BayCare Best Practice Medical Guideline

Lab Evaluation for work-up of Syphilis

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BayCare Medical Standard

This BayCare Medical Guideline utilizes an evidence-based approach to the lab evaluation of possible Syphilis with a particular focus on the so-called **Reverse Algorithm in evaluating suspected cases and the use of a new test titled "Syphilis screening".**

Purpose

Syphilis is a clinical disease caused by the bacterial spirochete, *Treponema pallidum*. It is classified as a sexually transmitted infection and if it is not treated early, it can lead to a chronic infection. Primary syphilis usually includes a painless genital ulcer or chancre. Secondary syphilis typically includes weakness, lymphadenopathy, fever, and a skin rash. Tertiary syphilis involves more systemic and serious complications that involve inflammatory lesions in the skin, bone, cardiovascular and nervous systems. Early detection and treatment is important because the long-term clinical effects can be significant. Unfortunately, the clinical signs and symptoms can be quite broad and general. In addition, laboratory testing for syphilis can often lead to confusion for providers.

Procedure

What are the benefits of using the Reverse Algorithm? Why did BayCare Laboratories make the switch to the Reverse Algorithm?

The traditional algorithm includes a non-treponemal test such RPR as the primary/screening test and a treponemal test such as FTA-ABS as the secondary/confirmatory test. The reverse algorithm switches this order. Major advantages of starting with a treponemal test include: high throughput/automated testing, objective results, and high sensitivity/specificity through all stages of syphilis, even in low-prevalence areas. This assay is more expensive, however total healthcare costs should be less due to a higher number of patients being treated as well an increase in identification of at-risk sexual partners.

The new test name is: **Syphilis Screening** (Initial Test – Treponema Ab reflex to RPR reflex to TP Confirmation).

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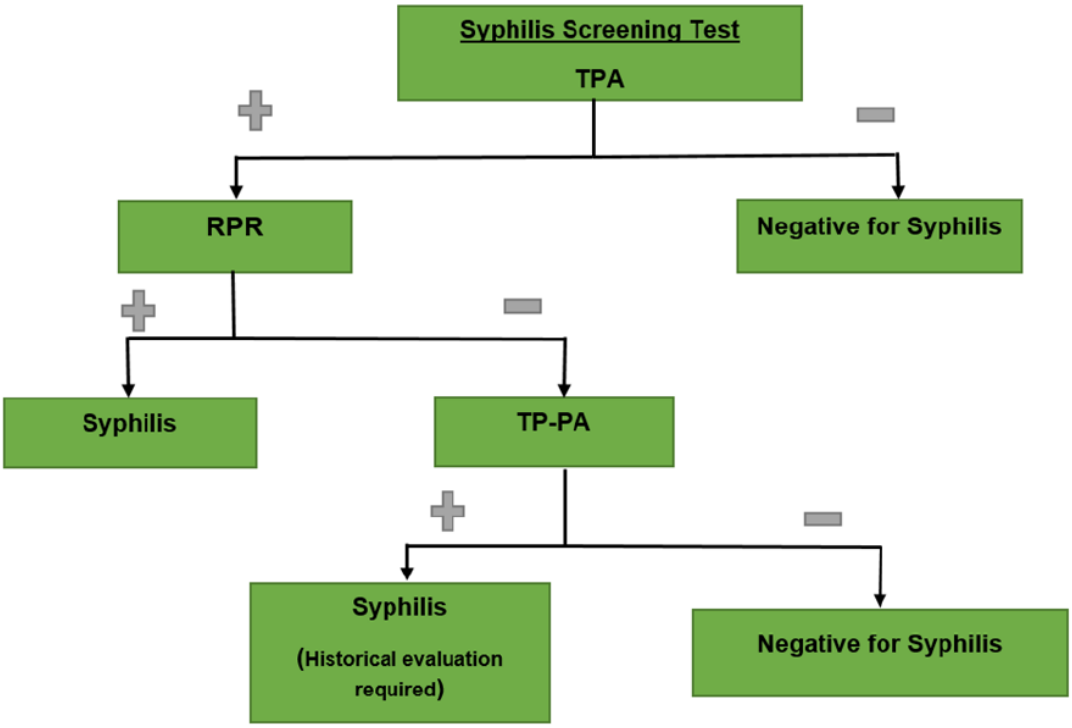
Syphilis Diagnosis Flow Chart (2)



What about discrepant results?

If the treponemal Ab test is negative, the process stops here and the patient is considered negative for syphilis. If the treponemal Ab test is positive, it will reflex to the RPR test and if positive, it will confirm the result and the patient will be considered positive for syphilis. If the treponemal and the RPR test are discrepant, it will reflex to a 3rd test that is sent to a reference laboratory, the ***Treponema pallidum* Particle Agglutination (TP-PA)** assay, which will resolve the discrepancy. TP-PA is a treponemal specific test that involves a long incubation period to test for agglutination between patient serum with syphilis antibodies and commercial syphilis antigens in a microplate well.

If a patient has a positive screening treponemal test, a negative RPR and a positive TP-PA, this likely represents a possible past successfully treated syphilis case as well possible early or latent syphilis, which would require a thorough review of the patient history (2). If a sample is positive for a treponemal test and negative for both the RPR and TP-PA, this likely represents a false positive treponemal screen and no further or repeat testing should be needed unless there is a strong clinical suspicion (2).

Review of Laboratory Testing Options for Syphilis

Dark Field Microscopy: this method involves direct visualize of the spirochete under the microscope. While this is a traditional method, it is fraught with many issues including proper collection of skin lesions, proper transport to a laboratory, increased turn-around-time (TAT) and the skill of the observer to make the diagnosis. This method is quite rare in most laboratories.

Molecular Methods: while molecular tests such as PCR have revolutionized other areas of microbial detection (Strep A, COVID-19, Influenza A, etc), this has not proven to be true for syphilis, especially in later stages. One study showed that the **sensitivity of PCR in secondary syphilis is 50% (1).**

Serology Tests: serology testing is the gold standard for the diagnosis of syphilis and as such it is used by BayCare Laboratories. Serology tests can be divided into 2 general categories: **1). Non-treponemal serology** and **2). Treponemal serology**

What are Non-treponemal serology tests?
These are serology tests in serum or CSF against cardiolipin-cholesterol-lecithin antigens, which are not specific to syphilis, but they are commonly seen in syphilis patients. The 2 well known examples are: **Rapid Plasma Reagin (RPR)** and **Venereal Disease Research Laboratory (VDRL).**

What are Treponemal serology tests?
These are serology tests that detect the patient's immune response to *T. pallidum* by measuring IgM and/or IgG, just like any other infectious disease serology test. Well known examples of these methods include: **Fluorescent Treponemal Antibody Absorption (FTA-ABS), Treponema Pallidum Particle Agglutination (TP-PA)** and a standard enzyme immunoassay.

What are the pros and cons of the Non-treponemal vs treponemal tests?

Test	Pro	Con
Non-Treponemal	Inexpensive High sensitivity in early infection Easy to perform Good monitor for treatment	Not specific for syphilis Less reliable in low prevalence areas and in late stage infections Subjective test Longer turn-around-times (TAT)
Treponemal	Specific for syphilis Faster TAT Automated/High throughput Objective result reporting	Expensive Less established as primary screening method

What about monitoring known syphilis positive patients or newborns from known syphilis positive mothers?
If a patient has a known diagnosis of syphilis, the preferred laboratory test for monitoring is an RPR titer.

The test name is: **Syphilis Titer** (RPR Titer – Only for monitoring known Syphilis positives or newborns)

Epidemiology in Florida
According to a recent article from the Florida Department of Health, in 2008-2010 there were 3,266 syphilis cases in Florida and in 2013-2015 there were 5,340 cases, which represents a 63% increase (3). This number comes from the traditional algorithm. The authors analyzed the diagnostic yield using the reverse algorithm by looking at a specific set of patients from March 8, 2017 to April 5, 2017 and they found that the **sensitivity of the traditional algorithm was 72.9%** and the **sensitivity of the reverse algorithm was 98.3%** (3). This study is similar to many other studies from other public health departments and it is a major impetus for many laboratories making the switch to the reverse algorithm.

In addition to many hospital laboratories such as BayCare Laboratories switching to the reverse algorithm, two well-known national examples include Quest Diagnostics and Mayo Clinic Laboratories.

References

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