Syphilis

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To assess trends in disease patterns, understand the impact of syphilis and better target population-level disease prevention efforts.
2. To assure adequate treatment for infected individuals, curtail infectiousness, and prevent complications of late syphilis (e.g., late neurologic complications, cardiovascular disease).
3. To prevent congenital syphilis by screening and treatment of infected pregnant women.
4. To prevent transmission by identifying, informing, and referring to treatment recent sexual contacts of reported cases, and screening others at risk.

1.2 Legal Reporting Requirements

1. Physicians and other health care providers must report a case or suspected case of syphilis within one working day to the Local Health Department (LHD) (OAR 333-018-0015).
2. Laboratories must report all positive test results indicative of *Treponema pallidum* infection to the LHD of the county where the individual resides within one working day from the time of positive result. Reportable results are tests indicated of syphilis, including but not limited to non-treponemal and treponemal serologic tests. (§2.3)

1.3 Local Health Department Investigation Responsibilities

1. Begin follow-up case investigation within 2 working days after receiving the case report.
2. Upon receipt of reactive serologic test results for syphilis, but before initiating a new case report, search for a record of the person in the Public Health Division's online integrated disease reporting system (Orpheus) or contact the STD Registry Clerk, Public Health Division Sexually Transmitted Disease Control Program for assistance with this task. (971-673-0152) If the person has a record in Orpheus, check whether the person has an associated syphilis case report or "reactor case." (Registry or cases can be distinguished by an "R" in the co-morbidity panel of Orpheus case entry.) All individuals recorded in Orpheus with one or more presumptive or confirmed cases of syphilis should have one and only one registry case. A registry case is a trick used by Orpheus developers to make longitudinal serologic titers visible across multiple acute or recurrent cases of syphilis and to record periodic titers from someone who was successfully treated long ago but has persistently measurable titers, or has recurrent falsely reactive tests. Each person who has a past case of confirmed or presumptive syphilis of any stage should also have a registry case. If one is not present for that person, contact the STD program for assistance in creating a registry case for this person if you don't already know how to do this yourself. If a registry case, or past presumed or confirmed syphilis case of any stage is present, a newly received positive test might represent persistent reactive serology after previous treated syphilis infection or a persistent false positive test. If you can verify that a person was previously treated for syphilis and the current titer is less than 2 dilutions higher than the titer after treatment (or than the previous titer if the person has been determined to be a "reactor"), enter the current result in the laboratories associated with the registry case in Orpheus and move on to your next task. (§2.3) If your LHD uses an independent electronic system for tracking syphilis disease data, speak with your manager

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about how to determine whether the person is a chronic reactor. Sometimes a person will report syphilis testing or treatment in another state, but does not yet have a reactor case recorded in Orpheus. In this circumstance, identify, to the best of your ability, the city, state, and approximate year of treatment. Forward this information to the STD Control Program via phone or Orpheus note to request that state staff contact the other state for records of past treatment and testing.

2. Report all presumptive and confirmed cases to the Public Health Division HIV/STD/TB (HST) Program by the end of the calendar week of initial physician or laboratory report by completing the case report directly in the Public Health Division's online integrated disease reporting system (Orpheus) by submitting a completed copy of the syphilis case report form available from the HST website, or by submitting an electronic file in mutually acceptable format that includes all information indicated collected by the case entry layout in Orpheus.

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

Treponema pallidum, a bacterium of the order Spirochaetales.

2.2 Description of Illness

Syphilis is a complex, systemic, sexually transmitted infection that has a highly variable clinical course. The etiologic agent, *T. pallidum* cannot be grown in culture. Untreated, it progresses through stages: primary, secondary, latent, and late syphilis with clinical manifestations, that are often separated by long periods of latency. Congenital infections can occur in infants after *in utero* or intrapartum inoculation. Central nervous system infection (neurosyphilis) can occur at any stage. Approximately 30–40% of untreated persons will develop complications of late syphilis, sometimes many years after infection.

Primary. Primary syphilis is the first stage after an incubation period of 10–90 days (average 21 days), characterized by an ulcer (chancre, sore, or primary lesion) that is typically concave, with a raised border. Primary syphilis is sometimes referred to by its traditional CDC code, "710." It is typically painless, appears at the site of inoculation, generally the genitalia or anus. Primary lesions can occur at other sites of inoculation such as the lip, breast or mouth and might be located at ordinarily invisible locations such as the cervix, vagina or rectum. Commonly, only one lesion is present, but more than one ulcer might be present. Inguinal lymphadenopathy is common. The primary lesion persists for 1–5 weeks (3 weeks average) then goes away. This is the most infectious stage of syphilis. Treponemal and non-treponemal tests might be negative when a primary syphilis ulcer first appears. (§2.3)

Secondary. After the primary lesion disappears, a latency period of 0–10 weeks (average of 4 weeks) typically ensues, after which the secondary stage appears in about 25% of individuals with untreated infection. Secondary syphilis is sometimes referred to by its traditional CDC code, "720." Common symptoms include a generalized body rash, lymphadenopathy, mucous patches, patchy hair loss (alopecia), and malaise. Rash is famously protean, often appears as faint coppery macules on palms of hands ("palmar") and soles of feed ("plantar"). Secondary symptoms typically persist from 1–6 weeks. One ordinarily finds both treponemal and non-treponemal tests to be reactive during secondary syphilis. (§2.3)

Early latent. During latent syphilis *T. pallidum* organisms persist in the body of the infected person but no symptoms manifest. For epidemiologic purposes, we separate latent syphilis into two categories: *early latent*, which is defined as an infection of one year or less, and *late latent*, which is an infection lasting >1 year. Early latent syphilis comprises the interval between the resolution of secondary symptoms (up to 6.5 months after infection) and 1 year after infection (exposure). In some instances, earliest date of infection (exposure) can be inferred from a documented negative serologic test collected before the current diagnosis, or from onset of documented signs of primary or secondary syphilis. When the earliest date of infection or exposure can be determined with confidence to have occurred within a year of diagnosis a case should be classified as *early latent*. Early latent syphilis is sometimes called by its traditional CDC code, "730."

Late latent. In many other instances, exact date of infection (exposure) cannot be known or constrained with certainty. These cases should be considered to be *late latent.* If the case remains untreated latent syphilis can persist for the remainder of the person's life. Late latent syphilis is sometimes called by its traditional CDC code, "745."

Late syphilis with clinical manifestations other than neurosyphilis. Sometimes called "late syphilis," or "tertiary syphilis," this stage typically becomes evident 15–30 years after untreated primary infection. Late syphilis with clinical manifestations other than neurosyphilis is sometimes referred to by its traditional CDC code, "750." Clinical manifestations most commonly include inflammatory lesions of the cardiovascular system, skin, and bone. Less commonly, late syphilis causes clinical manifestations in other anatomic locations such as the respiratory tract, mouth, eye, viscera, lymph nodes, or skeletal muscle.

Neurosyphilis. Central nervous system *T. pallidum* infection defines neurosyphilis. Neurosyphilis used to be considered a distinct stage of syphilis but syphologists no longer consider neurosyphilis to be a distinct stage of syphilis in the sequential sense; neurosyphilis can occur during any stage of syphilis. Nevertheless neurosyphilis is still sometimes referred to by its now-obsolete traditional CDC code, "760." Laboratory findings include a reactive treponemal serologic test for syphilis and a reactive VDRL test in cerebrospinal fluid (CSF). (§2.3) When signs or symptoms are present in early syphilis, these can include manifestations of meningitis, ocular syphilis (such as posterior uveitis), hearing loss (otosyphilis), and arteritis leading to stroke. Neurosyphilis during early syphilis can resolve spontaneously and might be asymptomatic. Late neurosyphilis can manifest as a progressive dementing illness (general paresis, dementia paralytica), or tabes dorsalis (locomotor ataxia), a disease of the posterior columns of the spinal cord and dorsal roots.

Congenital. Fetal infections occur with high frequency in untreated early syphilis infections of pregnant women and with lower frequency when pregnancy occurs during latent infection or late syphilis. The fetus acquires the infection while *in utero* via maternal circulation or during delivery by exposure to primary or secondary lesions. Congenital syphilis can cause abortion or stillbirth and may cause infant death due to pre-term delivery of low birth weight infants or from generalized systemic disease. If an expectant mother at term were to have visible primary syphilis lesion of the cervix, vulva, or vagina physicians might consider cesarean delivery to reduce risk of intrapartum infection. However in most instances fetal exposure has already occurred and cesarian section is not beneficial for reducing complications of congenital syphilis. The Oregon STD Program and CDC request collection of unique case-report information for cases of congenital syphilis. A special case reporting form can be downloaded from the Health Division website (http://public.health.oregon.gov/DiseasesConditions/CommunicableDisease/ReportingCommunicableDisease/ReportingForms/Pages/index.aspx) or obtained by contacting the STD Program directly (971-673-0153).

2.3 Serologic Tests for Syphilis

Non-Treponemal Tests.

These test for non-specific antibodies in a person's blood after syphilis infection. Typically become reactive (positive) ≥3 weeks after exposure (infection). Can be non-reactive (negative)in primary syphilis. Almost always positive in secondary and subsequent stages if untreated. Non-treponemal tests (most commonly RPR) can be reported qualitatively as "positive" ("reactive") or "negative," ("non-reactive") or quantitatively as a "titer" or "dilution," e.g., "1:4," "1:8", "1:16" ..., or simply "4", "8", "16"... The higher the dilution (titer) number, the greater the amount of antibody present. Titers can be very high (e.g. ≥1:1024) in early syphilis. On occasion, non-treponemal tests can be falsely negative in patients with very high titers. This is known as the "prozone effect." If early syphilis is strongly suspected, ask the laboratory to check for the prozone effect. Even without treatment, titers fall after early syphilis and can be relatively low (e.g. 1:4, 1:8) in untreated latent syphilis. Titers typically fall after treatment but can remain at low positive levels indefinitely. People with persistently reactive non-treponemal tests are said to be "chronic reactors" or are said to be "sero-fast." Non-treponemal tests are used to monitor response to treatment. A titer decline ≥4 fold (e.g., from 1:32 to 1:8) within 12 months of treatment is generally considered be indicative of appropriate response to treatment. If a non-treponemal test is reported qualitatively as "positive," ("reactive") it is important to arrange with the laboratory for quantitative estimate of dilution titer as the titer value will be necessary for staging, treatment and follow-up. If the specimen is not available another specimen should be collected prior to treatment and quantitative titer specifically requested. Often, non-treponemal tests will become positive ("convert") after traditional treponemal test such as FTA-ABS (below). So, in circumstances where recent syphilis exposure is highly likely, consider collecting a blood specimen for treponemal serology despite negative non-treponemal test.

Rapid Plasma Reagin (RPR)

Most commonly used non-treponemal test. RPR is the initial test in the traditional test algorithm used to screen asymptomatic people for syphilis. False-positive RPRs do occur; all reactive (positive) RPR tests should be confirmed by a treponemal test before making a diagnosis of syphilis in someone without symptoms or exposure history.

Venereal Disease Research Laboratory (VDRL)

Preferred test for non-treponemal testing of cerebrospinal fluid (neurosyphilis). Rarely used for peripheral blood testing.

Treponemal Tests

These test for specific antibodies to the T. pallidum bacterium in a person's blood after syphilis infection. Should be reported qualitatively as reactive (positive) or non-reactive (negative) but can be reported as a numeric value from 1 to 4, with higher numbers representing stronger test response. Values from 2 to 4 should be treated equivalently as reactive (positive) without reference to numeric strength of response. Treponemal tests typically become reactive (positive) ≥3 weeks after exposure (infection). Once reactive (positive) treponemal tests generally remain so for life and are not useful for diagnosing reinfection or inadequate treatment. In the latter instances quantitative titers of non-treponemal tests should be used. On occasion, a laboratory might report the result of a treponemal test as "weakly reactive," or with a quantitative value of "1," or "1+." Such a result should be thought of as indeterminate and the test repeated or another type of treponemal test conducted.

Fluorescent Treponemal Antibody-Absorbed (FTA-ABS)

This is the treponemal test available at Oregon State Public Health Lab and is most commonly used treponemal test in Oregon.

Microhemagglutination Test for Antibodies to Treponema pallidum (MHA-TPA)

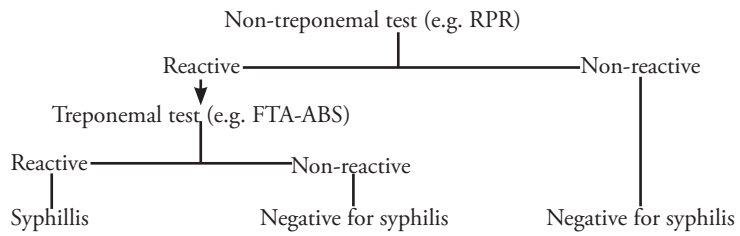
Treponema pallidum agglutination test (TP-PA)

Treponema pallidum enzyme immunoassay (TP-EIA)

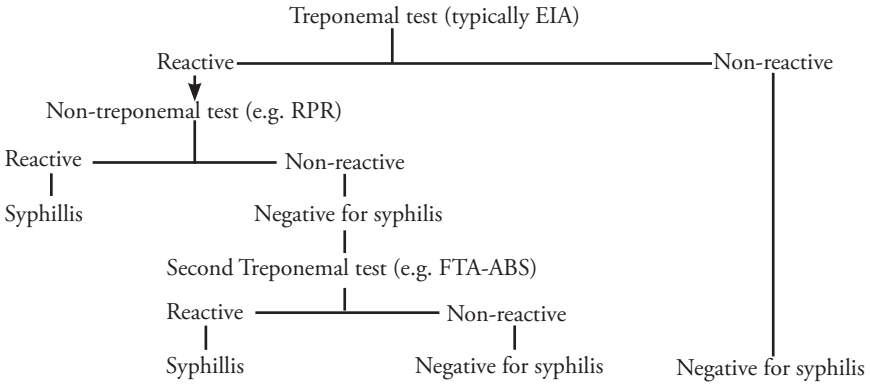
This test has been automated and consequently is often used as the first test in the so-called "reverse algorithm" screening for syphilis. False positives are common and should be confirmed by a non-treponemal test. If the non-treponemal test is non-reactive (negative), another treponemal test (e.g., FTA-ABS) should be conducted before making a diagnosis of syphilis infection.

Current Syphilis Screening Algorithms

"Traditional" Syphilis Screening



"Reverse Sequence" Syphilis Screening



2.4 Reservoirs

Infected humans only.

2.4 Sources and Modes of Transmission

1. Sexual

   Direct contact with infectious exudates from obvious or concealed moist, primary or secondary lesions of skin, and with mucous membranes of infected people during sexual intercourse. From 1997 until this writing, infectious syphilis has disproportionately occurred among men who have sex with men, many of whom have HIV. During this period, cases among women have often been linked epidemiologically to a male sex partner who also has sex with other men. This can be an important subject to explore during case investigation.

2. Vertical.

   Transmitted from mother to fetus *in utero* or during delivery. During the first decade and a half of the 21st century congenital syphilis has been exceedingly rare in Oregon, 4 cases having been observed.

3. Bloodborne.

   Transmitted via transfused blood if donor in early stages of disease. (This is a rare event.)

2.5 Incubation Period

Ten to 90 days, (average 21 days). Length of incubation may be related to the amount (number of organisms) to which the person is exposed; the greater the number (amount of inoculum), the shorter the incubation period.

2.6 Period of Communicability

Infections are communicable to sex partners during primary and secondary stages. Direct physical contact with primary lesions is highly infectious. Also, *T. pallidum* can be identified from dry syphilitic rashes and these are thought to be infectious, at least in theory. However, transmission by physical contact with a dry rash is thought to be rare. Other secondary lesions such mucous patches and condyloma lata (wart-like rash of genital and occasionally other intertriginous areas) and are believed to be more infectious than dry rashes. Infected pregnant women can pass the infection to the fetus during pregnancy regardless of stage of infection. Pregnant women with genital lesions can infect a newborn by exposure to lesions during birth.

2.7 Treatment

(If more than a few days have elapsed between most recent quantitative non-treponemal test was collected, it is prudent to collect another at treatment. Sometimes titers rise rapidly in early syphilis. If a post-treatment titer is compared to a titer that is drawn more than a few days befoe treatment, one might be led to (falsely) conclude that treatment response was less than 4 dilutions.)

Primary, secondary, and latent infections known to be of <1 year duration.

Adults: benzathine penicillin G, 2.4 million units intramuscularly in a single dose. (Note that standard packaging consists of syringes pre-filled with 1.2 million units each of benzathine penicillin. Always read packaging instructions carefully, but if you have syringes pre-filled with 1.2 million units, a complete adult dose typically requires administration of 2 full pre-filled syringes, one in each gluteus (preferably) or quadriceps muscle. At room temperature, benzathine penicillin is quite viscous and must be injected slowly. Patients who receive injectable penicillin should be observed for signs of severe allergy for ≥ 20 minutes after injection.)

Infants and children: benzathine penicillin G, 50,000 units/kg intramuscularly, up to the adult dose of 2.4 million units in a single dose.

Penicillin allergy (adults)

Doxycycline 100 mg orally twice daily for 14 days (Doxycycline should not be used to treat syphilis in pregnant women.), OR

Tetracycline 500 mg orally four times daily for 14 days (Tetracycline should not be used to treat syphilis in pregnant women.), OR

Azithromycin, 2 g orally in a single dose (Azithromycin should be used with caution; azithromycin resistance and treatment failures have been documented in the U.S. Azithromycin should not be used to treat syphilis in pregnant women.), OR

Ceftriaxone 1 g intramuscularly or intravenously daily for 10–14 days (Optimum dose and duration have not been defined. Approximately 2% of individuals with skin-test proven allergy to penicillin have allergy to cephalosporins. Ceftriaxone should not be used to treat syphilis in pregnant women.), OR

Skin testing for penicillin allergy and desensitization if expertise to perform these is available.

Late latent infections (>1 year or unknown duration since infection) and late syphilis with clinical manifestations other than neurosyphilis.

Adults: benzathine penicillin G, 7.2 million units total, administered as 3 doses of 2.4 million unit

intramuscularly each at one-week intervals.

Infants and children: 150,000 units/kg total up to the total adult dose of 7.2 million units, administered as 3 doses of 50,000 units/kg up to the adult single dose of 2.4 million units each at on-week intervals.

Penicillin allergy (adults)

Doxycycline 100 mg orally twice daily for 28 days (Doxycycline should not be used to treat syphilis in pregnant women.), OR

Tetracycline 500 mg orally four times daily for 28 days. (Tetracycline should not be used to treat syphilis in pregnant women.),

(Ceftriaxone might be effective for treatment of late latent or unknown latency infections. However, the optimal dose and duration have not been defined. Use of ceftriaxone for treatment of late syphilis should be discussed with a specialist. Ceftriaxone should not be used to treat syphilis in pregnant women.)

Neurosyphilis (Individuals with early syphilis and cerebrospinal fluid abnormalities in the absence of clinical neurological findings can be treated as early syphilis [above].) If clinical evidence of neurologic involvement is observed, such as cognitive dysfunction, motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies or meningitis, a cerebrospinal fluid analysis should be performed.)

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.

Alternative:

Procaine penicillin G 2.4 million units intramuscularly once daily, PLUS

Probenecid 500 mg orally four times a day, both for 10–14 days.

(Consider administering benzathine penicillin intramuscularly once weekly for 3 weeks after completion of the neurosyphilis regimen to provide a comparable duration of therapy to that recommended for latent syphilis >1 year duration and late syphilis with complications other than neurosyphilis.)

Congenital syphilis.

Aqueous crystalline penicillin G 100,000–150,000 units/kg/day administered as 50,000 units/kg/dose intravenously every 12 hours during first 7 days of life and every 8 hours thereafter for a total of 10 days, OR

Procaine penicillin G 50,000 units/kg/dose IM in a single daily dose for 10 days.

2.7 Assessing for other Sexually Transmitted Infections

All clients diagnosed with syphilis should be offered testing for HIV, gonorrhea, and chlamydia.

3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

3.1 Confirmed Case

Primary syphilis. A clinically compatible case with one or more ulcers (chancres) in which *T. pallidum* is demonstrated in a clinical specimen by dark field, fluorescent antibody, or equivalent microscopic methods.

Secondary syphilis. A clinically compatible case (i.e., localized or diffuse mucocutaneous lesions, often with generalized lymphadenopathy) in which T. *pallidum* is demonstrated in a clinical specimen by dark field, fluorescent antibody, or equivalent microscopic methods.

Late syphilis with clinical manifestations other than neurosyphilis. Demonstration in specimens from lesions suggestive of late syphilis of *T. pallidum* by fluorescent antibody or special stains in a clinically compatible case (i.e. inflammatory lesions of the cardiovascular system, skin and bone or respiratory tract, mouth, eye, viscera, lymph nodes or skeletal muscle).

Congenital syphilis. Demonstration of *T. pallidum* by dark field microscopy, fluorescent antibody, or other specific stains in specimens from lesions, placenta, umbilical cord, or autopsy material obtained from an infant.

3.2 Presumptive Case

Primary syphilis. A clinically-compatible case with one or more ulcers (chancres) and a reactive treponemal or non-treponemal serologic test for syphilis.

Secondary syphilis. A clinically-compatible case with a reactive, non-treponemal test (RPR or VDRL) titer > 4 dilutions (1:4) . (Immunologically deficient clients may exhibit unusual test results such as non-reactive RPR or FTA.)

Early latent syphilis.

No current clinical signs or symptoms of syphilis, with either of the following:

A reactive non-treponemal test, and a reactive treponemal test, without a prior history of syphilis, or

A past history of treatment for syphilis and a current non-treponemal test titer ≥ four times the previous non-treponemal test titer. (e.g., current titer of 1:32, previous titer 1:8, 32 = 4 x 8)

AND,

Evidence of syphilis acquisition within the past 12 months including any of the following:

Documented seroconversion from non-reactive to reactive treponemal test, or ≥ fourfold increase in titer of a non-treponemal test *during* the previous 12 months, or

Signs or symptoms consistent with primary or secondary syphilis during the previous 12 months without having been treated for syphilis, or

Sex partner of someone with confirmed or presumptive primary or secondary or early latent syphilis during the past 12 months without a history of treatment, or

Reactive non-treponemal and treponemal tests from an individual whose only possible sexual exposure occurred within the preceding 12 months.

Late latent syphilis.

No current clinical signs or symptoms of syphilis, with either of the following:

A reactive non-treponemal test, and a reactive treponemal test, without a prior history of syphilis, or

A past history of treatment for syphilis and a current non-treponemal test titer ≥ four times (2 dilutions) the previous non-treponemal test titer . (For example, current titer of 1:32, previous titer 1:8, 32 = 4 x 8)

AND

Case does *not* have evidence for syphilis acquisition within the past 12 months. (See Early Latent Syphilis.)

Late syphilis with clinical manifestations other than neurosyphilis.

Characteristic abnormalities or lesions of the cardiovascular system, skin, bone or other structures with a reactive treponemal test, in the absence of other known causes of these abnormalities, and without CSF abnormalities and clinical signs or symptoms consistent with neurosyphilis.

3.3 Suspect Case (not reportable to Oregon Health Division)

Primary syphilis. A clinically-compatible case without laboratory or serologic confirmation. In this instance a blood test for syphilis may have been done, but it is possible that there hasn't been time for an antibody response, so the non-treponemal and treponemal tests may be nonreactive. Confidence is strengthened if the case is related epidemiologically to a known early syphilis infection.

Secondary syphilis. A clinically-compatible case without laboratory or serologic confirmation. Because blood tests for syphilis tend to be almost 100% sensitive during the secondary stage, a suspect case diagnosis should be considered only after carefully weighing all the evidence. Confidence is strengthened if the

suspect case is related epidemiologically to a known early syphilis infection.

(Exposed sexual contacts who can be located should be treated "preventively" with the same treatment that would be used for a confirmed or presumptive case of primary or secondary syphilis (§2.7). Case reports needn't be completed for suspect or preventively treated cases though information about sexual contacts to confirmed cases—including dates and doses of preventive treatment should be collected and recorded as described below (§4.3). If laboratory or serologic evidence of *T. pallidum* infection subsequently becomes available for a suspect case, a case report should be completed and the case recorded as confirmed or presumptive as described.)

3.4 Services Available at the Oregon State Public Health Laboratory (OSPHL)

OSPHL performs RPR and FTA-ABS testing of serum. (Typically these are done in batches; current practice is to run the batches on Tuesday.) Contact the laboratory with questions, 503-693-4100.

(Multnomah County Health Department performs dark-field microscopy. Successful visualization of spirochetes such as *T. pallidum* requires vigorous abrasion of the suspected syphilis lesion with immediate application of exudate to a microscope slide and immediate microscopy on site by an experienced dark-field microscopist. If you are seeing a patient with a lesion consistent with primary or secondary syphilis, would like to have dark field examination done, and it is feasible to send the patient to Multnomah County Health Department examination and dark-field microscopy without unnecessarily delaying treatment, contact the Multnomah County Sexually Transmitted Disease Clinic to arrange for the case to be examined. [503-988-3700])

4. ROUTINE CASE INVESTIGATION

4.1 Provider Interview

Contact the health care provider to verify treatment, complete missing, ambiguous, or erroneous elements of the initial case report and inform the provider that you or another public health professional will contact the case-patient directly for interview. A provider interview can be done by telephone, or paper case report forms can be faxed or delivered online for completion by the provider.

4.2 Patient Interview

A confidential interview should be attempted for all presumptive and confirmed cases. Client privacy should be carefully guarded and ensured, and confidentiality of information preserved throughout the interview and case investigation. Telephone and face-to-face approaches are acceptable. Electronic communication such as text and e-mail might be acceptable alternatives if confidentiality, privacy and security can be reasonably assured. Check with a manager or LHD administrator for guidance about permissibility of these alternative electronic communication methods for interviewing syphilis cases. Some patients are reluctant to disclose or not forthcoming about pertinent information about sex partners during the initial interview. In these circumstances, consider second or even third interviews ("re-interviews"). Often patients who are mistrustful, distracted, or simply adapting to their diagnosis will provide more actionable information when they are re-interviewed in a confidential and respectful way. Repeat interviews can be particularly important when women of childbearing age are believed to have been exposed in an effort to prevent congenital syphilis.

In cases where the client is aged <13 years, speak with the parent or legal guardian first. Exercise professional judgment about the need to interview the child separately or in the presence of the parent or guardian.

4.3 Managing Sexual Partners

One should attempt to identify, interview, examine, and test all sex partners of the case within the appropriate interview period for the stage of syphilis (Table, *infra*). Sex partners exposed within 3 weeks of interview should be treated "preventively," since serologic tests will not reliably be positive if the partner is infected. Other sex partners should be treated "preventively" if the partner is likely to be difficult to find or is expected to have difficulty returning for results of testing and treatment if indicated. If a client has not had sex within the interview period, the most recent sex partner should be examined and tested if possible, and treated based on test results.

Long term sex partners of cases with late latent or late syphilis should be offered testing.

Interview periods by syphilis stage*

Stage	Interview Period
Primary	90 days before date of onset of primary lesion through date of treatment
Secondary	6.5 months before date of onset of secondary symptoms through date of treatment
Early latent	1 year before start of treatment

*Attempts should be made to interview, examine, test and treat "preventively" partners exposed during the appropriate interview period.

During the confidential interview, ask cases with early syphilis for the names and contact information of everyone with whom the case has had sex within the appropriate interview period (Table). If the case denies any sex partners during the interview period, record the name and contact information for the most recent sex partner regardless of the interval since most recent sexual contact. Remember to collect from the case if known: the partner's nicknames, address, telephone numbers including cell phones, e-mail addresses, social network sites where patient meets partners along with usernames, race, sex, age, primary language spoken and earliest and most recent dates of sexual contact (regardless of condom use) for each sexual partner recorded.

Visual case analysis (VCA) is a tool that can sometimes be quite helpful in constraining the most likely period during which the case was inoculated and the periods during which the case was most likely to have been infectious. When used for each case within a related cluster of cases, it can help identify the most likely source of infection of each case. In circumstances where a case's inoculation occurred during a peiod which no other member of teh cluster was highly infectious, VCA can highlight that a yet unrecognized case or cases are still to be identifed. Instructions and forms for VCA are available on the communicable disease forms web page under "Syphlis" (http://public.health.oregon.gov/DiseasesConditions/CommunicableDisease/ReportingCommunicableDisease/ReportingForms/). Contact the Oregon STD Program if you'd like assistance with visual case analysis.

Using available information, named sexual contacts should be contacted within 2 working days of the initial case interview by telephone, field (in-person) visit, or other method, and referred to their LHD or another health care provider for evaluation, testing, and treatment. Generally, LHD staff should try to contact the sex partner 3 times before determining that the partner cannot be located. Attempts should be made to contact the partner on alternate days and times of day. When possible, alternate contact method should also be tried. For example, if telephone calls have not been successful, an field (in-person) visit should be considered. If the client prefers to refer the partner, health department staff should determine how they will verify that the partner has been examined or treated. If the contact's treatment cannot be verified within a reasonable time frame (2–5 days), one should attempt to notify and refer the partner for examination and treatment. If locating information is not available for the sex partner, health department staff should call or contact the client for additional information.

When a partner is reached, all outstanding personal information indicated by the "Contacts" tab of the Orpheus case entry form or on the contacts section of the paper form not previously provided by the health care provider should be collected and any that the health care provider reported should be confirmed. The date and outcome of each attempt to interview each partner should be recorded along with the dates and results of any laboratory tests conducted and the dates and details of any presumptive treatment or treatment of laboratory-confirmed infection. When the attempt to notify and treat the partner have been completed the date and outcome (disposition) of the efforts (e.g., "infected, brought to treatment," "unable to locate," "refused preventive treatment," etc.) should be recorded and any additional useful information collected retained.

In some circumstances, such as a local outbreak or widespread cluster of cases, it might become useful to identify and test or treat friends of cases and members of the same social or sexual network. If you collect information about people who are friends or members of the same sexual or social network for purposes of testing or treatment, these too can be listed with other contacts.

The "Lot System" is a traditional sexually transmitted disease investigation tool. When records were kept on paper, a "lot" represented a single folder containing all records related to a cluster of related cases with a goal of making all information related to an investigation available to all responsible workers for use in

interview or re-interview, treatment or followup of cases, partners or associates. Orpheus provides a mechanism to create lots and to assign patients to lots (§4.4). Lots can be assigned for any "logical" reason, for example: 1) patients are related, i.e., they name one another as sex partners or are linked through clustering or 2) cases share something in common, such as working for the same company or living in the same apartment building.

4.4 Documentation

If using Orpheus:

Basic, Risk and Clinical and Follow-up tabs.

Enter information collected from the client into the appropriate areas of the Orpheus case report interface — Basic, Risk and Clinical and Follow-up tabs.

If the client provides personal (non-clinical) information such as demographic or sexual exposure history that contradicts information collected from health care provider/s, overwrite the provider response with the client response and make a note of the change in the notes section of the Orpheus case report.

Contacts tab:

Record information about contacts directly into the "Contacts" and related sub-tabs of the case entry interface. Use the "+ Contact" button on the "Contacts" tab of the Orpheus case report to add each new contact. Alternatively, you can record the contact information on the paper case report form for later transfer into Orpheus, or into your local database. This list should include all named contacts within the appropriate interview period (Table, p. 9) including those from whom the client might have acquired infection and others whom the client might have exposed. If you have decided to collect information about associates and sex partners named by others, record their information here too. Record the type of contact (Table *infra*) in the field labeled 'Referral basis.' Record the date and final outcome ('disposition;' Table *infra)* of your efforts in the "Contacts" tab of the case entry form. Be sure that the name of the partner about whom you wish to enter information has been highlighted in the right side of the "Contacts" tab before entering data in any of the sub-tabs.

Contact Type Codes

Disposition code	Use
Partners	
P-1	Sex partner
P-2	Needle partner
P-3	Sex and needle partner
"Suspects"	
S-1	Named by this case patient; has symptoms suggestive of disease
S-2	Named by this case patient; is a sex partner of *another* person who is known to be infected
S-3	Named by this case patient; needs exam; not S-2 or S-3
"Associates"	
A-1	Named by someone who is not infected; has symptoms suggestive of disease
A-2	Named by someone who is not infected; is a sex partner of someone who is infected
A-3	Named by someone who is not infected; could benefit from exam; not A-2 or A3

Disposition Codes for Sex Partners and Associates

Disposition code	Use
A - Preventive Therapy	Sex partner or associate of case, treated, no treponemal or non-treponemal test available
B - Refused Preventive Therapy	Sex partner or associate of case, refused treatment, no treponemal or non-treponemal test available
C - Infected, Brought to Treatment	Sex partner or associate meets probable or confirmed case definition (any stage), treated.
D - Infected, Not Treated	Sex partner or associate meets probable or confirmed case definition (any stage), not treated (e.g. refused, lost to follow-up).
E - Previously Treated for this Infection	Sex partner or associate meets probable or confirmed case definition (any stage), treated by another healthcare provider prior to interview.
F - Not Infected	Serologic tests results available for sex partner or associate and not consistent with probable or confirmed case definition (any stage).
G - Insufficient Information to Begin Investigation	Named suspect or associate without sufficient available information (such as telephone, address, or email) to attempt to contact.
H - Unable to locate	Attempted but unable to locate sex partner or associate.
J - Located, Refused Examination	Successfully located sex partner or associate, but refused testing or treatment.
K - Out of Jurisdiction	Sex partner or associate resides in another state, country or county.
L - Other	Outcome of attempt to locate other than listed elsewhere in table.
M - Reverse Contact Link	Sex partner or associate also meets probable or confirmed case definition (any stage) and is likely source to current case. In this circumstance laboratory and treatment outcome is stored with the sex partner or associate's case information. This code is used to avoid "double counting" partners who are "reciprocally listed" on cases for which they were the source.

Demographic sub-tab:

Enter partner information in the “Demographics” sub-tab of the “Contacts” tab.

Exposure:

Record the date of the first sexual encounter between this partner and the client and the date of the most recent encounter in the “Exposure” sub-tab of the “Contacts” tab. Record the outcome of efforts to contact the partner in the exposure sub-tab.

Notes sub-tab:

Record the date and outcome of each attempt to interview each partner and record this information in the “Notes” sub-tab of the “Contacts” tab of the Orpheus case entry interface. Retain any useful information in the “Notes” sub-tab of the “Contacts” tab of the Orpheus case entry form.

Labs & Treatment sub-tab:

Record the dates and results of any laboratory tests conducted and the dates and details of any presumptive treatment or treatment of laboratory-confirmed infection in the “Labs & Treatment” sub-tab.

Epilinks sub-tab (lots):

If you wish to assign a lot number (§4.3) to each case within a logical group or cluster to facilitate investigation, contact the STD Control Program (971-673-0153) to request that a lot be assigned. To assign a case to a lot, go to the "Epilinks" sub-tab and select the assigned lot number from the drop down list.

5. CONTROLLING FURTHER SPREAD

5.1 Education

During the interview, clients with early syphilis (primary, secondary or early latent) should be counseled to complete all recommended treatment, avoid sex until treatment has been completed and any sores or rashes have resolved, avoid sex with untreated sex partners until they too have been treated and their sores or rashes resolved, and to use condoms to reduce the risk of acquiring sexually transmitted infections in the future. Clearly other behaviors associated with sexually transmitted disease such as multiple concurrent, or anonymous sex partners should be discouraged, but to be effective, counseling should be personalized to the client by taking a "client-centered" approach. In general, sexually transmitted disease interviews involve a single encounter with the client, so the focus of the interview, by necessity, must be fairly narrow. Give attention to those behaviors that the client seems willing or able to change.

5.2 Case Follow-up

Every individual with a reported case of syphilis should be advised to seek medical attention for persistent symptoms and to undergo clinical evaluation and serologic testing (non-treponemal test, typically RPR) at 6 months and 12 months after treatment. If the case was treated with an alternative to penicillin because of allergy or other reason, serologic follow-up should begin at 3 months after treatement. In circumstances where adherence to follow-up recommendations is in doubt or access to follow-up might be limited, some settings elect to conduct earlier follow-up testing at 2 and 3 months. (Recommended follow-up intervals for serologic testing for pregnant women and individuals who also have HIV infection are different [§6.1 & §6.2].)

Treatment failure should be assumed and re-treatment initiated if a case exhibits persistent or recurrent signs or symptoms or sustains a fourfold (2 dilutions) increase in non-treponemal test titer compared with titer at the time of treatment. Such cases should also be re-evaluated for HIV infection and undergo a cerebrospinal fluid evaluation.

Failure of non-treponemal test titers to decline fourfold (2 dilutions) within 6–12 months after therapy might be indicative of treatment failure, though some people with successful treatment will not manifest the 2 dilution decline in titer. If titers do not decline, patients should receive additional clinical and serologic follow-up, and consideration given to cerebrospinal fluid examination and re-treatment.

6. MANAGING SPECIAL SITUATIONS

6.1 Case Also Has HIV/AIDS

All persons who have syphilis should be tested for HIV infection and other sexually transmitted infections including gonorrhea and chlamydia. Consider retesting for HIV after 3 months if the first HIV test is negative.

Though uncommon, unusual serologic responses have been observed among HIV-infected persons who have syphilis. Most commonly, serologic titers have been higher than expected, but false negative serologic tests and delayed appearance of antibodies have been reported. Serologic titers should be interpreted in the usual manner for diagnosis and treatment of *T. pallidum* infection.

Unless neurologic symptoms are present, cerebrospinal fluid examination is not necessary in individuals with HIV and syphilis.

HIV-infected individuals with syphilis should be treated with the same regimens recommended for HIV-negative individuals.

Compared with HIV-negative individuals with syphilis, HIV-infected individuals with syphilis might be at increased risk for neurologic complications and might have higher rates of serologic treatment failure.

Follow-up non-treponemal serologic tests should be collected from HIV-infected individuals after treatment for syphilis at 3, 6, 9, 12 and 24 months after syphilis treatment.

Treatment failure in HIV-infected individuals with syphilis should be managed in the same manner as treatment failure in HIV-negative individuals.

6.2 Case is Pregnant

Parenteral penicillin G is the only therapy with documented efficacy for syphilis at any stage during pregnancy. Pregnant women with syphilis who report penicillin allergy should be desensitized and treated with

penicillin.

Pregnant women with reactive non-treponemal (RPR) serologic tests should have confirmatory testing with a treponemal test. Where prenatal care is not optimal or syphilis prevalence is high, treatment should be provided at the time a non-treponemal test is reactive while awaiting results of treponemal tests.

Where prevalence is high or a pregnant woman is believed to be at high risk for syphilis, serologic testing should be performed twice during the third trimester at 28–32 weeks and again at delivery.

Women with reactive treponemal tests (seropositive) should be considered to be infected unless an adequate treatment history is documented clearly in the medical records with decline in non-treponemal serologic titers after treatment.

Jarish-Herxheimer reaction (§6.3) with treatment might precipitate premature labor or fetal distress; women should receive obstetric attention if they note any fever, contractions, or decrease in fetal movements.

Follow-up treponemal serologic tests should be collected at 28–32 weeks gestation and again at delivery, and at 6 and 12 months after treatment. If a woman is believed to be at high risk for reinfection, titers can be checked monthly during pregnancy.

6.3 Jarisch-Herxheimer Reaction

The Jarisch-Herxheimer reaction is an acute febrile reaction frequently accompanied by headache, myalgia, fever, and other symptoms that usually occur within the first 24 hours after the initiation of any therapy for syphilis. Patients should be informed about this possible adverse reaction. The Jarisch-Herxheimer reaction occurs most frequently among patients who have early syphilis, presumably because bacterial burdens are higher during these stages. Antipyretics such as acetaminophen or non-steroidal anti-inflammatories like ibuprofen or aspirin can be used to manage symptoms, but they have not been proven to prevent this reaction. The Jarisch-Herxheimer reaction might induce early labor or cause fetal distress in pregnant women, but this should not prevent or delay therapy.

6.4 Outbreak Situations

If a higher than expected number of early syphilis cases occur and are clustered in time and place, consider preventive treatment of friends and associates of cases who are not named sex partners. Contact the Oregon STD Control Program to discuss expanded use of preventive treatment under such circumstances.

Consider circulating advisories to local physicians and other clinicians to inform them of local increases in incidence of syphilis and advise them to heighten their consideration of syphilis in a patient with consistent complaints or history and lower their threshold for screening asymptomatic patients for syphilis.

In communities and populations where syphilis prevalence is high, serologic testing of pregnant women should be carred out at the initial prenatal visit, at 28–32 weeks gestation, and again at delivery. Serologic titers can be checked monthly in women at high risk for reinfection after treatment or in geographic areas in which prevalence of syphilis is high.

If prevalence of syphilis in a specific population, such as men who have sex with men or persons with HIV infection, annual or more frequent screening with non-treponemal test such as RPR is appropriate.

7. APPLICABLE RULES

6.1 Reporting

OAR 333-018-0000 through 333-018-0020

6.2 Investigation

OAR 333-019-0000 and 333-019-0002

8. OTHER RESOURCES

Centers for Disease Control and Prevention. 2010 STD Treatment Guidelines. 2012 (Update). Available at www.cdc.gov/STD/treatment/2010

Centers for Disease Control and Prevention. The National Electronic Telecommunications System for Surveillance (NETSS) CDC Implementation Plan for STD Surveillance Data. January 2014. Available at www.cdc.gov/std/Program/STD-NETSSIMPLN-V4_2014Jan.pdf.

Centers for Disease Control and Prevention. STD Surveillance Case Definitions. Available at www.cdc.

gov/std/stats10/app-casedef.htm

9. UPDATE LOG

April 2014. Created. (Schafer)

June 2014. Revised after comments from CLHO. Fixed typos and errors. Added screening alogorithm graphic. (Schafer)