SYPHILIS INFECTION

Syphilis is a sexually acquired infection which may become chronic without treatment. Nearly all cases of syphilis are acquired by direct sexual contact with lesions of an individual who has primary or secondary syphilis. Transmission can occur vertically from mother to child during pregnancy by transplacental passage of treponemes to fetus at any syphilis stage.

1. **Agent**: Organisms of the genus Treponema; Treponemal species of public health importance: Treponema pallidum (causative agent of venereal syphilis).

2. **Identification**:

   a. Symptoms: Syphilis is a chronic, systemic infection characterized by periods of active clinical disease that are interrupted by periods of latency. Many patients appear asymptomatic.

      Syphilis is divided into (4) stages (primary, secondary, latent, and tertiary), which reflect the clinical progression of disease. Any stage of syphilis which occurs <1 year of acquisition is considered early syphilis and any stage of syphilis which occurs after 1 year of acquisition or the duration is unknown is considered as late syphilis Neurosyphilis as well as ocular and otic syphilis can occur at any stage of the disease although more common in the early stages.

      Primary Syphilis: Characterized by a painless ulcer (chancre) appears 10-90 days (average 21 days) after contact with an infected partner. A chancre is highly infectious and teeming with spirochetes and heals spontaneously, in 1-6 weeks. Minimal tender lymphadenopathy may occur.

      Secondary Syphilis: Secondary Syphilis: The signs and symptoms usually appear 3-6 weeks after the primary chancre appears. Untreated secondary syphilis manifestations will resolve spontaneously after weeks to months. The chancre and secondary syphilis may also occur simultaneously.
      a) Skin rash (~75-90% of patients) - May be generalized or localized at the genitals, ~60% involve the palms and soles, usually non-pruritic.
      b) Generalized lymphadenopathy (~70-90% of patients) Constitutional symptoms (~50-80% of patients) – fever, headache, and/or malaise.
      c) Mucous patches (~5-30% of patients) - Flat to slightly raised and usually painless patches found in the oropharynx or anogenital regions.
      d) Condyloma lata (~5-25% of patients) - Moist wart-like papules and occur in warm, intertriginous areas such as the perineum and gluteal folds.
      e) Alopecia (~10-15% of patients) – Patchy hair loss, resembling a motheaten appearance, hair loss can also occur on the eyelashes and eyebrows.

      Early Latent Syphilis: Characterized by the absence of symptoms and signs. Categorized as early (≤ 1 year duration) or late (> 1 year duration). Early latent syphilis is infectious to sex partners, though patients are usually asymptomatic. In order to be diagnosed as early latent, the patient must have had one of the following within the past year:
      a) Documented seroconversion or fourfold or greater increase in titer of a non-treponemal test.
      b) Unequivocal prior symptoms of primary or secondary syphilis.
      c) A sex partner documented to have primary, secondary, or early latent syphilis.
      d) Reactive non-treponemal and treponemal tests when the only possible exposure occurred within the previous year.

      Late Latent Syphilis: Characterized by the absence of symptoms and signs. Categorized as early (≤ 1 year duration) or late (> 1 year duration). Late latent syphilis is generally less communicable through sexual contact. However, this can result in maternal-fetal transmission. Characterized by the absence of symptoms and signs- late (> 1 year duration). In order to be diagnosed as late latent, the patient must have had:
      a) No current clinical symptoms of syphilis and negative exam, **and**

b) No prior reactive serologic test for syphilis.
c) No recent (< 1year) serologic test.

Tertiary Syphilis: Tertiary syphilis is rarely diagnosed. If syphilis remains untreated, ~30% of patients may progress to tertiary disease. Tertiary syphilis may include the following lesions:

- Gummas – Average onset of gummatous lesions is ~10-15 years after initial infection.
- Cardiovascular syphilis lesions – Average onset of cardiovascular syphilis is 20-30 years after initial infection.
- Central nervous system (CNS) lesions – Generally occur decades after initial infection may include the following symptoms- general paresis, tabes dorsalis, dementia, psychosis, gait disturbances.

Neurosyphilis: Treponemal invasion of the CNS in early syphilis is common, occurring in ~30-40% of syphilis cases. Neurosyphilis can occur and be asymptomatic at any stage of disease. Symptomatic early neurosyphilis usually occurs a few months to a few years after initial infection. Evidence suggests HIV positive patients may be at increased risk for neuro-syphilis.

Common manifestations of early neurosyphilis are:

a) Acute syphilitic meningitis – typical meningitis symptoms (headache, fever, photophobia, neck stiffness, nausea, and vomiting).
b) Cranial nerve palsies – especially involving cranial nerves VI, VII, and VIII with possible auditory complications (hearing loss).
c) Meningovascular syphilis – typical symptoms include seizures or a stuttering stroke-like syndrome.
d) Ocular Syphilis – manifestations may include uveitis, neuroretinitis, and optic neuritis. Ocular involvement can occur with both early and late stages of syphilis. The most common manifestation in early syphilis is uveitis.
e) Otic Syphilis- manifestations may include hearing loss, tinnitus or vestibular abnormalities such as vertigo, imbalance or gait instability. Otic involvement can occur with both early and late stages of syphilis.

The most common manifestation in early syphilis is new onset sensorineural hearing loss, tinnitus, and vertigo.

Prenatal Syphilis: The clinical presentation of syphilis does not change during pregnancy. Benzathine penicillin G is the only therapy with documented efficacy for syphilis during pregnancy. Pregnant women with syphilis in any stage who report penicillin allergy should be desensitized and treated with penicillin.

Clinical follow-up of prenatal syphilis is vital. This includes coordinated prenatal care and treatment. Since LA County is considered a high syphilis morbidity area, at a minimum, serologic titers should be obtained at entry into prenatal care, repeated at 28–32 weeks' gestation and at delivery. Serologic titers should be checked more frequently (monthly if needed) in women at high risk for reinfection. Pregnant women with late or sporadic prenatal care, no prenatal care, women with history of substance abuse/mental illness, history of recent incarceration, or women whose sex partners may have other partners are at risk for syphilis and congenital syphilis sequalae.

Congenital Syphilis: Congenital syphilis is a preventable condition that results from untreated syphilis during pregnancy, with potentially severe consequences for infected infants. Congenital syphilis can lead to stillbirth, neonatal death, birth defects involving the nervous system or bones, blindness or deafness, skin lesions and scarring, and other manifestations. Manifestations of congenital syphilis are not always apparent at delivery. Even if a syphilis-exposed infant appears healthy at birth, if the mother had syphilis and was not properly treated at least 30 days before delivery, the infant requires an evaluation for congenital syphilis as well as treatment.

Clinical-Follow Up of congenital syphilis is vital. All neonates with reactive nontreponemal test should receive careful follow-up examinations and serologic testing (i.e., a nontreponemal test) every 2-3 months until the test becomes nonreactive.

- Nontreponemal antibody titers should decline by age 3 months and be nonreactive by age 6 months.
- At 6 months, if the nontreponemal test is nonreactive, no further evaluation or treatment is needed.
- Treated neonates that exhibit persistent nontreponemal test titers by 6-12 months should be re-evaluated through CSF examination and managed in consultation with an expert.

Syphilis Infections among Infants and Children: Sexual abuse must be considered a cause of syphilis infections in infants and children. This type of case requires consultation with the DHSP clinical guidance and nursing unit.

b. Differential Diagnosis: Differential Diagnosis: Syphilis is the great imitator and can mimic the manifestations of several systemic diseases. The skin rash of secondary syphilis may be confused with HSV, pityriasis, rosea, erythema multiform, generalized papular eruption, and other common rashes.

3. **Diagnosis**:

a. History: Determine if patient is at risk for syphilis—has exposure to known case of early syphilis, signs/symptoms of syphilis in sex partners, sexual practices, prior syphilis history, non-treponemal/treponemal testing, and history of past STDs.

b. Physical Examination: Thorough examination of the oral cavity, lymph nodes, skin, palms and soles, genitalia, pelvic area, and perianal region should be done to look for signs of syphilis. Neurologic, ophthalmic and otic examination to assess for signs of neurosyphilis, ocular and otic syphilis respectively.

c. Laboratory: There are two types of tests for syphilis 1) non-treponemal and, 2) treponemal.

1. Non-treponemal tests are used for:
   - Screening
   - Follow-up assessment after treatment
   - Evaluation of patients with symptoms or possible re-infection

Non-treponemal tests measure IgM and IgG antibody directed against a cardiolipin-lecithin- cholesterol antigen. They are not specific for T. pallidum. The most common non-treponemal tests are the Rapid Plasma Reagin (RPR) and Venereal Disease Research Laboratory (VDRL).
Quantitative non-treponemal titers usually correlate with disease activity, making it a useful measure of response to therapy.

2. Treponemal tests are used for:
   - Confirmation of positive non-treponemal tests
   - Screening. Treponemal tests are qualitative (not able to titer)

Treponemal tests are specific for T. pallidum and measure antibody (IgM and IgG) directed against T. pallidum antigens by particle agglutination for the Treponema Pallidum Particle Agglutination test (TP-PA) or by immunofluorescence for the Fluorescent Treponemal Antibody-Absorbed test (FTA-ABS).

Automated enzyme immunoassays/ichemoluminescene immunoassays (EIA/CIA) are also used as confirmatory treponemal tests but have led to a shift in syphilis serologic testing in many laboratories. While the traditional screening algorithm consists of a non-treponemal test followed by a treponemal test, the automation of EIA/CIA in particular, has allowed laboratories to reverse the testing sequence by first screening with a treponemal test and then re-testing reactive results with a nontreponemal test to determine titer. This reverse syphilis algorithm is considered the preferred method for screening. However, in patients with a with a known history of syphilis when the treponemal test is likely to be reactive, a follow up non-treponemal (RPR) test alone is sufficient to detect new infection as indicated by a four-fold rise in the RPR titer.

Note: All persons who have syphilis should be tested for HIV. All people who have syphilis and who are at risk for HIV infection (e.g., do not have HIV) should be counseled about biomedical prevention of HIV including

pre-exposure (PrEP) and post-exposure prophylaxis (PEP).

d. Biologic false positive (BFP): Individuals with reactive non-treponemal tests and non-reactive confirmatory treponemal tests are called BFP. A variety of conditions can cause false positive such as: viral illness, recent immunizations, injection drug use, autoimmune disorders, malignancy, aging and pregnancy.

4. **Incubation**: Usually 10 days to 3 months (average range 21 to 28 days).

5. **Reservoir**: Humans are the only reservoir for T. pallidum. Syphilis cannot be spread by non-living reservoir.

6. **Source**: Source: The T. Pallidum spirochete is able to pass through contact with any mucous membrane or compromised skin.

7. **Transmission**: Sexual or direct contact with the primary lesion (through broken skin or mucous membranes), or transplacental during pregnancy from a mother to her fetus. Transmissible via oral, vaginal, and anal sex. Can be transmitted via blood products/needle sharing.

SPECIFIC TREATMENTS

1. Treatment of Primary, Secondary, and Early Latent Syphilis:

   a. Antibiotic of Choice
   Benzathine penicillin G 2.4 million units, intramuscular/ IM (once)

   b. Alternative (for non-pregnant, penicillin-allergic patients)
   Doxycycline 100mg orally, BID for 14 days may be substituted (can also use tetracycline 500mg PO QID for 14 days but more GI side-effects and compliance is likely to be worse, compared to doxycycline).

2. Treatment of Late Latent Syphilis

   a. Antibiotic of Choice
   Benzathine penicillin G 2.4 million units (BPG) IM, intramuscular/ IM (administered once each week for three weeks).

   Note: Patients receiving three doses of penicillin must restart their treatments over if more than 14 days has elapsed between doses. They should receive their bicillin no earlier than five days since the preceding dose. (In pregnancy, doses must be 7 days apart; the maximum interval between doses is 9 days.)

3. Treatment of Neurosyphilis

   a. Antibiotic of Choice
   Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days.

   b. Alternative (for non-pregnant, non-penicillin allergic patients)
   Procaine penicillin G 2.4 million units IM once daily PLUS Probenicid 500 mg orally four times a day, both for 10-14 days.

   Note: For patients with possible penicillin allergy, please contact DHSP Nursing Unit for assistance.

TREATMENTS FOR SYPHILIS IN PREGNANCY & CONGENITAL SYPHILIS

Benzathine penicillin G (BPG) is the only appropriate treatment for syphilis during pregnancy.

Early Latent Syphilis: Receive one dose of 2.4 million units of BPG intramuscular (IM).

Late Latent Syphilis: Require 3 doses of BPG intramuscular (IM) each exactly 7 days apart. Treatment must be completed at least 28 days before delivery.

Jarisch-Herxheimer Reaction: The Jarisch-Herxheimer reaction is an acute febrile reaction frequently accompanied by headache, myalgia, fever, and other symptoms that can occur within the first 24 hours after the initiation of any therapy for syphilis. The Jarisch-Herxheimer reaction occurs in up to 45% of pregnant women and can cause uterine contractions, potentially leading to miscarriage or preterm labor.

Note: Treating a pregnant woman for syphilis also treats her fetus. Pregnant women with syphilis who have penicillin allergy must be desensitized

so that they can receive proper treatment. Missed doses are not acceptable for pregnant women. If a dose is missed, then therapy must be restarted. (In pregnancy, doses must be 7 days apart; maximum interval between doses is 9 days.)

Treatment of Congenital Syphilis: Treatment of an infant exposed to syphilis in utero depends on several factors and requires consultation with DHSP Clinical Consultation Guidance and Nursing Unit.

- **Option 1**: Aqueous crystalline penicillin G 100,000–150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days and every 8 hours thereafter for a total of 10 days. If more than 1 day of therapy is missed, the entire course should be restarted.

- **Option 2**: Procaine penicillin G 50,000 units/kg/dose IM in a single daily dose for 10 days.

- **Option 3**: Benzathine penicillin G 50,000 units/kg/dose IM in a single dose. Before using the single-dose benzathine penicillin G regimen, the complete evaluation (i.e., CSF examination, long-bone radiographs, and CBC with platelets) must be normal, and follow-up must be certain. Call DHSP for further guidance if using this option.

CLINICAL FOLLOW-UP OF PRIMARY & SECONDARY SYPHILIS

Day of treatment titer is recommended to establish titer baseline. Afterwards, clinical and serologic evaluation should be performed at 6 and 12 months after treatment; more frequent evaluation might be prudent if follow-up is uncertain or if repeat infection is a concern (e.g., pregnant female). Serologic response (i.e., titer) should be compared with the titer at the time of treatment. Failure of nontreponemal test titers to decline fourfold within 6–12 months after therapy for primary or secondary syphilis may be indicative of treatment failure. However, clinical trial data have demonstrated that 15%–20% of persons with primary and secondary syphilis treated with the recommended therapy will not achieve the fourfold decline in nontreponemal titer used to define response at 1 year after treatment. HIV infected persons have an increased likelihood of remaining serofast at higher titers than non-HIV infected persons.

CLINICAL FOLLOW-UP OF LATE LATENT SYPHILIS

Quantitative nontreponemal serologic tests should be repeated at 6, 12, and 24 months. A CSF examination should be performed if 1) a sustained (>2 weeks) fourfold increase or greater in titer is observed, 2) an initially high titer (≥1:32) fails to decline at least fourfold within 12–24 months of therapy, or 3) signs or symptoms attributable to syphilis develop. In such circumstances, patients with CSF abnormalities should be treated for neurosyphilis.

Note: There is no natural immunity to syphilis and past infection offers no protection to the patient.

Public Health Nursing Protocol:
Home visit is required for syphilis cases.

Refer to "Public Health Nursing STD Algorithms" in B-73 Part IV Public Health Nursing STD Protocol

CONTROL OF CASE AND SEXUAL CONTACTS

1. Persons with either confirmed non-treponemal and treponemal tests and/or those with syphilis symptoms may transmit the disease, however the transmissibility varies based on the stage of the disease.

2. Cases at highest risk for transmission:
   - Primary Syphilis
   - Secondary Syphilis
   - Early Latent Syphilis
   - Prenatal Syphilis, any stage

3. Sexual Contacts of a person who receives a diagnosis of primary, secondary, or early latent syphilis are at high risk of contracting the infection. The **Interview Period** is the time from the earliest date the patient could have been infected to the date of treatment. The following are the syphilis interview periods for each stage:
   - Primary Syphilis - If the sexual partner (SP) had sexual contact with index case within 3 months plus the duration of symptoms.
   - Secondary Syphilis - If SP had sexual contact with index case within 6 months prior, through the resolution of symptoms.

- Early Latent Syphilis - If SP had sexual contact with index case within 1 year of diagnosis.
- All Sexual Partners of pregnant females require immediate presumptive treatment for syphilis. Do not wait for laboratory results.

4. Cases at lower risk for transmission:
   Late Latent Syphilis - Long-term sex partners of patients who have late latent syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the evaluation.

Note: All persons reporting sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis within 90 days preceding the diagnosis should be evaluated and treated presumptively for early syphilis, even if serologic test results are negative.

REPORTING PROCEDURES

Report any case or suspected cases: Syphilis laboratory results and CMR's must be reported to the Department of Public Health within one working day by Sexually Transmitted Disease Confidential Morbidity Report (Title 17, Section 2500. California Code of Regulations)

REPORT FORM: STD-CMR

For more information on reporting visit: http://www.publichealth.lacounty.gov/dhsp/ReportCase.htm

PREVENTION / EDUCATION

Partner Services (PS) / Targeted Case Management (TCM) (PHN/PHI)
Targeted Case Management is the systematic pursuit, documentation, and analysis of medical and epidemiologic case information that focuses on opportunities for disease intervention. Partner services are a broad array of services such as partner notification, prevention counseling, STD testing and treatment and linkage to care, or other types of prevention services (e.g., reproductive health, prenatal care, substance abuse referral, HIV PrEP & PEP, etc.).

PRE-Interview Analysis
1. Establish the reason for the initial examination (RFE).
2. Establish possible history of syphilis infection.
3. Establish a critical period and interview period based on available medical or case-related information, and
4. Establish information objectives (e.g., relationship to other cases).
5. Review all available medical and case information, assess missing elements to provide Partner Services. (i.e., inadequate/ missing treatments, missing laboratory tests).
6. Review Case Number/Patient Name/Date of Interview/Diagnosis, etc.
7. Review interview record.
8. Review laboratory results/medical reports.
9. Review a copy of the infected patient's Field Record (FR)/Health Department Follow-Up (HDFU), if applicable/all associated field records (partners, suspects, and associates). Initiate case documents/field notes in a logical sequence.

PHN/PHI will Conduct Index or Contact Interviews:
The PHN/ PHI conducts these interviews preferably in person and always in confidence. Telephone interviews are permissible per approved algorithms.

Child Abuse/Child Neglect-Mandated Reporting
Sexual abuse and child neglect reporting are required by California law. PHNs/PHIs are mandated reporters. This includes the reporting of sexual partners of disparate age and is required regardless of disease intervention priorities. California Penal Code §§11165.7, 11166, and 11167.

PHN/PHI initiates interview:
The primary objective of the interview is to help the client manage their infection. The PHN/PHI ensures that each client is educated regarding syphilis. The following topics shall be discussed with patient:

Interview Process:
1. Introduce her/himself, explain his/her professional role and the purpose of the session.
2. Maintain confidentiality, in the context of (PS). Confidentiality refers to keeping information about index, partners, or contacts in confidence.
3. Manage risk through prevention counseling.
4. Ensure patient understands mode of transmission, symptomatic/asymptomatic

nature of disease/risk of re-infection, and complications and consequences.
5. Assess patient's self-perception of risk, higher chance of getting/giving other STDs/HIV, and the importance of referral of sex partners and other high-risk persons (i.e., pregnant partners) for treatment to protect their health and reduce the spread of disease.
6. If applicable, assess the patient's understanding of negative consequences to fetus if she delivers while being infected with syphilis.
7. Link patient to medical evaluation and treatment, plan counseling/testing or referral for other STDs (i.e., Chlamydia, Gonorrhea, HCV), HIV medical care if HIV positive, and HIV prevention services (including PrEP/PEP) as applicable.
8. Plan to follow-up regarding any pending referral/treatment plans.

Partner Elicitation/Field Records (FR)

1. Initiate a Field Record for all Interview Period partners that have adequate locating information. The Interview Period is the time from the earliest date the patient could have been infected to the date of treatment.
2. The following are the syphilis interview periods for each stage:
   - Primary Syphilis - If the sexual partner (SP) had sexual contact with index case within 3 months plus the duration of symptoms.
   - Secondary Syphilis- If SP had sexual contact with index case within 6 months prior, through the resolution of symptoms.
   - Early Latent Syphilis- If SP had sexual contact with index case within 1 year of diagnosis.
3. Initiate a Field Record for other high-risk individuals such as non-sexual partners who are symptomatic or someone who is part of index's sexual network if applicable).

DOCUMENTATION

The PHN/ PHI documents the results of interviews, referral forms and laboratory results in STD Case Watch (CW).

Ensure CW referral forms include the following:

1. Client's understanding of reason for the initial examination (RFE).
2. Establish possible history of syphilis infection, medical and case information in such a manner
   as to establish the reason for the initial examination.
3. Syphilis Interview Period based on available medical or case-related information.
4. Case number/Patient Name/Date of Interview/Diagnosis.
5. Complete interview record.
6. Syphilis treatment/preventive treatments.
7. Laboratory results & follow up testing/medical reports.
8. Infected patient's FR/HDFU, if applicable/all associated field records (partners, suspects, and associates).
9. Case documents/field notes in a logical sequence.

QUALITY ASSURANCE & CLOSURE REVIEW (LEVEL I and LEVEL II)

Cases are to be closed within 30 days from assignment to PHN/PHI with all associated/ required case management forms. Documents must be legible, thorough, and concise. Closure date may be extended by supervisor if needed. Cases not meeting closure criteria will be re-routed for further investigation.

OTHER RESOURCES

1) CDC. Recommendations for partner services programs for HIV infection, syphilis, gonorrhea, and chlamydial infection. MMWR Rep 2008; 57(No. RR-9).
2) CDC. Sexually Transmitted Diseases Treatment Guidelines, 2021
3) DHSP Syphilis and STD resources
4) Syphilis in Women Action Toolkit