

**Syphilis Serology Review**

The causative organism of syphilis, *Treponema pallidum*, cannot be cultured in the clinical microbiology lab. Therefore, serologic tests are necessary for the diagnosis of the disease in any stage. Serologic tests for syphilis are classified as either nontreponemal or treponemal.

Nontreponemal tests include RPR and VDRL. These tests detect IgM and IgG anti-cardiolipin antibody, which is produced in response to host cell damage and cardiolipins released from treponemes. Consequently, false positive nontreponemal tests occur in the presence of other anti-cardiolipin antibody-producing conditions including autoimmune disease, various other infections, pregnancy, and previous transfusions. All reactive nontreponemal tests should be followed up with treponemal testing. Titers of reactive nontreponemal tests can be monitored for effectiveness of therapy—a fourfold decrease in titer indicates therapeutic response.

Treponemal tests include FTA-ABS and TP-PA. These tests are not used for initial screening, due to slightly higher (1%) false positive rates than nontreponemal tests in the general population. The FTA-ABS test measures treponemal antibodies by indirect fluorescence, while TP-PA is a particle agglutination test that has widely replaced MHA-TP. A reactive treponemal test in addition to a reactive nontreponemal test is highly specific for infection. Treponemal tests may remain reactive indefinitely, and are not useful for monitoring therapy.

Clinically, syphilis has four defined stages. The primary stage is defined by the presence of a chancre at the site of infection. In secondary syphilis, the organism disseminates to multiple sites, causing rashes & lymphadenopathy. Primary and secondary syphilis generally occur in the first 6 months of untreated infection. Latent syphilis is asymptomatic infection, occurring after or between primary & secondary stages. Tertiary syphilis consists of late complications of the disease, including aortic aneurysm and neurosyphilis, usually occurring years or decades after primary infection. Serologic tests have variable sensitivity at each stage of disease. The % sensitivity of each serologic test by stage of infection is:

<table>
<thead>
<tr>
<th>Test</th>
<th>Primary</th>
<th>Secondary</th>
<th>Latent</th>
<th>Tertiary</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDRL</td>
<td>78</td>
<td>100</td>
<td>95</td>
<td>71</td>
</tr>
<tr>
<td>RPR</td>
<td>86</td>
<td>100</td>
<td>98</td>
<td>73</td>
</tr>
<tr>
<td>FTA-ABS</td>
<td>84</td>
<td>100</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>TP-PA</td>
<td>88</td>
<td>100</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>Syphilis IgG</td>
<td>97</td>
<td>97</td>
<td>97</td>
<td>97</td>
</tr>
</tbody>
</table>

The specificity for all tests in all stages of infection is 96-99%. Of note, nontreponemal tests have low sensitivity (70%) in tertiary syphilis. Therefore, treponemal tests should be performed regardless of RPR/VDRL results when late complications of the infection, such as aortic aneurysm or neurosyphilis, are suspected.

VDRL testing on CSF for the diagnosis of neurosyphilis is highly specific (99.8%), but has low sensitivity (50%), therefore a reactive CSF VDRL is diagnostic, but a non-reactive result does not rule out neurosyphilis. FTA-ABS can also be performed on CSF, and has 100% sensitivity, but lower specificity than VDRL (94%).

Saint Luke’s Regional Laboratories performs RPR’s daily and CSF VDRL weekly. All specimens with reactive RPR’s have confirmatory testing performed by FTA-ABS. Syphilis IgG antibodies are useful when primary infection is suspected and other serologic tests are negative, and when false positive results are suspected. Syphilis IgG antibody testing is available through Mayo Medical Laboratories.

**Hemolysis as a Laboratory Interferent**

Year-to-date, 527 venipuncture specimens out of 100,835 collected at Saint Luke’s Hospital have been rejected for laboratory testing because of hemolysis. Hemolysis may cause erroneous laboratory results by interfering with chemistry instrument performance or releasing intracellular...
red cell contents, such as potassium and lactate dehydrogenase, into the plasma. Interference studies performed on the DXC 600 chemistry analyzer used in the laboratories of Saint Luke’s Health System showed that hemolysis led to erroneously high or low results for the following analytes: alanine aminotransferase (ALT), alkaline phosphatase (ALP), ammonia, amylase, anti-streptolysin-O (ASO), aspartate aminotransferase (AST), bilirubin, C3, C4, creatine kinase (CK), creatinine, C-reactive protein (CRP), iron, gamma-glutamyl-transferase (GGT), high density lipoprotein (HDL), haptoglobin, IgA, IgG, IgM, lactate dehydrogenase (LD), prealbumin, phenytoin, potassium, rheumatoid factor (RF), tobramycin, transferrin and triglycerides.

Laboratory results suggestive of in vitro hemolysis include a parallel increase in potassium, AST and LD with a normal haptoglobin and reticulocyte count.

The most common causes of hemolyzed specimens are improper specimen collection, storage or transport. Specific examples include:
- forceful aspiration during venipuncture
- prolonged tourniquet time
- vigorous shaking or mixing
- centrifugation of a serum specimen before completion of clotting
- prolonged storage or delayed transport at room temperature

For inpatients and clinic patients, the laboratory notifies the nurse or client if an analyte cannot be reported due to moderate or gross hemolysis. The analyte is reported as “not done” with the comment “Specimen is hemolyzed, unable to report ___.” Exceptions to this comment are made for total and direct bilirubin ordered on infants less than 1 year of age and for haptoglobin. For moderate hemolysis on bilirubin orders, a comment is attached to the result stating “Specimen is moderately hemolyzed, which will falsely elevate the bilirubin result”. If a bilirubin specimen is grossly hemolyzed, it is rejected. For all hemolyzed haptoglobin specimens, a comment stating “In-vitro hemolysis may falsely depress the haptoglobin result” is reported. Ideally, hemolyzed specimens should be redrawn.

**Pseudohyponatremia**

Pseudohyponatremia is an artifactual hyponatremia most commonly caused by severe hypertriglyceridemia (>1500 mg/dL), or less often, by severe hyperproteinemia (>10 g/dL). Sodium is most commonly measured with an ion specific electrode (ISE). Two types of ISE exist; indirect and direct. Sodium is dissolved only in the water portion of plasma. When triglyceride or protein levels are extremely high, they occupy more space in a given volume of plasma, resulting in a decrease in the percentage of water with its sodium content. Consequently, an artifactualy low sodium concentration is obtained because less sodium is present in a given volume of plasma, even though the concentration of sodium in the water phase is unaltered. Pseudohyponatremia can occur when sodium is measured with an indirect ISE, which is the method used by most automated chemistry analyzers. This phenomenon is not seen when sodium is measured with an instrument that uses direct ISE, such as point of care instruments and blood gas analyzers. These instruments use whole blood, instead of plasma, and do not require predilution of the sample. Pseudohyponatremia can be confirmed by measuring sodium on an instrument using direct ISE and also measuring serum osmolality and comparing the result to a calculated osmolality. In a patient with hyponatremia, an increased osmolal gap suggests the presence of pseudohyponatremia.

**NovoSeven Changes**

Novoseven is a recombinant human coagulation Factor VIIa concentrate that promotes hemostasis by combining with tissue factor at the site of injury and activating the extrinsic pathway of the coagulation cascade. Previously, it was supplied as a freeze dried powder in three vial sizes: 1.2, 2.4 and 4.8 mg that were reconstituted with sterile water. This product required refrigerated storage.

Beginning in August, a reformulated product will become available that can be stored at room temperature. Vial sizes will change to 1.0, 2.0 and 5.0 mg, making dose calculation easier. Each vial will come prepackaged with a histidine buffer for reconstitution. Novoseven and diluent vials will be color coded to insure that the correct volume of diluent is used for reconstitution. Infusion volumes will be approximately one half of the previous volume. Clinical dosing guidelines will not change.