GENETRACK Diagnostics

Syphilis

WHAT IS SYPHILIS?

Syphilis is a sexually transmitted disease caused by the bacterium *Treponema pallidum* subspecies *pallidum*. It has been called "The Great Pretender", as symptoms can resemble other diseases. If syphilis is untreated it can cause serious health complications.

TRANSMISSION

The syphilis-causing bacterium is able to pass through intact mucous membranes or compromised skin, and is primarily transmitted during sexual contact, or during pregnancy or childbirth from an infected mother to her infant. Transmission can occur by kissing near a lesion (chancre), and through oral, vaginal, and anal sex. The majority of cases in the United States (60%) occur in men who have sex with men, with 20% of these cases transmitted through oral sex alone (1).

Syphilis transmission through sharing needles appears to be limited (1), and transmission does not often occur through sharing of utensils, or contaminated toilet seats, hot tubs etc. (2). Condom use helps reduce the risk of syphilis transmission. However, if the condom does not cover a syphilis chancre, transmission can still occur during sexual contact. Syphilis infections are associated with a 2- to 5-fold increased risk of acquiring HIV, particularly when syphilis-associated genital sores are present (3).

Syphilis during pregnancy is associated with miscarriage, stillbirth, or infant death shortly after delivery in up to 40% of cases. Congenital syphilis occurs when an infected pregnant woman passes syphilis to her baby during pregnancy. For infected infants, treatment must begin immediately to prevent developmental delays, seizures, and other fatal complications (4).

SYMPTOMS

Primary Stage

A skin lesion, called a chancre, is the first sign of a syphilis infection. Chancres appear at the location where *T. pallidum* entered the body anytime from 10-90 days after infection, with an average onset of 21 days post-infection. In approximately 40% of cases, only a single, firm, round, and painless chancre of approximately 0.3-3 cm occurs (1). In others, multiple chancres appear that may be painful and tender. Chancres generally occur on the cervix for women (44% of cases), penis for heterosexual men (99%), and anally and rectally for men who have sex with men (34%) (5). In 80% of cases, lymph node swelling in the area of the infection also occurs (1). Chancres last for three to six weeks and heal whether or not treatment is received. If untreated, the infection progresses to the secondary stage (2).

Secondary Stage

Skin rashes and/or lesions in the mouth, vagina, or anus occur during the secondary stage of infection. These may appear when the primary chancre is healing or several weeks after it has healed. In addition, many individuals who present with the later secondary symptoms either do not develop a chancre or the chancre is unnoticed (6). Syphilis rashes vary in appearance, and can include rough red spots on the palms, large, raised, gray or white lesions (condyloma lata) in the mouth, underarm or groin, or rashes that are so faint that they are unnoticed (1). Additional symptoms in the secondary stage can include fever, sore throat, hair loss, weight loss, swollen lymph glands, headaches, muscle aches, and fatigue. Rare complications include inflammation of the liver, joints, and optic nerve, kidney disease, and interstitial keratitis. Like the primary symptoms, secondary symptoms will also disappear whether or not treatment is received. However, the syphilis infection will progress to the latent stage if adequate treatment does not occur (2).

Latent Stage

There are no visible signs or symptoms of syphilis during the latent (hidden) stage. However, syphilis-causing bacteria (*T. pallidum*) are still present. In the early latent phase (less than two years after original infection), transmission can still occur as up to 25% of individuals can develop a recurrent secondary infection (7). Individuals are not as infectious in the late latent phase (more than two years after the original infection). The latent stage can last for many years, with 15-40% of untreated individuals developing tertiary syphilis (8).

Tertiary Stage

In rare cases, the latent stage progresses to a potentially fatal tertiary stage. This can occur 10-30 years or more after acquiring a syphilis infection. Multiple different organ systems can be affected including the brain, nerves, eyes, heart, liver, bones, and joints. The associated symptoms vary depending on the affected body parts.

Neurosyphilis and Ocular Syphilis

At any stage of infection, *T. pallidum* can invade the nervous system causing neurosyphilis, or the eyes causing ocular syphilis. Neurosyphilis symptoms can include headaches, paralysis, dementia, sensory deficits, and altered behavior. Ocular syphilis can cause vision changes, decreased visual acuity, and blindness (2).

PREVALENCE

In 2018, there were 115,045 new syphilis cases reported in the United States. Primary and secondary syphilis (the earliest and most transmissible stages) accounted for 35,063 of these cases, with the majority occurring in gay, bisexual and other men who have sex with men. Congenital syphilis (transmitted from an infected pregnant woman to her infant) was reported in 1,306 cases in 2018, with a significantly higher rate among black and Hispanic mothers compared to white mothers (2).

RISK POPULATIONS

The primary high-risk populations for syphilis are men who have sex with men, and HIV-positive individuals. Other high-risk populations include individuals who have been incarcerated, sex workers, and members of certain racial groups with higher syphilis incidence (blacks, Hispanics, Native Hawaiian/Pacific Islander, American Indian/Alaska Native) (9).

DIAGNOSIS

Syphilis diagnosis is by two types of laboratory analyses of a blood sample – nontreponemal and treponemal tests. Both are required for an accurate diagnosis.

Nontreponemal tests are a useful screening option, but are not specific for syphilis, and can produce false-positive results. Any reactive samples in a nontreponemal test must also be analyzed with a treponemal test to confirm a syphilis diagnosis.

Treponemal tests detect antibodies that are specific to syphilis, but these antibodies usually remain detectable for life even after successful treatment; hence these tests identify both current and past, resolved infections (10).

The traditional 'classic' testing approach requires a nontreponemal test

followed by a treponemal test. However, advances in testing techniques now mean that the 'reverse screening' approach (treponemal then nontreponemal) is more commonly used. This package insert describes a treponemal assay. Additional testing with a nontreponemal assay should be conducted on all samples that are reactive in this treponemal assay.

TREATMENT

Primary, secondary, and early latent stage syphilis (infection within 2 years) is treated with a single intramuscular dose of Benzathine penicillin G. Late latent stage syphilis (more than 2 years after original infection) requires three intramuscular doses of Benzathine penicillin G at weekly intervals. Neurosyphilis and ocular syphilis are treated with Acqueous crystalline penicillin G for 10-14 days. Although treatment cures the disease and prevents disease progression, it does not repair any tissue damage that has already occurred, and does not prevent reinfection at a later date. There is currently no effective vaccine available for syphilis (11).

TESTING RECOMMENDATIONS

The CDC recommends syphilis testing for anyone showing symptoms that are suggestive of a syphilis infection. All individuals with an oral, anal, or vaginal sexual partner with a recent syphilis diagnosis should also be tested. Routine testing should also occur in any individuals who are pregnant, and up to every three months in sexually active HIV-positive individuals, and in sexually active men who have sex with men (9).

TEST PROCEDURE

Correct specimen collection and handling is required for optimal assay performance.

This test requires a blood sample from a finger prick. All supplies for sample collection are provided in this kit. First wash and dry hands. Warm hands aid in blood collection. Clean the finger prick site with the alcohol swab and allow to air dry. Use the provided lancet to puncture the skin in one quick, continuous and deliberate stroke. Wipe away the first drop of blood (as it may be contaminated with tissue fluid or skin debris). Massage finger to increase blood flow at the puncture site and hold in a position that gravity facilitates the collection of blood on the fingertip. Transfer the blood to the blood collection card or blood collection tube (microtainer).

Avoid squeezing or 'milking' the finger excessively. If blood flow stops, perform a second skin puncture on another finger if more blood is required.

Dispose of all sharps safely and return sample to the laboratory in the provided prepaid return shipping envelope.

Upon receipt at the laboratory, the blood sample is analyzed by the fully automated Alinity i Syphilis TP chemiluminescent microparticle immunoassay on the Alinity ci series analyzer. This assay detects antibodies to recombinant antigens representing TpN15, TpN17, and TpN47 of the *T. pallidum* genome. The amount of syphilis antibodies in the blood sample is measured in relative light units by a chemiluminescent reaction.

SPECIAL INSTRUCTIONS

No additional preparation or dietary/medication changes are required before collecting a sample for testing.

TEST INTERPRETATION

A reactive result indicates that syphilis antibodies are present in the specimen tested. This result does not distinguish between current infections and past treated infections. Additional testing with a nontreponemal assay should be conducted on all samples that are reactive in this treponemal assay.

A nonreactive result indicates that syphilis antibodies were not detected in the specimen tested. This may be due to sample collection during the window period post-exposure. Retesting is recommended if potential exposure to syphilis has occurred or other laboratory or clinical information indicates a syphilis infection.

An indeterminate result indicates that a new specimen should be tested.

DISCLAIMERS/LIMITATIONS

This report is not intended for use in medico-legal applications. These results are intended for screening for syphilis antibodies and should be interpreted in conjunction with other laboratory and clinical information.

Correct specimen collection and handling is required for optimal assay performance. The assay is unaffected by triglycerides ≤ 3000 mg/dL, bilirubin ≤ 20 mg/dL, protein ≤ 12 g/dL, and hemoglobin ≤ 500 mg/dL.

A negative (nonreactive) result does not exclude the possibility of infection. False-negative test results may occur due to specimen collection in the very early stage of infection.

A reactive result does not mean that an individual definitely has syphilis, as a reactive result will occur in samples from previously treated individuals. Additional testing with a nontreponemal assay is required for confirmation.

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