Public Health Ontario | Santé publique Ontario

Labstract – October 2017

Syphilis *(Treponema pallidum)* Serologic Testing Update - Changes to Screening test and Algorithm

Audience

Health Care Providers who order syphilis serology testing.

Overview

Effective October 22, 2017:

- Public Health Ontario Laboratory (PHOL) is changing the syphilis screening serology testing methodology on serum from Chemiluminescent Immunoassay (CLIA) to Chemiluminescence Microparticle Immunoassay (CMIA). The change is the result of an evaluation of several Health Canada approved syphilis serologic assays.
- The syphilis (*Treponema pallidum*) serology algorithm will no longer include Fluorescent Treponema Antibody Absorbance assay (FTA- ABS) that is currently used as the third confirmatory test.

Background Information

Syphilis is a disease caused by infection with the bacterium *Treponema pallidum* (TP). Route of transmission is through sexual contact, congenital infection or rarely blood transfusion. Syphilis typically follows a progression of stages including primary, secondary, latent and rarely tertiary stages that can last for weeks, months or even years. Serologic testing is the primary method for routine diagnosis and monitoring of treatment.

Change to Syphilis Screening Serology Testing Methodology

Results will be reported as either 'Reactive' or 'Non-reactive' for the detection of antibodies (IgG and IgM) to *Treponema pallidum* (TP) in human serum using the new CMIA qualitative test. The manufacturer's stated performance claims are are ≥ 99.0% for each sensitivity and specificity.

False positive results can occur and are dependent upon the characteristics of the population tested. Other infections (including HIV), rheumatological illness, intravenous drug use, pregnancy and recent immunization may cause a false positive result. False negative results may arise at the very early stage of infection. Confirmatory testing is performed to clarify a reactive serological screen test result.

Change to the Syphilis Serology Test Algorithm

An initial screening with a treponemal serology test is followed by a non-treponemal Rapid Plasma Reagin (RPR) test and a treponemal test, *Treponema pallidum* Particle Agglutination (TPPA). If both RPR and TPPA tests fail to confirm a reactive screening result, another treponemal test, Fluorescent Treponemal Antibody Absorption (FTA-ABS) has been performed.

The FTA-ABS test will be discontinued for syphilis confirmatory serologic testing for the following reasons:

1. Limited benefit of the FTA-ABS test as a means of resolving inconclusive confirmatory results and overall interpretation following RPR and TPPA assays.
2. To align the PHOL syphilis serology algorithm with the Canadian and CDC best practice standards and recommended testing guidelines[1,2,3].
3. To improve turnaround time for reporting of syphilis serology results.

Interpretation of the Most Common Results Using the Revised Syphilis Algorithm

Screening Test (CMIA)	Confirmatory Test (RPR)	Confirmatory Test (TPPA)	Possible Interpretations/ Recommendations
Non-reactive	Not tested	Not tested	No confirmatory testing is performed if syphilis screen result is non-reactive • Early incubating syphilis can be non-reactive before antibodies have developed. • If clinical suspicion of early syphilis, suggest single repeat serology in 4 weeks if not repeated already.
Reactive	Reactive	Reactive	Consistent with recent or prior syphilis infection
Reactive	Non- reactive	Reactive	Consistent with recent or prior syphilis infection
Reactive	Non- reactive	Non- Reactive	• Results consistent with false reactive screening test. • Rare alternate interpretations include early syphilis, previously treated, or late latent syphilis. • Repeat serology in 4 weeks if not already repeated.
Reactive	Non-reactive	Indeterminate	Inconclusive syphilis serology results • Possible interpretations include false positive, or early, old treated or untreated syphilis. • Repeat serology in 4 weeks if not already repeated.
Reactive	Reactive	Non- Reactive	Inconclusive syphilis serology results • Possible interpretations include false positive, or early, old treated or untreated syphilis. • Repeat serology in 4 weeks if not already repeated.
Reactive	Reactive	Indeterminate	Consistent with recent or prior syphilis infection

Screening Test (CMIA)	Confirmatory Test (RPR)	Confirmatory Test (TPPA)	Possible Interpretations/ Recommendations
Age < 12 Months Reactive	Reactive	Reactive	• Maternal antibody (can be present in infant for up to 12 months) • Congenital infection • If congenital or early syphilis is suspected, consider ordering repeat serology at the recommended intervals according to the PHAC Canadian Guidelines on Sexually Transmitted Infections, Section 5-10, Table 8(b) (see references)
Age < 12 Months Reactive	Non- reactive	Reactive	• Maternal antibody (can be present in infant for up to 12 months) • Does not rule out congenital infection • If congenital or early syphilis is suspected, consider ordering repeat serology at the recommended intervals according to the PHAC Canadian Guidelines on Sexually Transmitted Infections, Section 5-10, Table 8(b) (see references)

The positive predictive value (PPV) is dependent on the prevalence of the infection in the population being tested. Interpretation of results is best conducted in conjunction with clinical findings.

Specimen collection requirements

Human serum is acceptable for syphilis serology testing. Whole blood should be allowed to clot. Serum separator tubes (SST) are acceptable. Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens. Heat inactivated, haemolysed, icteric, lipemic or microbially contaminated sera are not recommended for testing.

Note: This document does not apply to testing for syphilis in primary lesions and cerebrospinal fluid (CSF). Syphilis testing information for primary lesions and CSF is available at:
http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Syphilis_Chancre_Direct_Fluorescence.aspx;
http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Syphilis_CSF.aspx

Testing Turnaround time (TAT)

TAT may be up to 6 days.

References

1. Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2014 http://www.cdc.gov/std/stats14/ (Accessed on February 06, 2017)

2. Hicks CB, Clement M. Syphilis: Screening and diagnostic testing. In: UpToDate, Hynes NA, Mitty J (Ed), UpToDate, Waltham, MA. (Accessed on April 03, 2017)

3. Levett PN, Fonseca K, Tsang RSW, et al. Canadian Public Health Laboratory Network laboratory (CPHLN) guidelines for the use of serological tests (excluding point-of-care tests) for the diagnosis of syphilis in Canada. Can J Infect Dis Mid Microbiol 2015;26(Suppl A):6A-12A.

4. PHAC Canadian Guidelines on Sexually Transmitted Infections; Section 5-10: Management and Treatment of Specific Infections, Table 8(b) at https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/sexually-transmitted-infections/canadian-guidelines-sexually-transmitted-infections-27.html

For further information

- Contact the PHOL Customer Service Centre at 416-235-6556 or 1-877-604-4567 (toll-free), or by email at CustomerServiceCentre@oahpp.ca
- For PHOL specimen collection information and previous Labstracts, refer to publichealthontario.ca/Labs
- The current version of the PHOL General Test Requisition and other forms are available at publichealthontario.ca/Requisitions
- To subscribe to future Labstracts, email labstracts@oahpp.ca
- To register for Autofax and receive laboratory reports by fax directly from our laboratory information system as soon as they are released, contact the PHOL Customer Service Centre.