Lupus Anticoagulant Testing Made Simple

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Learning objectives

- Describe antiphospholipid syndrome (aPS) and role of the lupus anticoagulant (LA) in thrombosis
- Present current guidelines for LA screening and confirmation
- Discuss recommended LA testing methodologies
- Correlate LA and aPS to specific clinical cases
Antiphospholipid Syndrome (aPS) Overview
Clinical Manifestations of aPS

- Transient ischemic attacks
- Stroke
- Autoimmune hemolytic anemia
- Pulmonary embolism
- Myocardial infarction
- Valve thickening/dysfunction
- Pre-eclampsia/eclampsia
- Live birth with prematurity
- Livedo reticularis
- Skin ulcers
- Thrombocytopenia
- Early pregnancy loss
- Live birth with intrauterine growth restriction
- Late pregnancy loss
- Deep vein thrombosis
- Inferior extremity superficial thrombophlebitis
Antiphospholipid Syndrome (aPS) Diagnosis

Antiphospholipid Syndrome (aPS) is an auto-immune condition characterized by a hypercoagulable state:
- Blood clots in arteries and veins
- Pregnancy complications such as recurrent miscarriages or severe preeclampsia

Rare syndrome, more prevalent in women than in men.

Primary aPS: absence of any other related disease
Secondary aPS: with other auto-immune disease such as Lupus erythematosus (SLE)

In rare cases, aPS can lead to rapid organ failure due to generalized thrombosis = Catastrophic antiphospholipid syndrome

Lupus Anticoagulants are Part of aPS

Treatment
Anticoagulation (UFH) to reduce thrombosis risk & improve pregnancy prognosis (no VKA / teratogenic)
Antiphospholipid syndrome (aPS) is caused by antiphospholipid antibodies (APL):

- Heterogeneous group of antibodies
- Able to bind phospholipids (PL) to prolong PL-dependent tests

- In vivo APL cause Thrombosis: Modulate TF expression, enhance binding to platelets, and interfere with antithrombotic mechanisms

- In vitro APL cause prolongation of clotting time: Normally thrombosis state = time shortening. In vitro artifact due to test principle: in clotting time factors are activated by PL in the assay. If PL are monopolized by APL, factor activation is decreased (prolongs clotting time).

Lupus Anticoagulants are Part of aPS

Why we use PL dependent tests
aPTT Reagent – PL Concentration

Routine aPTT
50%
PL

Sensitive aPTT
25%
PL

Confirmatory
100%
PL

= PL particles
LA Effect on Clotting Tests

Patient without LA

Patient with LA

Clotting Time
Normal

Clotting Time
Prolonged

FXa

Lupus
Phospholipid Dependency of Protein C Pathway

FXa/FVa/Ca$$^{++}$$  \[=\text{PL}\]

Prothrombin $\xrightarrow{\text{fPS}}$ IIa

fPS $\xrightarrow{\text{APC}}$ IIa

free PS $\xrightarrow{\text{PL}}$ IIa  \[=\text{PL}\]

Va or VIIIa $\xrightarrow{\text{PL}}$ VIIIai or Vai

Inactivated Cofactors

Indicates any phospholipid-dependent activation step
Lupus Anticoagulant Diagnostic Guidelines
LA Guidelines - Chronology

- **1995**

- **2006**

- **2009**

- **2012**

- **2014**
  - Clinical and Laboratory Standardization Institute (CLSI) Laboratory Testing for the Lupus Anticoagulant, H60-A, April 2014
LA Diagnostic Flow Chart (2009 ISTH Guidelines)

**If family history for aPS OR abnormal screen test**

- **PT/aPTT**
  - NORMAL → STOP
  - ABNORMAL → RUN TT

- **RUN TT**
  - ABNORMAL → STOP
  - NORMAL → DRVV Screen

- **DRVV Screen**
  - NORMAL → STOP
  - ABNORMAL (add mixing step) → DRVV Confirm

- **DRVV Confirm**
  - ABNORMAL (add mixing step) → Staclot LA
  - NORMAL → PTT LA

- **PTT LA**
  - ABNORMAL (add mixing step) → Calculate delta
  - NORMAL → Calculate normalized ratio

**It may be necessary for the lab to rule out other coagulopathies that could coexist**
LA Testing Guidelines – ISTH SSC 2009

Step 1 – Screen (low PL reagent)
- LA sensitive aPTT reagent
- dRVVT screen reagent
- Thrombin Time – eliminate prolonged clotting times due to anticoagulation

Step 2 – Mixing studies
- Repeat screening tests using a patient 1:1 mix
- 1:1 mix = 1 part patient + 1 part pool normal plasma

Step 3 – Confirm (high PL reagent)
- Hexagonal phase PL reagent (Staclot® LA)
- dRVVT confirm

Tests must be repeated > 12 weeks after initial testing; need to demonstrate persistence
Other Helpful Tests to Consider

- **Full laboratory aPS profile should include:**
  - LA testing (clotting based)
  - Anti β2-GPI ELISA (aβ2-GPI) IgG, IgM
  - Anticardiolipin (aCL) IgG, IgM

- **Presence of medium-high titers of aCL and aβ2-GPI of same isotype (i.e. IgG) is in agreement with positive LA and IDs patients with high thrombotic risk**

- **Thrombin time can help to rule out heparin and other anticoagulant contamination**

- Lupus anticoagulants
- Anti-β2GPI
- Anticardiolipin
## Persistence of Testing Results

<table>
<thead>
<tr>
<th>Test</th>
<th>% positive on repeat testing</th>
<th>Mean follow up time</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA</td>
<td>39 of 51 patients (77%)</td>
<td>2.4 years</td>
</tr>
<tr>
<td>Anticardiolipin antibody (moderate – high titer)</td>
<td>65 of 86 patients (75%)</td>
<td>3.5 years</td>
</tr>
<tr>
<td>Anti-β2GPI antibody (moderate – high titer)</td>
<td>11 of 15 patients (76%)</td>
<td>1.0 year</td>
</tr>
</tbody>
</table>

- Repeat aPS results remain stable for at least ¾ of patients regardless of laboratory performing test.
- Variation not correlated with aspirin, warfarin, or hydroxyquinoline use.
- Indefinite anticoagulation is indicated for most aPS patients.

LA is the primary predictor of adverse pregnancy outcome after 12 weeks’ gestation in aPL-associated pregnancies. Anticardiolipin antibody and anti-2GPI, if LA is not also present, do not predict adverse pregnancy outcome.

Comparison of LA Guidelines

### Preanalytical conditions

<table>
<thead>
<tr>
<th>Area of recommendation</th>
<th>ISTH 2009</th>
<th>BCSH 2012</th>
<th>CLSI 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample preparation</td>
<td>Double centrifugation</td>
<td>Double centrifugation</td>
<td>Double centrifugation</td>
</tr>
<tr>
<td>Assays to use</td>
<td>dRVVT and aPTT</td>
<td>dRVVT plus aPTT or others</td>
<td>dRVVT and aPTT and/or others</td>
</tr>
<tr>
<td>Testing order</td>
<td>Screen-mix-confirm</td>
<td>Screen-mix-confirm</td>
<td>Screen-confirm-mix</td>
</tr>
<tr>
<td>Ratio derivation</td>
<td>NPP denominator</td>
<td>NPP denominator</td>
<td>RI mean denominator</td>
</tr>
<tr>
<td>RI/cutoffs</td>
<td>99th percentile</td>
<td>97.5th percentile (if Gaussian)</td>
<td>97.5th percentile (if Gaussian)</td>
</tr>
<tr>
<td>Calculations for phospholipid-dependence</td>
<td>% correction of screen by confirm, or LA ratio (screen/confirm)</td>
<td>% correction of screen by confirm, or LA ratio (screen/confirm)</td>
<td>% correction of screen by confirm, or LA ratio (screen/confirm)</td>
</tr>
<tr>
<td>Mixing test</td>
<td>Perform on 1:1 mixture with NPP; interpret with ICA or mixing test-specific cutoff</td>
<td>Perform on 1:1 mixture with NPP</td>
<td>Perform on 1:1 mixture with NPP; interpret with ICA or mixing test-specific cutoff</td>
</tr>
<tr>
<td>Testing patients on VKAs</td>
<td>Undiluted plasma if INR &lt; 1.5; mix with NPP if INR &gt; 1.5 &lt; 3.0</td>
<td>Screen and confirm on 1:1 mixture with NPP; TSVT + ET or PNP</td>
<td>Screen and confirm on 1:1 mixture with NPP; TSVT + ET or PNP</td>
</tr>
<tr>
<td>Testing patients on UFH</td>
<td>Interpret with caution</td>
<td>Not recommended</td>
<td>Can detect LA in some cases where heparin neutralizer is effective</td>
</tr>
<tr>
<td>Interpretive reporting</td>
<td>Recommended</td>
<td>Recommended</td>
<td>Recommended</td>
</tr>
</tbody>
</table>

Lupus Anticoagulant Laboratory Tests
LA Testing: Preanalytics

- Double centrifugation (stay away from the platelet layer)
- Platelet Poor Plasma (PPP); < 5000 platelets/µL
- No hemolysis or traumatic draw, discard 1st tube
- Pooled normal plasma (PNP) should be from multiple donors, well characterized for all coagulation factors and platelet poor
- -70°C preferred for freezing; CLSI recommends no more than two weeks at -20°C (H21-A5, H57-A)
Coagulation Assay Mechanisms

aPTT Based

dRVVT Based
Activated Partial Thromboplastin Time (aPTT)

- Involves activation of FXII by PL and CaCl$_2$
- Reagent composition
  - PL
  - Activator
  - Tests for factors VIII, IX, IX and XII
- Clinical uses for aPTT
  - Factor deficiencies
  - Heparin therapy
  - Circulating anticoagulants
  - Disseminated intravascular coagulation (DIC)
- Potential interference from anticoagulant drugs
  - Warfarin
  - Rivaroxaban, edoxaban (not sensitive to apixaban)
  - Argatroban, dabigatran
Differential Diagnosis of Coagulation Inhibitors

1. Inhibitors associated with clinical bleeding
   anti-Factor VIII
   anti-Factor II, VII, IX, X, XI
   anti-Fibrinogen/Fibrin
   Heparin-like anticoagulants

2. Inhibitors with or without bleeding
   anti-Factor V

3. Inhibitors usually not associated with bleeding
   Lupus anticoagulant
   anti-Factor XII

dRVVT Screen & Confirm – Principle

**Screening Tests**
DRVV Screen

- Patient without LA – Low [PL] test

**Confirmation Tests**
DRVV Confirm

- Patient without LA – High [PL] test

**Clotting Time**
- Normal

**Ratio** < 1.2
Screening Tests
DRVV Screen
Patient with LA – Low [PL] test

FXa
FX

Clotting Time
Prolonged

Confirmation Tests
DRVV Confirm
Patient with LA – High [PL] test

FXa
FX

Clotting Time
Shorter than low [PL] test

Ratio > 1.2
Effect of LA (+) Sample on Screening aPTT

In the cuvette, LA overwhelms the PL in the aPTT reagent
- Reduced concentration of PL results in prolonged clotting times
- Clotting times (example):
  - Normal plasma: 28.0 – 36.0 seconds
  - LA positive: 55 seconds

Screening aPTT

50% PL

= PL particles

= LA
Effect of LA (+) on aPTT and dRVVT Screen

- In the cuvette, LA overwhelms the PL in the aPTT/dRVVT reagent
- Reduced concentration of PL results in prolonged clotting times
- Clotting times (example):
  - PTT-LA
    - Normal: 34.3 – 40.4 seconds
    - LA positive: 62.0 secs.
  - dRVVT screen
    - Normal: 36.8 – 42.8
    - LA positive: 58.0 secs

25% PL

= PL particles
= LA
Mixing Studies

- Use in order to rule out factor deficiencies which may prolong clotting times (CT)
- Perform as a 1:1 or 50/50 mix of PNP and patient
- Compare immediate mix to 60 min preincubated mix

Calculate Index of circulating anticoagulant (ICA):

\[
\text{ICA} = \frac{(\text{CT}_{\text{mixture}} - \text{CT}_{\text{PNP}}) \times 100}{\text{CT}_{\text{patient}}}
\]

Results

1. Correct
2. Fail to Correct
## Mixing Study Interpretation

**APTT normal range = 25-35 sec**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Immediate</th>
<th>60 min</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>46</td>
<td>48</td>
<td>Complete Correction</td>
</tr>
<tr>
<td>PNP</td>
<td>31</td>
<td>32</td>
<td>C/W Factor Deficiency</td>
</tr>
<tr>
<td>1:1 Mix 1</td>
<td>33</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Patient 2</td>
<td>46</td>
<td>48</td>
<td>Incomplete Correction</td>
</tr>
<tr>
<td>PNP</td>
<td>31</td>
<td>32</td>
<td>C/W Inhibitor</td>
</tr>
<tr>
<td>1:1 Mix 2</td>
<td>36</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Patient 3</td>
<td>46</td>
<td>60</td>
<td>Incomplete Correction</td>
</tr>
<tr>
<td>PNP</td>
<td>31</td>
<td>32</td>
<td>Prolongation at 60 min</td>
</tr>
<tr>
<td>1:1 Mix 3</td>
<td>35</td>
<td>48</td>
<td>C/W time dependent inhibitor (Factor VIII Inhibitor)</td>
</tr>
</tbody>
</table>
Borderline Screening aPTT Results (1 - 5 sec)

- Use a LA sensitive aPTT (more sensitive than the routine aPTT) in a 4:1 patient:PNP mixing study

LA Effect on dRVVT Confirm

- In the cuvette, LA overwhelms the PL in the aPTT/dRVV reagent
- Reduced concentration of PL results in prolonged clotting times
- Clotting times (example):
  - dRVVT confirm
    - Normal: Ratio <1.2
    - LA positive: 1.8
  - Staclot® LA
    - Normal: Δ <8.0 secs
    - LA positive: Δ 25 secs

= PL particles
= LA

*Sago*
Sta clot® LA – Integrated Test System

Steps 1 and 2

<table>
<thead>
<tr>
<th>Patient Buffer</th>
<th>Patient Hex Phos</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNP</td>
<td>PNP</td>
</tr>
<tr>
<td>aPTT-LS</td>
<td>aPTT-LS</td>
</tr>
<tr>
<td>CaCl₂</td>
<td>CaCl₂</td>
</tr>
</tbody>
</table>

Low PL concentration Tube #1

High PL concentration Tube #2

T1 - T2 = Δ Time
Staclot LA - Principle

**Tube 1**
Without hexagonal PL

Patient without Lupus

FX → FXa → Clotting Time Normal

**Tube 2**
With hexagonal PL

Patient without Lupus

Specific Hexagonal PL neutralizing LA

FX → FXa → Clotting Time Normal

CT1 – CT2 < 8 sec
Staclot LA - Principle

**Tube 1**
Without hexagonal PL
Patient with LA

**Tube 2**
With hexagonal PL
Patient with LA

Specific Hexagonal PL neutralizing LA

Clotting Time
Prolonged

CT1 – CT2 > 8 sec

Tube 1 
Without hexagonal PL
Patient with LA

Tube 2 
With hexagonal PL
Patient with LA

Specific Hexagonal PL neutralizing LA

Clotting Time
Shorter than CT1

Staclot
Thrombin Time Principle and Applications

- **Principle:** measure clotting time in presence of known thrombin concentration

- **Recommended by 2009 ISTH SSC guidelines to exclude contamination by anticoagulant drugs**

- **Prolongation of the thrombin time indicates:**
  - Presence of UFH, LMWH, argatroban, dabigatran
  - Fibrinogen abnormalities
  - Qualitative (dysfibrinogenaemia)
  - Quantitative could be from congenital or acquired hypofibrinogenemias
  - The presence of fibrin degradation products
TT and LA Testing Panels

17% of LA-positive cases contained some heparin, and 4% of LA-positive cases contained a significant amount of heparin.

13% of cases diagnosed as LA positive had less than significant levels of heparin, but 4% had significant levels of heparin (or another anticoagulant).

TT and Reptilase should be used together to rule out heparin or other anticoagulant contamination before specialized tests such as LA testing are performed.

## Influence of Anticoagulant Drugs on LA Testing

<table>
<thead>
<tr>
<th></th>
<th>Prevalence of abnormal results (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dabigatran (110 mg bid)</td>
</tr>
<tr>
<td>PT activity &lt;70%</td>
<td>95</td>
</tr>
<tr>
<td>TT ratio &gt;1.2</td>
<td>100</td>
</tr>
<tr>
<td>aPTT &gt; 40 sec</td>
<td>100</td>
</tr>
<tr>
<td>aPTT &gt; 40 sec, ICA &gt; 10%</td>
<td>100</td>
</tr>
<tr>
<td>dRVVT screen &gt;40 sec</td>
<td>100</td>
</tr>
<tr>
<td>dRVVT &gt;40 sec, ICA &gt;13%</td>
<td>100</td>
</tr>
<tr>
<td>dRVVT screen/confirm NR &gt;1.17</td>
<td>81.8</td>
</tr>
</tbody>
</table>

Conclusions

- Nomenclature for LA can be confusing

- **Tests for aPS**
  - Clotting studies to detect LA
  - Confirm tests should be based on same format as screen
  - Direct detection of the antibodies using ELISA

- **Diagnosis of aPS** requires the presence of at least one of the clinical entities: thrombosis, pregnancy morbidity; and at least one positive test

- The positive findings must be persistent when retesting at >12 weeks
Case Studies
Case Study # 1

- 11 year old female presents with epistaxis and fever, along with malaise and anorexia. She had an unremarkable physical history with a tonsillectomy at age 9 without excessive bleeding, no relatives with bleeding histories, but taking aspirin for fever.

- Physical exam showed she was afebrile and well nourished but cervical lymphadenopathy present.

# Case Study # 1 Laboratory Results

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULT</th>
<th>REFERENCE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>13.8 sec</td>
<td>11.3 – 14.6 sec</td>
</tr>
<tr>
<td>aPTT</td>
<td>55.0 sec</td>
<td>25 – 34 sec</td>
</tr>
<tr>
<td>aPTT 1:1 mix</td>
<td>43.0 sec</td>
<td>Correction to 25 – 34 sec</td>
</tr>
<tr>
<td>PTT-LA</td>
<td>108.0 sec</td>
<td>36 – 50.1 sec</td>
</tr>
<tr>
<td>dRVVT Screen</td>
<td>43.1 sec</td>
<td>29.6 – 42.9 sec</td>
</tr>
<tr>
<td>Prothrombin</td>
<td>82%</td>
<td>50 – 150%</td>
</tr>
<tr>
<td>Factor VIII</td>
<td>135%</td>
<td>60 – 160%</td>
</tr>
<tr>
<td>Staclot® LA</td>
<td>20.4 sec</td>
<td>Negative &lt; 8 sec</td>
</tr>
</tbody>
</table>

Case Study # 1 – Diagnosis

- Probability of hemophilia A (FVIII deficiency) and hemophilia B (FIX deficiency) are low, along with factor inhibitors.

- LA is most likely present; often are transient in children and associated with viral infections

- LA not expected to cause thrombosis in this case

- Cervical lymphadenopathy presence suggests infectious mononucleosis

Case Study # 2

- 43 year old male presents with an ischemic stroke.

- History of hypertension, but no surgical history available.

- Unremarkable family history, the only medication being taken is a multivitamin.

## Case Study # 2 Laboratory Results

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULT</th>
<th>REFERENCE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>PT</td>
<td>12.5 sec</td>
<td>11.3 – 14.6 sec</td>
</tr>
<tr>
<td>aPTT</td>
<td>78.0 sec</td>
<td>25 – 34 sec</td>
</tr>
<tr>
<td>PTT-LA</td>
<td>90.0 sec</td>
<td>36.1 – 50.1 sec</td>
</tr>
<tr>
<td>Thrombin time</td>
<td>16.0 sec</td>
<td>&lt; 18.0 sec</td>
</tr>
<tr>
<td>dRVVT screen</td>
<td>78.6 sec</td>
<td>29.6 – 42.9 sec</td>
</tr>
<tr>
<td>dRVVT Mix</td>
<td>56.0 sec</td>
<td>Correction to 29.6 – 42.9 sec</td>
</tr>
<tr>
<td>dRVVT Confirm</td>
<td>37.5 sec</td>
<td>N/A</td>
</tr>
<tr>
<td>dRVVT Ratio</td>
<td>2.1</td>
<td>&lt; 1.3</td>
</tr>
<tr>
<td>Factor VIII</td>
<td>200</td>
<td>50 – 186%</td>
</tr>
<tr>
<td>Factor VIII inhibitor</td>
<td>N/A</td>
<td>Undetectable</td>
</tr>
</tbody>
</table>

Case # 2 Diagnosis and Therapy

- LA is likely

- Due to stroke incidence along with presence of LA, diagnose as positive aPS

- LAs are found in 18% of stroke patients < 44 years old

- Provide LMWH or warfarin therapy

- aPTT cannot be used to monitor heparin therapy; will need to use anti-Xa

Case Study # 3

11 year old male presents with epistaxis 1 week prior, treated with fresh frozen plasma at a different facility where prothrombin deficiency was diagnosed.

Now apparently healthy, no distress or active bleeding. Fever and lymphadenopathy had occurred 6 months prior.

Previous surgical procedures (tonsillectomy, circumcision) produced no excessive bleeding, no family history for bleeding, no medications being taken.

## Case Study # 3 Laboratory Results

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULT</th>
<th>REFERENCE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td>287</td>
<td>130 – 400 x 10^3/μL</td>
</tr>
<tr>
<td>PT</td>
<td>25.0 sec</td>
<td>10.7 – 13.0 sec</td>
</tr>
<tr>
<td>INR</td>
<td>2.3</td>
<td>1.0 (before therapy); 2 – 3 (therapeutic range)</td>
</tr>
<tr>
<td>Prothrombin</td>
<td>6</td>
<td>50 – 150%</td>
</tr>
<tr>
<td>aPTT</td>
<td>62.0 sec</td>
<td>25.0 – 34.0 sec</td>
</tr>
<tr>
<td>PTT-LA</td>
<td>113.0 sec</td>
<td>36.1 – 50.1 sec</td>
</tr>
<tr>
<td>Staclot® LA</td>
<td>61.5 sec</td>
<td>Negative &lt; 8 sec</td>
</tr>
<tr>
<td>dRVVT screen</td>
<td>99.2 sec</td>
<td>29.6 – 42.9 sec</td>
</tr>
<tr>
<td>dRVVT Confirm</td>
<td>70.2 sec</td>
<td>N/A</td>
</tr>
<tr>
<td>dRVVT Ratio</td>
<td>1.4</td>
<td>&lt; 1.3</td>
</tr>
<tr>
<td>Factor VIII inhibitor</td>
<td>N/A</td>
<td>Undetectable</td>
</tr>
</tbody>
</table>

LA is likely with specificity for prothrombin; genetic prothrombin deficiency is most likely negative

Prognosis in patient of this age is good even with an acquired prothrombin deficiency

Supportive therapy should be done with management of bleeding episodes using prothrombin complex concentrates (PCCs)

Case Study # 4

69 year old female presents with easy bruising within past few weeks. Large hematoma at site of intramuscular injection; multiple ecchymoses in left arm with diffuse swelling.

History of hypertension, diabetes, arthritis, asthma, previous surgeries (cholecystectomy, hysterectomy) produced no excessive bleeding, no relatives with bleeding disorders.

Medications include Acetaminophen, atenolol, azithromycin, estradiol, glyburide, pravastatin sodium, prednisone, ramipril, and theophylline.

# Case Study # 4 Laboratory Results

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULT</th>
<th>REFERENCE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td>324</td>
<td>130 – 400 x 10(^3)/μL</td>
</tr>
<tr>
<td>PT</td>
<td>11.2 sec</td>
<td>10.7 – 13.0 sec</td>
</tr>
<tr>
<td>aPTT</td>
<td>99.5 sec</td>
<td>25.0 – 34.0 sec</td>
</tr>
<tr>
<td>PTT-LA</td>
<td>131.4 sec</td>
<td>36.1 – 50.1 sec</td>
</tr>
<tr>
<td>Staclot® LA</td>
<td>19.9 sec</td>
<td>Negative &lt; 8 sec</td>
</tr>
<tr>
<td>Thrombin time</td>
<td>15.3 sec</td>
<td>&lt; 18.0 sec</td>
</tr>
<tr>
<td>dRVVT screen</td>
<td>42.2 sec</td>
<td>29.6 – 42.9 sec</td>
</tr>
<tr>
<td>Factor VIII</td>
<td>&lt; 1%</td>
<td>50 – 186%</td>
</tr>
<tr>
<td>Factor VIII inhibitor</td>
<td>64 Bethesda Units</td>
<td>Undetectable</td>
</tr>
</tbody>
</table>

Case # 4 Diagnosis and Therapy

- Bleeding episode currently but not historically indicates presence of acquired hemophilia

- Most patients with acquired hemophilia are > 50 years old and half have an associated disorder such as arthritis, SLE, malignancy, or a drug reaction

- With such high inhibitor levels (> 5 BU), activated prothrombin complex concentrates or recombinant FVIIa are indicated to control bleeding

- Laboratory should continue monitoring FVIII and FVIII inhibitors going forward

Stago 24/7 Educational Webinar Sites

- **www.stago-edvantage.com**
  - US based KOLs
  - 1 hour; PACE accredited
  - Accessible from mobile devices
  - Virtual exhibit hall

- **www.stagowebinars.com**
  - Mostly European KOLs
  - 30 – 45 min including 15 min discussion
  - Accessible from mobile devices
Stago Educational Apps

- **Haemoscore**
  - Clinical scoring algorithms
  - Apple and Android
  - Tablet or phone

- **iHemostasis**
  - Coagulation diagrams
  - Case studies
  - Apple & Android
  - Tablet only