreatment

To assure that treatment was adequate, serologic titer follow-up, as noted on the previous pages, is mandatory. If the titer fails to decline fourfold (two dilutions) by 6 months after treatment for primary or secondary syphilis, treatment failure should be considered. In most cases of adequately treated primary syphilis the titer will be nonreactive by the end of one year and for secondary syphilis by the end of two years. Latent syphilis titers will decrease more slowly and may remain reactive in low titers even with adequate treatment. The possibility of reinfection should always be considered when the titer does not decrease as expected. A CSF examination is recommended unless reinfection and diagnosis of early syphilis can be established.

Retreatment is needed when:

1. Clinical signs or symptoms persist or recur.
2. There is a fourfold (two tube) increase in titer of a nontreponemal test (RPR/VDRL), without evidence of reinfection.
3. An initially high-titer nontreponemal test fails to decrease at least four-fold within a year.

Re-treat with a regimen effective against late latent syphilis unless CSF exam shows neurosyphilis.

C. Diagnosing and Treating Syphilis in HIV-Infected Patients

Since clinical manifestations, serologic responses, efficacy of treatment and occurrences of complications of syphilis may be altered in patients coinfecting with HIV, consultation should be obtained to evaluate unusual serologic test results in patients suspected of having syphilis or in those being followed for response to treatment. Careful medical follow up of co-infected patients must occur.

SYPHILIS IN PREGNANCY

A. Maternal Screening Serologies

The August 1990 Revised Department of Human Resources Rules, Chapter 290-5-21, "Serologic Test for Syphilis for Pregnant Women" mandates that such tests be performed:

1. At the initial prenatal care visit;
2. During the third trimester; and
3. At delivery, if the delivering physician cannot confirm that the previous testing was done.

It further states that reports of reactive serologies must be given to DHR within 24 hours of their receipt.

B. Evaluation of Seroreactive Women

Seroreactive women must be medically evaluated promptly and thoroughly. The evaluation should include a history and physical examination, a quantitative nontreponemal test and a confirmatory treponemal test unless there is documentation of a previous diagnosis of syphilis.

If a prompt and thorough evaluation of the cause of seroreactivity cannot be ensured, such as delay in obtaining confirmatory test results, the woman should be treated at the first evaluation visit. In general, delay in treatment of a seroreactive pregnant woman beyond two weeks should not be allowed.

If the patient has a reactive RPR or VDRL, a nonreactive confirmatory test, such as fluorescent treponemal antibody absorption (FTA-ABS), microhemagglutination assay for antibodies to *Treponema pallidum* (MHA-TP), or enzyme immunoassay (EIA), and no clinical or epidemiologic evidence of syphilis, no treatment is necessary. However, both the quantitative RPR/VDRL and the confirmatory test should be repeated within four weeks. If clinical or serologic evidence of syphilis is found, or if diagnosis of syphilis cannot be excluded with reasonable certainty, the patient should be treated.

Patients who have documented adequate treatment for syphilis in the past need not be retreated unless clinical, serologic or epidemiologic evidence of reinfection exists.

C. Treatment of Syphilis in Pregnancy

Pregnant women should be treated with the penicillin regimen appropriate for the diagnosed stage of syphilis. Tetracycline and doxycycline are contraindicated during pregnancy and erythromycin should not be used because of the high risk of failure to cure infection in the fetus.

Because of its failure to cure some adult infection, and most fetal infection, erythromycin treatment should not be considered except as an interim measure, for women with a history of allergy to penicillin, until skin testing can be performed, desensitization done if necessary and penicillin treatment is given.

If necessary, make arrangements to have the skin/testing desensitization done at a Regional Perinatal Center according to the following guidelines established in December 1995:

Standards for Referral of Penicillin-allergic Pregnant Women with Syphilis for Appropriate Treatment

- A. Referring Agency/Health Department
 - 1. Will arrange for services at the local level, if available.
 - 2. Will make the appointment for the client.
 - 3. Will have the client sign a Release of Information Form and give the referral agency as much information about the client's current medical history and previous reaction to penicillin as possible, at the time of making the appointment . A copy of the information will be given to the client and FAXed to the contact person at the Regional Center.
 - 4. Will clarify, with the agency and client, the expected method of payment for services with the referral agency when the appointment is made (e.g., Medicaid, referral agency paying under high risk pregnancy program, private insurance).
 - 5. Will assist the client to obtain transportation to and from the appointment, as needed.

- B. Participating Perinatal Center (see next page)
 - 1. Will assure that an alternate contact person is available to take a referral when the listed contact person is not available.
 - 2. Will schedule an appointment for the client as soon as possible, considering the ability of the client to receive transportation to the

- facility.
3. Will clarify the expected method of payment for services with the client/referral agency when the appointment is made.
 4. Will retain the prerogative to decide, based on the history of the client's previous reaction to penicillin and any other pertinent history, whether skin testing should be done prior to desensitization and subsequent treatment with penicillin.
 5. Will use the CDC 1998 STD Treatment Guidelines, or subsequent revisions, as a guide to treatment of penicillin-allergic clients.

REGIONAL PERINATAL CENTERS

Grady Memorial Hospital
 Atlanta
 Dr. Luella Klein, Director
 Contact: Diane Kelly
 (404)616-4936

Medical College of Georgia
 Augusta
 Dr. Bruce Work, Director
 Contact: Kathy Leopard
 (706)721-4959, Option 2, Option 3

Memorial Medical Center
 Savannah
 Dr. Gary Oakes, Director
 Contact: Jane Miller
 (912)350-5993

Medical Center of Central Georgia
 Macon
 Dr. Mark Boddy, Director
 Contact: Debra Kimsey
 (912) 738-0404

The Medical Center
 Columbus
 Dr. Robert Stauffer, Director
 Contact: Dr. Stauffer
 (706)572-1112

Phoebe Putney Hospital
 Albany
 Dr. Michael Edwards, Director
 Contact: Dr. Edwards
 (912)889-2557

If unable to make an appointment, contact Dianne Norris, RNC, at the Women's Health Unit, Atlanta, (404)657-3143.

In the event a mother receives only erythromycin treatment, she must have careful follow-up to assure response to treatment. It must also be assured that the neonate receives penicillin treatment at birth, even if asymptomatic.

Women who are treated in the second half of pregnancy are at risk for premature labor and/or fetal distress if the treatment precipitates a Jarisch-Herxheimer reaction. They should be advised to seek medical attention

if they notice any change in fetal movements or begin to have any contractions.

Monthly serologic follow-up is mandatory, so that retreatment can be given if needed. The antibody response should be appropriate for the stage of disease.

D. Transmission of Syphilis to the Fetus

The chances of a fetus becoming infected depend on the duration of the disease in the mother and the stage of pregnancy during which she is treated.

A mother with untreated primary or secondary syphilis represents a greater hazard to the fetus than if she had latent or late syphilis. The possibility of fetal infection is never entirely eliminated.

Spirochetes from an infected mother are transmitted via the maternal circulation, through the placenta, to the fetal circulation. The fetus receives a transfusion of spirochetes, with the result that the symptoms of early congenital syphilis resemble those of acquired secondary syphilis. If the fetus is infected during the first trimester, miscarriage may occur. Stillbirth is another possible outcome. The later the fetus becomes infected, the better its chances are for survival.

E. The Infected Neonate

The prognosis is poor for infants with symptoms at birth. However, most infected newborns appear healthy at birth, with signs/symptoms beginning to appear in a week or more. Those infected late in the third trimester may have a negative blood at birth and may not show signs/symptoms until at least the eighth week after birth.

F. Evaluation, Diagnosis and Treatment of the Neonate

Guidelines for infant evaluation, diagnosis and treatment may be found in the latest CDC [STD Treatment Guidelines](#), or other guidelines from CDC.

Syphilis Laboratory Tests

A. Type of test: Darkfield microscopic identification of *T. pallidum*.

Specimen: Abrade lesion to remove exudate, epithelium and crusts. Collect serum on slide. Use coverslip. Examine immediately.

Interpretation of results:

Motile spirochetes observed means a diagnosis of primary or secondary syphilis, depending on the type of lesion(s).

B. Type of test: STAT RPR card test, qualitative (undiluted serum)

Specimen: Serum from 5-10 ml. whole blood. Perform test per kit instructions, including use of control cards to test antigen daily.

Interpretation of results:

Positive test may support diagnosis of syphilis when other criteria are met for stage suspected.

(Send remainder of specimen to the Public Health Microbial Immunology Lab in Decatur, DHR Regional Lab or local lab for quantitative RPR or VDRL .)

C. Type of test: Quantitative RPR (or VDRL) nontreponemal serologic test (serially diluted to an endpoint)

Specimen: 5-10 ml whole blood (or serum, as above) in serologic outfit, with Serologic Test for Syphilis and Rubella form.

Send to: State Microbial Immunology Lab, DHR Regional Lab, or local lab.

Interpretation of results:

1. More than a reactive test is needed to justify a diagnosis of syphilis.

2. A negative test does not rule out syphilis.

a. The RPR or VDRL may not be reactive in primary syphilis until at

least one week after appearance of the chancre.

- b. In 1-2% of cases of secondary syphilis an initially negative test may be due to the "prozone phenomenon". In these cases, an initially nonreactive but "rough" pattern will become reactive upon further dilution. The lab should be asked to dilute an initially negative serum and continue titration in all cases where suspicious lesions are present. (If blood tube and upper right corner of lab form are marked with a red dot the state labs will do this.)
 - c. The nontreponemal tests may also be negative in congenital or late symptomatic syphilis.
3. A reactive nontreponemal test (titer usually 1:8 or less) may be a false positive. Though most remain unexplained, some causes are:

Acute False Positives (up to 6 months duration)

Various viral and bacterial infections
Immunizations
Drug use
Pregnancy

Chronic False Positives

Various autoimmune diseases, e.g., rheumatoid arthritis, systemic lupus erythematosus
Other conditions with abnormal globulins
Cancer chemotherapy
Chronic infections
Narcotic addiction
Genetic factors
Aging (over age 60)

A negative treponemal test (FTA-ABS/MHA-TP/EIA) will rule out a diagnosis of syphilis in a person with a false positive nontreponemal test.

4. Depending at the stage when treatment is given, the RPR or VDRL may remain positive in low titer, or even in relatively high pre-treatment titer, for life after adequate treatment. Follow-up tests, per protocol, are important to establish the stable titer level to facilitate evaluation of future test results. The patient should be given a written record of the results and encouraged to take it to future health care visits.

5. A sustained 4-fold (two dilution) rise in titer, such as 1:2 to 1:8, performed by the same lab indicates probable need for retreatment. The only exception is adequately treated congenital syphilis where the titer may fluctuate without particular significance.
 6. On occasion, such things as drug use, and possibly pregnancy, may produce unusual titer patterns.
- D. Type of test: Enzyme immunoassay (EIA) serology, for antitreponemal IgG antibody. Confirmatory test for syphilis.

Specimen: Same as for RPR.

This test will automatically be performed on all reactive RPRs sent to the Public Health Microbial Immunology Lab in Decatur, and DHR Regional Labs, unless there is a notation on the lab form that it is not needed.

To avoid unnecessary testing, the "No confirmatory test needed" box on the lab form should be marked when the patient has:

1. A history of a previous reactive treponemal test, such as an FTA-ABS, MHA-TP or EIA; or
2. A history of a previous diagnosis of syphilis; or
3. A darkfield positive lesion of primary or secondary syphilis; or
4. A newly reactive RPR and symptoms of primary or secondary syphilis.

NOTE: There are occasional instances when confirmatory test results may be needed on patients with negative RPR results (e.g., when a very early ulcer typical of primary syphilis is present or for newborn reactor follow-up). To request that the state Public Health or Regional lab perform an EIA when RPR results are negative, highlight, in green, the right edge of the Syphilis and Rubella Form (#3432).

Interpretation of results:

Reactive means confirmation for a diagnosis of syphilis.

Reactive, equivocal means that the test could not be called either reactive or nonreactive. The specimen was tested two more times and repeat test results were still equivocal. In these cases, the lab will also do an FTA-

ABS (see next page) on the specimen before reporting the results.

Nonreactive means no confirmation for a diagnosis of syphilis.

E. Type of test: FTA-ABS for treponemal antibody.

Specimen: Same as for RPR and EIA.

This test will only be done on specimens that have repeatedly equivocal EIA results or have an RPR \geq 1:16 and the EIA is negative.

Interpretation of results:

Reactive means confirmation for a diagnosis of syphilis.

Minimal reactive means that the test repeatedly showed minimally reactive results. If there are still concerns about a possible diagnosis of syphilis in the patient, another specimen may be submitted.

Nonreactive means no confirmation for a diagnosis of syphilis.

