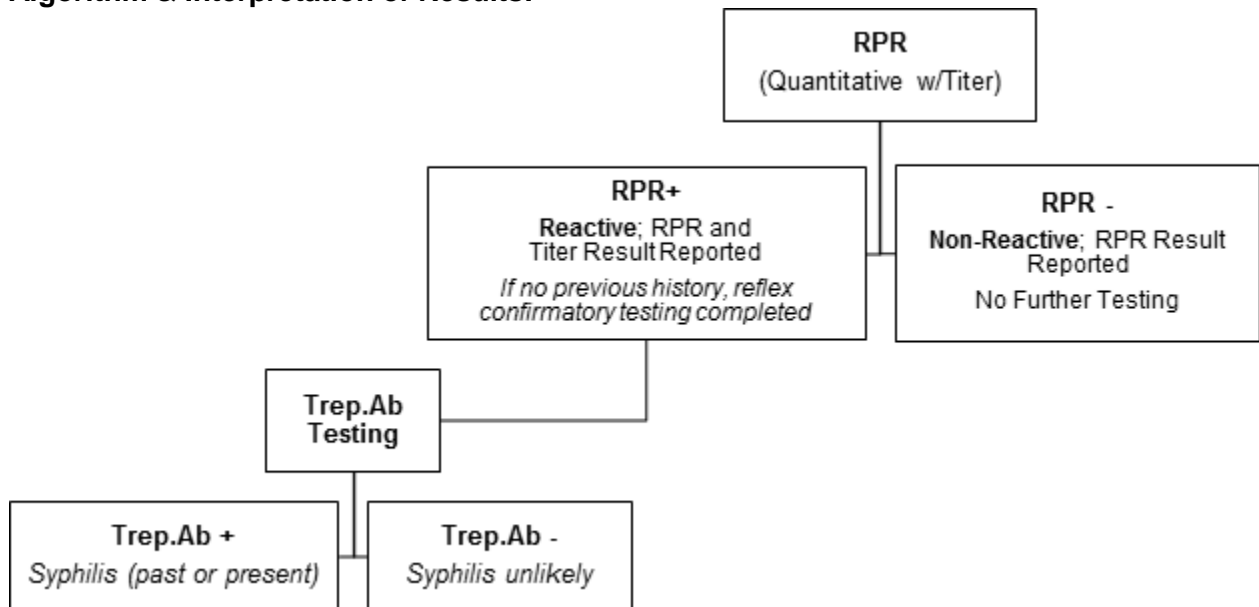


DATE: December 19, 2018  
TO: Attending Medical Staff, House Staff, Nursing, Clinics  
FROM: Dr. Amy Saenger, Dr. Sara Love and Dr. Fred Apple; Clinical Laboratories  
SUBJECT: Clarification of Syphilis Testing Algorithm, Methodology, & Positivity Rates

Effective Tuesday April 8, 2014, in concordance with Infectious Disease, a revised algorithm for syphilis testing was implemented. Presumptive diagnosis of syphilis requires two tests: a non-treponemal (qualitative) and a treponemal (confirmatory) test. Reflex testing using a specific assay to detect total IgG/IgM antibodies to *Treponema pallidum* (Trep.Ab) is performed based on the initial non-treponemal Rapid Plasma Reagin (RPR) results. This algorithm is consistent with the current recommendations by the CDC and the Minnesota Department of Health (MN DOH) for syphilis screening.

**Algorithm & Interpretation of Results:**



Additional caveats in interpretation of serology results are provided below, from the MN DOH.

- Non-Treponemal (RPR) Screening:
  - Non-treponemal antibody titers may correlate with disease activity and are used to follow treatment response.
  - A fourfold change in titer is necessary to demonstrate a clinically significant difference between two non-treponemal test results obtained using the same serologic test.
  - Non-treponemal test titers usually decline after treatment and may become non-reactive over time; however, in some individuals non-treponemal antibodies can persist for a long period of time.
- Treponemal Antibody Testing:

- Individuals with a reactive treponemal test will usually have a reactive test result for a lifetime.
- Treponemal assays do not predict response to treatment and should not be used for this purpose.
- In persons with HIV infection serologic tests are accurate and reliable for diagnosing syphilis and following a patient's response to treatment.
  - However, atypical non-treponemal serologic test results (i.e. unusually high, low, or fluctuating titers) may occur regardless of HIV infection status.
  - When serologic tests do not correspond with clinical findings suggestive of early syphilis, presumptive treatment is recommended for persons at risk for syphilis, and use of other tests (e.g. biopsy and PCR) should be considered.

### Review of Syphilis Algorithm Results at Hennepin Healthcare

The automated Trep.Ab assay has not changed since April, 2016. The RPR testing changed from a qualitative, manual assay to an automated, quantitative test in May, 2018. The RPR reactivity rates, as well as the Trep.Ab confirmation rates, for all Hennepin Healthcare patients tested between June 1 and October 31 in 2017 and 2018 are shown below.

<b>Syphilis Screening (All Patients)</b>				
<b>Date Range</b>	<b>RPR Orders (n)</b>	<b>Reactive RPR</b>	<b>RPR Reactivity Rate</b>	<b>Confirmation Rate (+RPR / +Trep Ab.)</b>
June 1 to Oct 31, 2017	9759	420	4.3%	59.2%
June 1 to Oct 31, 2018	11548	709	6.1%	44.8%

Data were evaluated to examine the discordance between RPR and Trep.Ab results using the traditional screening algorithm. Results were isolated to females under the age of 40 years, an age chosen arbitrarily to mimic a potential OB population.

<b>Syphilis Screening in Females &lt;40 Years</b>					
<b>Date Range</b>	<b>Assay</b>	<b>RPR Orders (n)</b>	<b>Reactive RPR</b>	<b>RPR Reactivity Rate</b>	<b>Confirmation Rate (+RPR / +Trep Ab.)</b>
June 1 – Oct. 31, 2017	RPR (Qualitative)	3834	47	1.23%	60%
June 1 – Oct. 31, 2018	RPR (Automated)	4560	179	3.92%	14%

There are limited data available which evaluate the traditional vs. reverse algorithm syphilis screening in a high-risk OB population. Studies have evaluated traditional vs. reverse screening algorithms in low-risk OB populations and the rate of discordant results between RPR and Trep.Ab testing are similar (50% using traditional algorithm vs. 46% using reverse algorithm).

Overall positivity rates using the reverse algorithm are also directly correlated with prevalence and shown to increase discordant results using the reverse algorithm (Trep.Ab +/RPR- /confirmed false + with second Trep. Test).

Due to the high-risk population we serve, coupled with the known issues with antibody testing during pregnancy, it is unclear that switching to the reverse algorithm will reduce analytical false positive results.

Testing is performed Monday through Saturday.

Please contact Dr. Fred Apple (873-3324), Dr. Amy Saenger (873-8709), Dr. Sara Love (873-2813) or Jennifer Nicholson (Chemistry Supervisor 873-3017) with questions.