SYPHILIS

I. DEFINITION:

A. Syphilis is a systemic, sexually transmitted disease (STD) caused by the *Treponema pallidum* bacterium.

B. It can cause long-term complications if not treated correctly. Symptoms in adults are divided into stages. These stages are described below in the Clinical Features. Syphilis has been called 'the great imitator' because it has so many possible symptoms, many of which look like symptoms from other diseases. The painless syphilis chancre that clients get after they are first infected can be confused for an ingrown hair, zipper cut, or other seemingly harmless bump. Many times the client does not know they had a sore. The non-itchy body rash that develops during the second stage of syphilis can show up on the palms of the client's hands and soles of their feet, all over the body, or in just a few places. The rash is usually bilateral, meaning it appears equally on both sides of the body.

C. The three means of syphilis transmission are:

1. Person to person via vaginal, anal, or oral sex through direct contact with a syphilis chancre.
2. Person to person during foreplay, even when there is no penetrative sex (much less common).
3. Pregnant mother with syphilis to fetus - very serious complications may occur (fetal demise, long bone deformities, "saddle nose").

II. CLINICAL FEATURES:

If left untreated, the disease progresses through several stages during which the infected person may or may not be symptomatic. The DIS and 'Syphilis Diagnosis and Treatment Algorithm' (Appendix 1) can assist with staging.

A. Primary Syphilis

1. One or more chancres (usually firm, round, small, and painless) appear at the site of infection (most often the genital area) 10 to 90 days after infection.
2. The chancres heal on their own in 3-6 weeks, even without treatment.
3. Client is highly infectious in the primary stage.

B. Secondary Syphilis

1. Rashes occur as the chancre(s) fades or a few weeks after the chancre heals.
2. Rashes typically appear on the palms of the hands, the soles of the feet, or on the face, but also may appear on other areas of the body. The skin lesions are bilaterally symmetrical.
3. Sometimes wart-like “growths” may appear on the genital area.

4. Rashes and syphilitic warts tend to clear up on their own within 2-6 weeks, but may take as long as 12 weeks.

5. May have lymphadenopathy, oral and/or genital mucous patches, hepatitis, optic neuritis, arthritis and peripheral neuropathy.

6. Client may be highly infectious in the secondary stage.

C. Early Non-primary Non-secondary Syphilis

1. Infection was acquired within the previous 12 months, but there are no signs or symptoms of primary or secondary syphilis.

2. Client is potentially infectious.

D. Syphilis of Unknown Duration

1. There is insufficient evidence to conclude if infection was acquired during the previous 12 months.

2. Client is potentially infectious

E. Late Syphilis

1. Infection was acquired >12 months previously.

2. Client is not infectious

F. Late Syphilis with Clinical Manifestations

Late clinical manifestations usually develop after a period of 15-30 years of untreated infection. Therefore, if the patient has late clinical manifestations of syphilis, the case should be reported with the appropriate stage of infection (for the vast majority of cases, unknown duration or late syphilis) and late clinical manifestations should be noted in the case report data.

1. Evidenced by inflammatory lesions of the cardiovascular systems (e.g.) aortitis, coronary vessel disease, skin (gummatous lesions), gone (e.g. osteitis), or other tissue.

2. Rarely, other structures (e.g., the upper and lower respiratory tracts, mouth, eye, abdominal organs, reproductive organs, lymph nodes, and skeletal muscle) may be involved. In addition, certain neurologic manifestations (e.g., general paresis and tabes dorsalis) are also late clinical manifestations of syphilis.

G. Neurologic Manifestations

Neurologic manifestations (previously known as neurosyphilis) can occur at any stage of syphilis. If the patient has neurologic manifestations of syphilis, the case should be reported with the appropriate stage of infection (as if neurologic manifestation were not present) and neurologic manifestations should be noted in the case report data.

1. Infection of the central nervous system with T. pallidum as evidenced by manifestations including syphilitic meningitis, meningovascular syphilis, general paresis, including dementia, and tabes dorsalis.

Syphilis - 2
H. Ocular Manifestations

Ocular manifestations (previously known as ocular syphilis) can occur at any stage of syphilis. If the patient has ocular manifestations of syphilis, the case should be reported with the appropriate stage of infection (as if ocular manifestations were not present) and ocular manifestations should be noted in the case report data.

1. Infection of any eye structure with *T. pallidum* as evidenced by manifestations including posterior uveitis, panuveitis, anterior uveitis, optic neuropathy, and retinal vasculitis. Ocular syphilis may lead to decreased visual acuity including permanent blindness.

I. Otic Manifestations

Otic manifestations can occur at any stage of syphilis. If the patient has otic manifestations of syphilis, the case should be reported with the appropriate stage of infection (as if otic manifestations were not present) and otic manifestations should be noted in the case report data.

1. Infection of the cochleovestibular system with *T. pallidum*, as evidenced by manifestations including sensorineural hearing loss, tinnitus, and vertigo.

III. MANAGEMENT PLAN:

A. Laboratory Studies – collect specimens for appropriate testing:

1. **Specimen for Syphilis:**

   Collect by venipuncture a sufficient amount of blood 2 mL into a Serum Separator Tube (SST) to allow for initial test and any reflex testing needed. (Minimal acceptable volume for syphilis testing is 1mL blood; however, this volume is only sufficient for initial screen test and does not allow for reflex testing if the specimen is screen-reactive).

   - *T. pallidum* induces the production of at least two types of antibodies in human infection: anti-treponemal antibodies that are produced against *T. pallidum* antigens, and anti-non-treponemal antibodies (reagin) produced as the result of reaction to cellular breakdown due to infection. Diagnosis of syphilis relies of the use of two types of serologic tests: one that detects non-treponemal antibodies, such as the Rapid Plasma Reagin Test (RPR) and one that detects treponemal antibodies. The use of only one type of serologic test is generally insufficient for diagnosis because each test has limitations. Syphilis testing performed by the OSDH Public Health Laboratory (PHL) uses the reverse sequence algorithm. This involves using an initial treponemal screening assay, the Lumipulse G TP-N chemiluminescent immunoassay, to detect antibodies (IgG and IgM) to *T. pallidum*. The use of a treponemal screen ensures greater sensitivity in detection of early infections in high risk individuals and individuals who appear with primary symptoms of syphilis. The standard algorithm, which uses the RPR as the screen would likely miss these early primary infections. All screen-reactive specimens are reflexed to an RPR test for the detection of reagin antibodies and endpoint titer determination. RPR-negative specimens are reflexed to a *T. pallidum* Particle Agglutination (TP-PA) treponemal test to verify the initial screen-reactive result.

   The reverse algorithm is also well suited for following treatment of syphilis patients; the treponemal screen test will remain positive on follow-up testing and these patients will be automatically reflexed to a quantitative RPR test.

2. **Specimen for C. trachomatis and N. gonorrhoeae:**
a) **Females:** Vaginal Swab is the preferred specimen collection method for *C. trachomatis* and *N. gonorrhoeae* testing. Collect vaginal swab if product is available refer to vaginal swab specimen collection procedure for instructions. If vaginal swab testing is not available, collect urine specimen. Ensure client waits 1 hour after last voiding before providing urine specimen.

b) **Males:** Collect urine for *C. trachomatis* and *N. gonorrhoeae*. Ensure client waits 1 hour after last voiding before providing urine specimen.

3. **HIV testing is recommended.**

4. **Clients who demonstrate any of the following symptoms or criteria should be referred to the nearest hospital emergency department for a prompt cerebral spinal fluid (CSF) examination:**
   a. neurologic or ophthalmic signs or symptoms; (e.g., abnormal gait, numbness or weakness in toes, feet, or legs, headache, stiff neck, seizure, visual changes/blindness, hearing loss, mental confusion, poor concentration, confusion, irritability, incontinence)
   b. evidence of late syphilis with clinical manifestations (e.g., aortitis, gumma);  
   c. serologic treatment failure.

B. **Assessing for Neurologic manifestations**

All clients who present with symptoms of primary and/or secondary syphilis, and all clients with confirmed positive serological test for syphilis are to be screened for neurologic, ocular, and otic manifestations using the Ocular Neurosyphilis Assessment Tool (ODH 1291).

C. **Treatment of Clients Infected with Syphilis and Contact(s)**

1. **Pregnancy Testing**

   If it is determined that the client has syphilis of any stage (using the Syphilis Diagnosis and Treatment algorithm, Appendix 1), urine testing for pregnancy is recommended for all women of childbearing age. Childbearing age includes the period of a woman’s life between puberty and menopause.

2. **Primary, Secondary, and Early Non-Primary Non-Secondary Syphilis**

   **Note:** The public health nurse must ensure that another employee, preferable CPR certified is present that can assist if an emergency occurs before any injections can be administered.

   **Option #1**  
   Benzathine penicillin G 2.4 million units IM in a single dose.  
   For non-pregnant, non-penicillin allergic adults (safe in pregnancy).  
   
   **Pregnant females should receive 1 dose of Benzathine penicillin G 2.4 million units IM followed by a second dose one week after the first dose.**

   **Option #2**  
   Doxycycline 100 mg orally 2 times a day for 14 days  
   Only if client is allergic to penicillin. This option cannot be used in
Option #3 Refer PREGNANT Penicillin-allergic clients to private physician for treatment.

3. Unknown Duration or Late Syphilis with no clinical symptoms of late syphilis or neurologic, ocular, or otic manifestations
   
   Option #1 Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 7-9 day intervals. For non-penicillin allergic adults (safe in pregnancy).
   
   See Note under 2, Option #1
   
   If treatment is interrupted (greater than 14 days between doses), the whole 3 week course of treatment must be restarted.

   Option #2 Doxycycline 100 mg orally 2 times a day for 28 days for client who is allergic to penicillin. This option cannot be used in pregnancy.

   Option #3 Refer PREGNANT Penicillin-allergic clients to private physician for treatment.

4. Syphilis with Neurologic Manifestation, Ocular Manifestation, or Otic Manifestation
   
   a. Treatment regimen of syphilis among clients with symptoms of or suspected neurosyphilis neurologic, ocular, or otic manifestations should be administered according to the stage of the syphilis diagnosis DIS will assist with staging, recommended treatment, and referral process.

   b. Client should then be referred to the nearest hospital emergency department for careful evaluation and treatment of neurosyphilis.

5. Treatment of Syphilis among clients with HIV
   
   Treatment regimen of syphilis among clients with HIV diagnosis should be administered according to the stage of the syphilis diagnosis, the same as those without HIV diagnosis.
   
   Clients with HIV infection and syphilis should be carefully assessed for symptoms of neurologic manifestations. If symptoms of neurologic manifestations are reported upon assessment, also contact DIS and coordinate for client to be referred to nearest emergency facility for further evaluation.

   Alternative non-penicillin treatment regimens in persons with HIV should only be used in conjunction with close serologic and clinical follow-up. Clients with HIV diagnosis and allergic to penicillin whose compliance with therapy or follow-up cannot be ensured should be referred to PCP for desensitized and treated with penicillin.

6. Treatment of syphilis in pregnancy (all stages)
   
   Treatment during pregnancy should be the penicillin regimen appropriate for the woman’s stage of syphilis. Some experts recommend additional therapy. (A second dose of benzathine penicillin 2.4 million units IM may be administered one week after the initial dose for women who have primary, secondary, or early latent syphilis). When possible, the clients PCP or OB provider should be made aware of treatment and/or refusal of needed treatment. When syphilis is diagnosed during the second or third trimester of pregnancy, management should include referring client for sonographic fetal evaluation for congenital syphilis.
**Doxycycline cannot be used to treat syphilis in pregnancy.**

There are no proven alternative nonpenicillin regimens for syphilis treatment during pregnancy. A pregnant female with a history of penicillin allergy must be referred to a private physician for treatment with penicillin, after desensitization, if necessary.

Females treated for syphilis during the second half of pregnancy are at risk for premature labor or fetal distress, or both, if their treatment precipitates the Jarisch-Herxheimer reaction. Advise these women to contact their physician if they notice any change in fetal movements or have contractions. Stillbirth is a rare complication of treatment, but concern for this complication should not delay necessary treatment.

### C. Client Education

1. **Client to remain in the county health department in a common area for at least 20 minutes to observe for reaction.**
2. Impress on client the importance of returning for injections when scheduled if a multiple dose treatment is needed. Explain if treatment is interrupted (greater than 14 days between doses), the whole 3 week course of treatment must be restarted. To eliminate the treponem, the penicillin blood level must be high and maintained for three weeks. If the blood level drops during the 3 weeks, the client may not be cured.
3. **Jarisch-Herxheimer reaction**
   a. Definition: An acute febrile reaction accompanied by headache, myalgia, and other symptoms that may occur within the first 24 hours after any therapy for syphilis.
   b. During pregnancy may induce early labor or cause fetal distress among pregnant women. This concern should not prevent or delay therapy.
   c. Common among clients with early syphilis.
   d. Antipyretics may be recommended.
4. If given doxycycline
   a. Provide with written instructions.
   b. Discuss possible side effects.
   c. Emphasize importance of completing regimen.
5. **Client should return for repeat RPRs at the recommended intervals according to the stage of the diagnosis (See Follow up section G) or as otherwise recommended by DIS.**
6. **For women:** Emphasize the risks of syphilis during pregnancy. If pregnant, return for follow-up serologic tests in the 3rd trimester.
7. **If client is positive for syphilis, encourage client to discuss sexual history with DIS.**
8. **Client and partner(s) should avoid sex until seven (7) days after their completion of treatment and the resolution of all symptoms. (Note: Symptoms could persist for greater than seven days.)**
9. **Return for evaluation should symptoms persist or recur.**
10. Prevention measures (e.g., condoms) to help prevent future infections.

11. Syphilis has been associated with an increased risk of acquiring HIV.

D. Disease Intervention Specialist (DIS)

1. DIS should be notified immediately upon client presenting with signs/symptoms of primary and/or secondary syphilis, and/or positive test.

2. DIS will assist in staging and recommend appropriate treatment for the client providing the treating nurse with a DIS Referral Form identifying their determination and recommendation. If the DIS is unable to provide the form when the client presents to the clinic, HIV/STD Service will fax the form to the county health department on behalf of the DIS.

3. DIS will determine if client is eligible for partner services (See Partner Services Eligibility, Appendix II). If client is not eligible for partner services, DIS will assist in arranging treatment for the client with the confirmed diagnosis.

4. DIS will interview and conduct partner notification if the client is eligible for partner services. DIS will refer eligible partners for examination and treatment.

5. Clients who are not eligible for partner services will refer his or her own sex partners in for examination.

6. DIS will refer clients who have tested positive at another agency for treatment and complete a DIS Referral form to provide testing information if needed.

7. Obtain serological and treatment history when applicable.

8. Assist in notifying client to return for follow-up serology if needed.

E. Management of Sex Partner(s)

Sexual transmission of *T. pallidum* occurs only when mucocutaneous syphilitic lesions are present; such manifestations are uncommon after the first year of infection. However, persons sexually exposed to a client with syphilis in any stage should be evaluated clinically and serologically according to the following:

1. Time periods for identifying at-risk sex partner(s)
   a. Source client has primary syphilis: Any sexual partner(s) within the last 4½ months;
   b. Source client has secondary syphilis: Any sexual partner(s) within the last 8½ months;
   c. Source client has early non-primary non-secondary syphilis: Any sexual partner(s) within the last year.

2. When to treat sex partner(s) presumptively (epi treat)
   a. Source client has primary, secondary, or early non-primary non-secondary (duration < 1 year) syphilis or unknown duration as reported by either the client or by the DIS.
Sex partner(s) exposed within the preceding 90 days may be infected even if blood tests are negative and therefore should be treated presumptively (epi treat).

b. Source client has late syphilis:
   1) Serologic test results are not available immediately;
   2) The opportunity for follow-up is uncertain;
   3) Long-term sex partners should be evaluated clinically and serologically for syphilis and referred to a private physician for further evaluation if tests are reactive.

3. Self-Referred Sex Partners

   Management of self-referred sex partners should follow the same guidelines as DIS referred sex partners unless the source client information is not available.

   a. If the name of the source client is known, PHN should call DIS to determine stage of the source client and then determine examination and treatment needs.
   b. If the name of the source client is not known, PHN should examine the client for syphilis.
      1) If the partner’s results are positive, treat accordingly.
      2) If the partner’s results are negative and they have had a sexual exposure within the last three months, recommend syphilis testing again in three months.

F. Consultation/Referral

1. Consultation
   a. Notify the DNM of any complications.
   b. Consult with the Disease Intervention Specialist (DIS) assigned to your county health department for all positive syphilis tests.

2. Refer to private physician for evaluation and treatment
   a. Pregnant women who have syphilis and are allergic to penicillin are referred to a physician for treatment.
   b. Neonates and older children suspected of having congenital syphilis.
   c. Clients suspected of having late syphilis with clinical manifestations.
      Clients with reactive serology and neurologic, ocular, or otic manifestations should be treated with bicillin regimen appropriate for the stage of the diagnosis and then referred to nearest emergency department for evaluation and treatment.

3. HIV Infected
   a. Client with HIV and syphilis are more likely to develop neurologic manifestation.
i. Client with HIV with confirmed syphilis and are allergic to penicillin should only be treated with a penicillin alternative treatment regimen if close serologic follow-up is ensured.

b. Serological titers may be higher or lower than expected.

c. Seroconversion may occur later than expected.

G. Follow-Up
(The PHN may obtain specimens serology testing for diagnosis purposes, as noted below and as requested by Disease Intervention Specialist.)

1. Early syphilis (< 1 year duration)

a. Primary and Secondary syphilis

1) Clients who present with active primary or secondary symptoms (e.g. chancre and/or rash) upon initial assessment should be scheduled to return to CHD 1 week after treatment to evaluate for resolution of symptoms.

2) Serology testing should be repeated at 6 and 12 months after therapy. (If client has HIV positive status, repeat at 3, 6, 9, 12 and 24 months after therapy) or more often if necessary in consult with DIS.

Note: The reverse sequence algorithm for syphilis testing performed by the OSHD PHL uses an initial treponemal screen, which if reactive is automatically reflexed to RPR. Because patients infected with syphilis remain positive for treponemal antibodies for life, specimens from clients being followed post-therapy will always be screen-reactive and will be reflexed to a quantitative RPR. Therefore, there is no necessity to indicate on the requisition that an RPR is needed for these patients; simply order Syphilis, serology (Reverse Algorithm).

3) Retreatment and evaluation required if (consult with DIS)

a) Signs/symptoms persist or recur.

b) Client has a sustained fourfold (two dilutions) increase in RPR titer when compared to either the baseline titer or a subsequent result (treatment failure or re-infected). (See Note Below)

c) RPR titer fails to decline fourfold (two dilutions) by 6 months after therapy. Client should be reevaluated for HIV infection. (See Note Below)

Note: RPR titers are reported as 1:1, 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:128, 1:256, 1:512, 1:1024, 1:2048, 1:4096, 1:8192, or > 1:8192 dilutions. Therefore, for example, if a client’s RPR titers increase from 1:32 to 1:128 or higher, this is at least a four-fold increase (i.e., 32 multiplied by 4 = 128). Alternatively, count 2 dilutions (e.g., 1:32 to 1:64 is one dilution and 1:32 to 1:128 is 2 dilutions).

b. Syphilis of Unknown Duration and Late Syphilis

1) Serology testing should be repeated at 6, 12, and 24 months (If client has HIV positive status, repeat at 6, 12, 18, and 24 months after therapy) or more often if necessary in consult with DIS.
after therapy) or more often if necessary in consult with DIS.

2) Client should be evaluated for neurologic manifestations and retreated appropriately if:

a) RPR titer increase fourfold (2 dilutions);

b) An initially high RPR titer (≥ 1:32) fails to decline at least fourfold (two dilutions) within 12-24 months;

c) Client develops signs or symptoms attributable to syphilis.

REFERENCES:

Centers of Disease Control and Prevention, 2015 Guidelines for Treatment of Sexually Transmitted Diseases. MMWR Recommendations and Reports, June 5, 2015 / Vol. 64 / No. 3, Pg. 34-51.


Sexually Transmitted Infections and HIV.
SYPHILIS STAGING, TREATMENT & FOLLOW-UP ALGORITHM

- **Patient has evidence of current infection?**
- **Pt has had a sexual exposure to syphilis?**
- **Sexual exposure was within the last 90 days as notified by client or DIS?**
- **Pt has signs of primary or secondary syphilis?**
- **SEROLOGIC TEST FOR SYPHILIS**
- **SEROLOGIC TEST FOR SYPHILIS & MAY PRESUMPTIVELY TREAT BIC x 1**
- **Pt has primary symptoms**
- **Pt has secondary symptoms**
- **Pt has current positive test AND one of the following?**
  - Negative test in the last 12 months or ≥4-fold titer increase from a previous test in the last 12 months?
  - 5/5 consistent with syphilis during the last 12 months?
  - A sexual exposure to early syphilis within the last 12 months?
  - Sexual debut within the last 12 months
- **UNKNOWN DURATION/ LATE SYPHILIS --BIC x 3**
- **PRIMARY SYPHILIS --BIC x 1**
- **SECONDARY SYPHILIS --BIC x 1**
- **EARLY, NON-PRIMARY, NON-SECONDARY SYPHILIS --BIC x 1**

**UNKNOWN DURATION / LATE SYPHILIS INVESTIGATIONS:**
Patients who have no signs or symptoms and have an RPR titer ≥ 1:8 are investigated by DIS as early non-primary, non-secondary syphilis. However, treatment should reflect unknown duration / late syphilis.

**STAGING EXCEPTIONS**
Diagnosis staging exceptions exist. DIS investigation may determine a different diagnosis stage.

*Evidence of current infection:*
- No prior history of syphilis AND current reactive treponemal test
  - OR-
  - Prior history of syphilis with a current nontreponemal titer demonstrating a ≥4-fold titer increase (unless the 4-fold increase was not sustained 2 weeks)

**Treatment alternatives for early syphilis:***
- If pt is pregnant treat with Bic x 2
- If pt is allergic to PCN, treat with Doxy 100 mg BID x 14
- If pt is pregnant and allergic to PCN, refer for PCN desensitization

**Treatment alternative for unknown duration/late syphilis:**
- If pt is allergic to PCN, treat with Doxy 100 mg BID x 28
- If pt is pregnant and allergic to PCN, refer for PCN desensitization

**RPR TITER FOLLOW-UP DATES**

<table>
<thead>
<tr>
<th>Primary / Secondary</th>
<th>6 &amp; 12 months</th>
<th>All stages other than primary or secondary</th>
<th>6, 12, &amp; 24 months</th>
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Revised 1/5/2018
PARTNER SERVICES (PS) ELIGIBILITY

SYPHILIS

ELIGIBILITY CRITERIA:
- Primary/Secondary Syphilis
- Syphilis Titer > 1:8
- Contact (P1) to a PSE Syphilis Case

ELIGIBLE CASE
- All Original Interviews conducted in person.
- Re-Interview may be omitted with certain criteria.

Partners:
- All Partners are initiated for PS and interviewed in person by DIS.
- Partners within last 90 days are referred to HD for preventative treatment.
- Partners >90 days can be tested by DIS in field.

Social Contacts:
- DIS may meet Social Contacts and test/interview.
- DIS may refer Social Contacts to HD for testing.

INELIGIBLE
- DIS does not interview client.
- DIS ensures the client receives treatment.
- DIS encourages provider to have client inform partners of exposure.

HIV

ELIGIBILITY CRITERIA:
- All Newly Identified HIV Cases
- HIV/Syphilis Co-Infection

ELIGIBLE CASE
- All Original Interviews conducted in person.
- Re-Interview may be omitted with certain criteria.

Partners and Social Contacts:
- All Partners and Social Contacts are Initiated and worked by the DIS.

To assist PS ineligible clients with partner notification:
www.sotheycanknow.org