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To: All Healthcare Providers

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Re: Change to Reverse Algorithm for Diagnostic Syphilis Testing at ZSFG

Starting January 11th, 2021, the ZSFG Clinical Laboratory will begin using the reverse algorithm for syphilis testing (*Treponema pallidum* infection).

**BACKGROUND**

Initial laboratory evaluation for syphilis includes multi-step testing for antibodies against both non-treponemal and treponemal antigens. The traditional syphilis testing algorithm employs a non-treponemal test screen followed by a reflexive treponemal test confirmation, if initially positive. Introduction of latest-generation treponemal serology assays has allowed for highly sensitive and specific screening for syphilis on an automated platform. In the “reverse algorithm” an automated treponemal antibody test is used as the initial screen, followed by a reflexive non-treponemal test. In discordant cases, a second treponemal antibody test is used to clarify infection status. **By switching to the reverse algorithm, we will continue to provide high-quality testing with faster turnaround time.**

**Syphilis Screening Algorithms**

**Traditional Algorithm**
- Non-treponemal Test (RPR)
  - Reactive
    - Treponemal Test (TP-PA)
      - Reactive
        - Syphilis
      - Non-reactive
        - Negative for Syphilis
  - Non-reactive

**Reverse Algorithm**
- Treponemal Test (Syphilis [*Treponema pallidum*] antibodies)
  - Reactive
    - Non- Treponemal Test (RPR)
      - Reactive
        - Syphilis
      - Non-reactive
        - Negative for Syphilis
  - Non-reactive

**ORDERING AND COLLECTION**

- The name of the syphilis panel of tests used in the reverse algorithm is Syphilis Antibody/RPR Serology.
- For testing after a prior diagnosis of syphilis, RPR alone can be ordered as: “RPR for prior history of syphilis” **This test is not indicated for initial syphilis testing.**
- Acceptable specimen: One gold top gel tube (serum).
- Note that the SF Public Health Laboratory will continue to only offer the traditional syphilis algorithm.

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RESULTS
- In EPIC, the test “Syphilis Antibody/RPR Serology” will include a panel of results for Syphilis (*T. pallidum*) antibodies, RPR, RPR titer, TPPA and interpretive comments.
- Comments will provide laboratory interpretation, including whether additional testing is being reflexively performed or not indicated, and what the combination of results may represent for infection status. Refer to table below.

TURNAROUND TIME
- Syphilis Antibody/RPR serology turnaround after specimen is received: STAT 1 hour; Routine 1-4 hours.
- RPR testing will be run once daily, Monday – Friday, excluding holidays.
- TP-PA testing will be run on Wednesdays.

### Interpretive Guidelines for Reverse Algorithm Testing

<table>
<thead>
<tr>
<th>Syphilis (<em>T. pallidum</em>) antibodies</th>
<th>RPR</th>
<th>TP-PA</th>
<th>Result Comment</th>
<th>Comment Location In EPIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Reactive</td>
<td>Not Indicated</td>
<td>Not Indicated</td>
<td>No laboratory evidence of syphilis. If clinically indicated, retest at a later date.</td>
<td>Under Syphilis (<em>T. pallidum</em>) antibodies</td>
</tr>
<tr>
<td>Equivocal/Reactive</td>
<td>Non-Reactive</td>
<td>Pending</td>
<td>Initial treponemal test positive, with non-treponemal test (RPR) non-reactive. Confirmatory treponemal test (TP-PA) is being reflexively performed. Refer to TP-PA for interpretation of results.</td>
<td>Under RPR</td>
</tr>
<tr>
<td>Equivocal/Reactive</td>
<td>Reactive</td>
<td>Not Indicated</td>
<td>Treponemal and non-treponemal antibodies detected, consistent with current or past syphilis infection.</td>
<td>Under RPR</td>
</tr>
<tr>
<td>Equivocal/Reactive</td>
<td>Non-Reactive</td>
<td>Non-Reactive</td>
<td>Treponemal antibodies not confirmed. Consistent with false positive or potential early syphilis infection. Correlation with clinical history and findings is suggested. If indicated, retest in 2-4 weeks.</td>
<td>Under TP-PA</td>
</tr>
<tr>
<td>Equivocal/Reactive</td>
<td>Non-Reactive</td>
<td>Reactive</td>
<td>Detection of Treponemal antibodies. Consistent with past/treated or potential early syphilis infection. Correlation with clinical history and findings is suggested. If indicated, retest in 2-4 weeks.</td>
<td>Under TP-PA</td>
</tr>
<tr>
<td>Equivocal/Reactive</td>
<td>Non-Reactive</td>
<td>Not Indicated (Previous reactive TPPA)</td>
<td>T.pallidum particle agglutination confirmatory test reactive on specimen from <em>date of previous reactive TPPA</em></td>
<td>Under RPR</td>
</tr>
</tbody>
</table>
INTERPRETATION OF SYPHILIS SEROLOGIES
Determining whether a patient has untreated syphilis and ascertaining the stage of syphilis relies on a combination of clinical history, diagnostic tests and physical examination. When interpreting syphilis tests, a provider should do the following:

1) **Ask:** Have you had a history of syphilis, recent symptoms (e.g. sore or rash), have any of your sex partners been diagnosed with syphilis?
2) **Assess** for risk factors for syphilis
3) **Examine:** Physical examination for ulcers (primary syphilis) or rashes and/or mucocutaneous lesions (secondary syphilis) with attention to the mouth, skin, and anogenital areas.
4) **Call:** To obtain prior RPR titers or syphilis treatment history for patients who live in San Francisco, call SF City Clinic: 415-487-5531.
5) **Consider treatment based on an initial positive Syphilis (T. pallidum) antibodies test (with other tests pending) if the patient does not have a prior history of syphilis and has risk factors for syphilis, or if the patient has signs or symptoms of syphilis or if the patient may be difficult to reach after the visit.

TIPS WHEN EVALUATING A PATIENT WITH POSSIBLE OR CONFIRMED SYPHILIS

- Initiate penicillin therapy--without waiting for laboratory confirmation of the diagnosis--in all patients with symptoms of syphilis and those who report sexual contact with someone who has syphilis; syphilis tests can be falsely negative during the incubation period after exposure.
- Obtain an RPR titer on the day of treatment (if > 48 hour since testing was done) as this establishes a baseline value that is used to determine whether treatment was effective. RPRs can fluctuate several fold within several days.
- Obtain a pregnancy test in all women diagnosed with syphilis.
- Test all patients diagnosed with syphilis for HIV and offer HIV pre-exposure prophylaxis (PrEP) to those who are negative for HIV.
- Emphasize the importance of partner treatment. Patients can anonymously notify sex partners that they have been diagnosed with an STI by sending a text from: [https://tellyourpartner.org/](https://tellyourpartner.org/)
- Report suspected syphilis cases within 24 hours of identification and let the SFDPH LINCS team know if a patient needs outreach to ensure treatment. Call 415-487-5531 or fax a confidential morbidity report (www.sfcityclinic.org) to 415-431-4628.
- **For more information on syphilis and reverse syphilis screening, visit:** [https://www.sfcityclinic.org/providers/guidelines](https://www.sfcityclinic.org/providers/guidelines)

For information on use of the reverse algorithm, you may access the **Clin Lab Manual** or refer to the following resources:

**2020 Educational resource for syphilis epidemiology, diagnosis and treatments**

**Syphilis Antibody Test FAQs**

For laboratory syphilis testing questions, please contact Jeffrey Whitman, MD at (628) 206-3595 or Barbara Haller, MD at (628) 206-3500.

For urgent clinical questions about outpatients, please call the SFCC clinician line: 415-487-5595. For non-urgent clinical questions about outpatients, send e-consult to ID. For questions about hospitalized patients please page the inpatient ID consult team.