Evaluation of Unexplained Prolonged APTT &/or PT
Review & Update 12-2015

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Special Coagulation Lab, Coagulation Clinic & Hemophilia Center
Prolonged APTT &/or PT

Disclosures + Outline-Objectives

• Disclosures
  – NO Financial Relationships or Conflicts
  – NO Off-label Therapeutic Products
  – Laboratory Diagnostic Products / Procedures: may or may not be FDA-approved and/or routinely available

• Outline - Objectives
  – Revisit the plasmatic procoagulant pathways
  – Recollect test procedures (APTT, PT, TT, DRVVT, Mix study)
  – Recount pathophysiologic categories of plasmatic coagulopathies
  – Discuss differing mechanisms and differential diagnostic features
  – Identify effective laboratory testing strategies
  – Describe basic management principles
Plasmatic Procoagulant Pathways & Tests

- **Intrinsic**
  - Prekallikrein
  - HMW-Kininogen
  - Surface
  - XI
  - XIIa
  - HMW-K
  - Phospholipid
  - Ca++/Zn++

- **Extrinsic**
  - Tissue factor
  - Phospholipid
  - Ca++

- **Common**
  - Prekallikrein
  - HMW-Kininogen
  - Surface

- **APTT**
  - XII
  - XI
  - Xla
  - IX
  - VIIIa
  - Vlla
  - Phospholipid
  - Ca++

- **PT**
  - VII-Vlla
  - Tissue factor
  - Phospholipid
  - Ca++

- ** DRVVT**
  - Prothrombin (II)
  - Thrombin (IIa)

- **TT**
  - Fibrinogen
  - Fibrin
Plasma (citrated) + Contact activator & phospholipid → Incubate 37°C 3-5 min + Ca++ → Measure clot time (37°C)

Intrinsic

Plasma (1 volume) + Tissue factor, Ca++ & Phospholipid (2 volumes) → Measure clot time (37°C)

Extrinsic

APTT

Fibrinogen

PT
Plasma (citrated) + Contact activator & phospholipid → Incubate 37°C 3-5 min + Ca++ → Measure clot time (37°C)

Intrinsic

Extrinsic

Plasma (1 volume) + Tissue factor, Ca++ & Phospholipid (2 volumes) → Measure clot time (37°C)

Fibrinogen
Prolonged Clotting Times - Mechanisms

- Coagulation factor deficiency(ies)
- Coagulation inhibition
- Both
- Neither (spurious)

"Mixing Test" for initial evaluation --> Interpretation
Inhibition vs Factor Deficiency

Mixing Patterns → Interpretation

**APTT (sec)**

- **Normal (%)**: 100, 80, 50, 20, 10, 0
- **Patient (%)**: 0, 20, 50, 80, 90, 100

**Upper normal**

**Inhibitor**

**Deficiency**

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Prolonged APTT &/or PT
MIXING STUDIES & ISSUES

• Mixing studies performed / interpretable only if baseline (screening) clotting time “significantly” prolonged = > upper normal (> +2SD or >97.5%ile vs. > +3SD or >99%ile cutoff)
  – 1 sec prolonged? • 2-5 sec prolonged? • >5 sec prolonged?

• 1:1 Mix (Pt:NPP) should normalize the prolonged clotting time (provides ≥50% of all factors) into the reference range if no inhibitor (but, weak inhibitor may “correct” - significance?)

• Incubated mixing studies (1-2 hrs): essential for detecting time-dependent inhibition (especially VIII inhibitors; rarely LA)
  – Compare w. incubated controls (Pt, NPP) mixed just before testing
  – Positive = incubated mix APTT ≥10-20% ↑ vs. control mix APTT

• Relatively few or limited studies - and evidence or guidelines - for performing & interpreting mixing studies (see CLSI LA testing guidelines 2014 = CLSI H60A document)

• Ratio reporting may be useful (ie, Pt:NPP ratio or normalized ratio)

• Laboratories should define reference ranges and “cut-offs” for mixing studies
Plasmatic Coagulopathies
Pathophysiologic Classification: SICKFAIL

- **S** = Spurious
- **I** = Inhibitors
- **C** = Congenital/Hereditary factor deficiencies
- **K** = Vitamin K deficiency
- **F** = Factor deficiencies (acquired) - single or multiple
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- **L** = Liver disease
Spurious Coagulopathies
Mainly Pre-Analytical = Sample or Patient Issues

- Hematocrit abnormal
  >55 or <25: ↑ PT, APTT
- Incomplete tube fill
- Wrong/No anticoagulant
  EDTA, heparin, serum
- Heparin contamination
  “Line draw”
- Anticoagulant Rx effects
  heparin, warfarin, DTI, etc.
- Other Rx effects
  Fibrinolytic Rx, DDAVP, etc.
- Transfusion effects
  FFP, Cryo, Factor concentrate
- Difficult venipuncture
  → clotting in vitro
- Lipemia, hemolysis, icterus
- Warm proteolysis
  loss of VIII & V: ↑ PT/APTT
- Cold activation
  VII → VIIa (short PT)
- Residual platelets
  ↓ LA sensitivity; ↓ thrombin time

Be aware (suspicious)! - these are not rare
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Vitamin K Deficiency

- **Common**: Neonates; Hospitalized patients

- **Limited body stores of fat-soluble Vitamin K**
  - 1-2 mg total stores in adults
  - Metabolic requirement ~0.1 mg / day

- **Function**: gamma carboxylation of glutamic acid --> “Gla”: binds Ca++ & phospholipids (PS, PE)

- **Vitamin K-dependent factors**: II, VII, IX, X, C, S,

- **Diagnosis**:
  - K-dependent factors low; others NL (I, V, VIII, XI, XII, etc.)
  - Response of PT (+/- factors) to Vitamin K Rx
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Anticoagulants

• **Coumarins**: Vitamin K antagonists (II, VII, IX, X, C, S)
  - Dicumarol
  - Warfarin (Coumadin®, generics)
  - Indanediones (Miradon®)
  - Superwarfarins (Brodifacoum®, others)

• **Heparins**: Antithrombin-thrombin (&/or AT-Xa) complex catalysis
  - Unfractionated heparins (UFH)
  - Low molecular weight heparins (LMWH) + fondaparinux (Arixtra®)
  - Endogenous heparinoids (rare)

• **Direct Thrombin Inhibitors**: Antithrombin - independent
  - Hirudins - Refludan®; Bivalirudin®; etc.
  - Others - Argatroban®; Pradaxa® (dabigatran); etc.

• **Direct Factor Xa Inhibitors**: Antithrombin - independent
  - Xaralto® (rivaroxaban); Eliquis® (apixiban); Savaysa® (edoxaban)
Anticoagulants (Coumarins)

- **Coumarins**: Vitamin K antagonists (II, VII, IX, X, C, S)
  - Typical test results:
    - PT>APTT prolongation; TT Normal; DRVVT prolonged
    - Mixing studies: no or minimal inhibition (PIVKAs)
    - K-dependent factors low; others normal (eg, F V)

- Unusual Coumarin Effects:
  - **Anticoagulant malingerers** ("Dicumarol eaters")
    - Warfarin toxicologic assay
  - **Superwarfarin poisoning** ("Rat poison")
    - Prolonged effect [weeks]; Vitamin K-resistance: 50-100 mg/day to Rx
    - Brodifacoum toxicologic assay
**Anticoagulants - Heparin**

**Coagulation Test Effects (Typical)**

Unfractionated Heparin (UFH)

- **APTT** -- Prolonged (variably)
- **PT** -- Normal (heparin neutralizer in PT reagent)
- **TT** -- Markedly prolonged (bovine thrombin)
- **RT** -- Normal
### Thrombin Time (TT) & Reptilase Time (RT)

#### Diagnostic Patterns*

<table>
<thead>
<tr>
<th>TT</th>
<th>RT</th>
<th>CAUSES</th>
<th>OTHER TESTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged</td>
<td>Normal</td>
<td>Heparin or inhibitor of bovine thrombin</td>
<td>Human TT &amp;/or heparin assays</td>
</tr>
<tr>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Hypo- or afibrinogenemia</td>
<td>Fibrinogen (endpoint assay) +/- kinetic</td>
</tr>
<tr>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Dysfibrinogenemia</td>
<td>Kinetic fibrinogen vs. antigen or endpoint assay</td>
</tr>
<tr>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Fibrin- split products</td>
<td>FSP or D-dimer assay (+ Fibrinogen)</td>
</tr>
</tbody>
</table>

*Typical patterns (exceptions exist); extent of abnormalities varies*
Other Anticoagulants Impacts on Coagulation Testing

- **Low Molecular Weight Heparins (LMWHs)**
  - Minimal (usually) but variable effects on APTT, TT
  - Rx monitoring - chromogenic heparin (anti-Xa) assay

- **Direct Thrombin Inhibitors (DTIs)**
  - Hirudins or Small molecules (argatroban, dabigatran)
  - Prolonged TT ± PT, APTT, DRVVT (not the RT)

- **Direct Coagulation Factor Xa Inhibitors**
  - Variably prolonged PT ± APTT, DRVVT (not TT, RT)
  - Chromogenic anti-Xa assay may detect . . .

LMWHs or Direct Inhibitors can interfere with diagnostic coag testing (false results) - especially if Rx unknown to laboratory!
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Liver Disease  
Hemostatic & Coagulation Effects (typical)

• Thrombocytopenia

• Prolonged clotting time tests; “no inhibition”
  • ↑PT, DRVVT > ↑APTT, (TT)

• Multiple coagulation factor / protein deficiencies
  • K-dependent factors: ↓ II, VII, IX, X, C, S
  • K-independent factors: ↓ I, V, XI, XII , AT
  • ↑ VIII

• Intravascular coagulation & fibrinolysis increased
  • Fibrin degradation products (D-dimer) ↑
  • Soluble fibrin monomer complex (SFMC) ↑

• Bleeding >> Thrombosis
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## Congenital Coagulation Factor Deficiencies

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Deficient factor</th>
<th>PT*</th>
<th>APTT*</th>
<th>Prevalence</th>
<th>Mode of inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophilia A</td>
<td>Factor VIII</td>
<td>Normal</td>
<td>Prolonged</td>
<td>1:5000†</td>
<td>X-linked recessive</td>
</tr>
<tr>
<td>Hemophilia B</td>
<td>Factor IX</td>
<td>Normal</td>
<td>Prolonged</td>
<td>1:30,000†</td>
<td>X-linked recessive</td>
</tr>
<tr>
<td>Hemophilia C</td>
<td>Factor XI</td>
<td>Normal</td>
<td>Prolonged</td>
<td>Up to 4%‡</td>
<td>Autosomal</td>
</tr>
<tr>
<td>von Willebrand disease (VWD)</td>
<td>VWF +/- F-VIII</td>
<td>Normal</td>
<td>Normal/prolonged</td>
<td>Up to 1%</td>
<td>Autosomal</td>
</tr>
<tr>
<td>Hageman factor deficiency**</td>
<td>Factor XII</td>
<td>Normal</td>
<td>Prolonged</td>
<td>Up to ~1% Rare§</td>
<td>Autosomal</td>
</tr>
<tr>
<td>Fletcher or Fitzgerald factors**</td>
<td>PK or HMWK</td>
<td>Normal</td>
<td>Prolonged</td>
<td>Rare§</td>
<td>Autosomal</td>
</tr>
<tr>
<td>Factor VII (Stable factor)</td>
<td>Prolonged</td>
<td>Normal</td>
<td>Normal</td>
<td>1:500,000</td>
<td>Autosomal</td>
</tr>
<tr>
<td><strong>Rarer coagulation factor deficiencies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Factor V (Labile factor)</td>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Prolonged</td>
<td>1:1 million</td>
<td>Autosomal</td>
</tr>
<tr>
<td>Factor II (Prothrombin)</td>
<td>Prolonged</td>
<td>Normal/prolonged</td>
<td>Rare§</td>
<td>Autosomal</td>
<td></td>
</tr>
<tr>
<td>Factor X (Stuart-Prower)</td>
<td>Prolonged</td>
<td>Normal/prolonged</td>
<td>1:500,000</td>
<td>Autosomal</td>
<td></td>
</tr>
<tr>
<td>Factor XIII (FSF)</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Rare§</td>
<td>Autosomal</td>
</tr>
<tr>
<td>Factor I (Fibrinogen)</td>
<td>Prolonged/NI</td>
<td>Prolonged/Normal</td>
<td>Rare§</td>
<td>Autosomal</td>
<td></td>
</tr>
<tr>
<td>Combined: V+VIII; II+VII+IX+X</td>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Rare§</td>
<td>Autosomal</td>
<td></td>
</tr>
</tbody>
</table>

*APTT = activated partial thromboplastin time; PT = prothrombin time.
† Male births. ‡Among Ashkenazi Jews. §Case reports. **No bleeding.

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Factor Deficiencies - Multiple Acquired (Patterns)

• Vitamin K Deficiency -- ↓ II, VII, IX, X, C, S
• Liver Disease -- ↓ Vit. K factors, I, V, XI (↑ VIII)
• ICF/DIC -- ↓ I, V, VII, AT, Plasminogen, Antiplasmin, etc.
• Inflammation -- ↓ XI, XII (↑ VIII & Fibrinogen)
• T-cell (peripheral) Lymphomas – ↓ I (± II, V, VII, AT, etc.)
• L-Asparaginase Rx -- ↓ Fibrinogen [I], AT (±C, S, etc.)
Factor Deficiencies - Single

**Acquired** (Non-immune or Immune: but no activity inhibition)

- **Factor II (Prothrombin)**
  - Lupus anticoagulant  (non-neutralizing antibodies)

- **Factor V**
  - Myeloproliferative disorders  (cell absorption, proteolysis?)

- **Factor X**
  - Systemic amyloidosis  (perivascular amyloid absorption)
  - Lupus anticoagulant  (non-neutralizing antibodies)

- **Factor VIII (+ Von Willebrand Factor: VWF)**
  - Acquired von Willebrand syndrome (AVWS)
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Fibrinolysis

- Urokinase (u-PA)
- (PAI)
- Plasminogen
- (PAI)
- Tissue plasminogen activator (t-PA)
- Proactivator
- Streptokinase
- (Antistreptokinase)
- Fibrin* (Fibrinogen)
- Fibrin (ogen) degradation products (FDP)
- Plasmin
- (Antiplasmin)
- Plasminogen
- (PAI)
- Fibrinolysis
- TAFI (thrombin-activatable fibrinolysis inhibitor)

*Fibrin enhances plasmin generation (binds plasminogen and t-PA)
Intravascular Coagulation & Fibrinolysis ("ICF")

- ICF -- a spectrum of increased responses of the coagulation system to stimuli

- Stimuli: "Physiological" ---> Pathological
  - Bleeding
  - Surgery, Trauma
  - Thromboembolism
  - Sepsis, Malignancy
  - Vascular or Obstetric Disorders
  - Liver failure, Snake bites, Etc.

- Clinical/Laboratory Scenarios:
  - Acute, Subacute, Chronic
  - Mild --> Severe
  - Compensated --> Decompensated
  - Bleeding, Tissue Ischemia, Thromboembolism & A[pre]symptomatic
ICF / DIC Laboratory Testing

Typical Results - Extent, Severity Vary

- Platelet count ↓
- PT ↑ ± APTT ↑
- Fibrinogen ↓
- D-dimer ↑↑ (increased thrombin & plasmin)
- SFMC ↑ (increased thrombin)

Supplemental DIC/ICF coag tests:

- Factor levels ↓ (II, V, VII, X, XI, etc.)
- Antithrombin, Plasminogen, Antiplasmin
- ↑Thrombin-Antithrombin (TAT complex)

ICF/DIC coagulation tests are not specific for diagnosis of clinical DIC

- “Positive” tests (e.g., D-Dimer & SFMC elevations) associated with:
  - Bleeding; Surgery; Trauma; Liver disease; Thromboembolism;
  - Hypercoagulable states, Etc.

Correlate lab data & clinical information!
Intravascular Coagulation & Fibrinolysis

“Primary” Fibrinolysis

• Activation of excessive Fibrinolysis -- without activation of coagulation (Thrombin generation)

• Bleeding

• Laboratory:
  – D-dimer & FDP elevation (increased Fibrinolysis)
  – SFMC typically negative (reflects Thrombin)
  – Fibrinogen may be low (Fibrinogenolysis)
  – Plasminogen & Antiplasmin low (also in DIC/ICF)
  – Antithrombin usually not low

• Associated diseases: Amyloidosis, Prostatic carcinoma, Cirrhosis, Thrombolytic therapy
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Coagulation Inhibitors

- **Specific Factor Inhibitors** (antibodies)
  - VIII, V, IX, II, X, XIII, VWF, etc. (neutralizing vs. non-neutralizing)

- **“Non-specific” Coagulation Inhibitors**
  - Lupus anticoagulants
    (“antiphospholipid” antibodies)
  - Dysproteinemias
    (MGUS, myeloma, Waldenström’s)
  - Other: Fibrin degradation products, etc.

- **“Global” Inhibitors** (thrombin & Xa inhibition)
  - Heparins, DTIs, Direct-acting Factor Xa inhibitors
Specific Factor Inhibitors
(Approximate Prevalence / Incidence Ranking)

1. Factor VIII (human, porcine)
2. Factor V (human, bovine)
3. Thrombin (bovine)
4. Factor IX (severe Hemophilia B)
5. Von Willebrand factor (VWF)
6. Other Factors (rare):
   I, II, VII, X, XI, XII, XIII, etc.
Factor VIII Inhibitors
(Prolonged APTT)

• Hemophilia A (severe) (alloantibodies)
  • Prevalence: up to 20-25%

• “Acquired Hemophilia” (autoantibodies)
  • Autoimmune disorders (5-10%)
  • Postpartum (5-10%)
  • Malignancies (?5%)
  • “Old healthy people” (70-85%)

• Allo- vs. Auto-antibody inhibitors differ:
  • lab features (kinetics of neutralization)
  • clinical features (pattern of bleeding syx)
Factor (VIII) inhibitor screen: incubated mixing test (APTT)

<table>
<thead>
<tr>
<th>Pool</th>
<th>Immediate</th>
<th>Result</th>
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<tbody>
<tr>
<td></td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>1 Hour</td>
<td>96</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Mixtures</th>
<th>(1 part pool + 4 parts patient)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate</td>
<td>27 100% 20 50% 18 25%</td>
</tr>
<tr>
<td>Expected:</td>
<td>21.8 + 0.8 = 22.6</td>
</tr>
<tr>
<td>Result</td>
<td>22</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient</th>
<th>Immediate</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 %</td>
<td>-</td>
<td>&lt;1</td>
</tr>
<tr>
<td>50 %</td>
<td>-</td>
<td>&lt;1</td>
</tr>
<tr>
<td>25 %</td>
<td>-</td>
<td>&lt;1</td>
</tr>
<tr>
<td>1 Hour</td>
<td>100 %</td>
<td>&lt;1</td>
</tr>
<tr>
<td>50 %</td>
<td>-</td>
<td>&lt;1</td>
</tr>
<tr>
<td>25 %</td>
<td>-</td>
<td>&lt;1</td>
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</table>

<table>
<thead>
<tr>
<th>1 Hour Together</th>
<th>Expected: 19</th>
<th>Result: 4</th>
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<tbody>
<tr>
<td>100%</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>50%</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>25%</td>
<td>-</td>
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<table>
<thead>
<tr>
<th>1 Hour Separate</th>
<th>Expected: 19</th>
<th>Result: 20</th>
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<tbody>
<tr>
<td>100%</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>50%</td>
<td>19</td>
<td></td>
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<tr>
<td>25%</td>
<td>15</td>
<td></td>
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</tbody>
</table>

No immediate, but progressive incomplete inhibition of FVIII activity (type II kinetics): POSITIVE SCREEN
### Bethesda FVIII Inhibitor Titrering Assay

**After 2 hours at 37°C**

<table>
<thead>
<tr>
<th>% Factor</th>
<th>% Residual</th>
<th>&quot;Factor&quot; from chart</th>
<th>X Dilution</th>
<th>= Bethesda Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pool</td>
<td>47</td>
<td>% factor in mixture</td>
<td>% factor in pool x 100</td>
<td></td>
</tr>
<tr>
<td>dilution + equal volume pool</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>undiluted</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1:2</td>
<td>44</td>
<td>55</td>
<td>0.85</td>
<td>4</td>
</tr>
<tr>
<td>1:4</td>
<td>26</td>
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<tr>
<td>1:8</td>
<td>34</td>
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<td>1:16</td>
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<td>1:128</td>
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Lupus Anticoagulants (LA) (Antiphospholipid Antibodies) Diagnostic Laboratory Criteria/Recommendations*

1. **Prolonged** phospholipid-dependent clot time(s)
   - APTT, DRVVT, PCT, KCT/SCT, (D)PT, etc. (≥2 tests - Δ principles)

2. **Inhibition** demonstrated -- mixing tests

3. **Phospholipid dependence** demonstrated
   - PNP (APTT); DRVVT “Confirm”; Staclot LA Hex PL; etc.

4. Evaluate for / Exclude **confounding coagulopathies** --
   - Factor defic./inhib., Heparin, Warfarin, DTI, etc.

5. For full APL eval. include supplemental testing (ELISA) for serum IgG/M anti-Cardiolipin/β-2 Glycoprotein I antibodies**


Dysproteinemic Coagulopathies
(Paraproteinemias inhibiting clot times)

- **Dysproteinemias**: MGUS, Myeloma, Waldenström’s macroglobulinemia
- **Monoclonal immunoglobulins** (G, M, A)
  - “Interfere” with coag protein assembly & function
    - Thrombin generation
    - Fibrin assembly
  - Specific inhibition of coag factor(s) - less common
- Prolonged, inhibited PT, APTT or both
- Asymptomatic > Bleeding
Coagulation Inhibitors - Differential Dx
(Listed by Descending Prevalence - approximate)

1. Anticoagulant Inhibitor Compounds and Substances
   - Heparin (unfractionated) & LMWHs
   - Direct thrombin inhibitors (DTIs) & Xa inhibitors
   - EDTA (ethylenediaminetetra-acetic acid) - instead of citrate plasma

2. Lupus Anticoagulant (LA) - “Antiphospholipid Abs”

3. Specific Coagulation Factor Inhibitors (Antibodies)
   - Factor VIII inhibitors (allo- and auto-antibodies)
   - Inhibitors of other coagulation factors (V, IX, II, X, XI, XIII)

4. Monoclonal Immunoglobulinopathies (Antibodies)
   - Monoclonal gammopathy of undermined significance (MGUS)
   - Macroglobulinemia, Multiple myeloma, Systemic amyloidosis (AL)

5. Fibrin Degradation Products (FDPs) & Other Non-specific Coagulation Inhibitors
Plasmatic Coagulopathies
Pathophysiologic Classification: SICKFAIL*

- **S** = Spurious
- **I** = Inhibitors
- **C** = Congenital/Hereditary factor deficiencies
- **K** = Vitamin K deficiency
- **F** = Factor deficiencies (acquired) - single or multiple
- **A** = Anticoagulants
- **I** = ICF (intravascular coagulation & fibrinolysis) or DIC (disseminated intravascular coagulation)
- **L** = Liver disease

*Thanks to Dr. Gerald Holcomb (Mayo Hem Emeritus) for the mnemonic idea, and to Dr. Paul Monahan (UNC Chapel Hill) for updating this one: SICKFAIL/SIKFAIL
Coagulation Test Panels

Reflexive Testing & Interpretive Reporting

“Consultative” Test Panels

- Mayo Medical Laboratories (MML) Testing Panels/Profiles
  - Lupus Anticoagulant (LA) (MML 83092 profile = LUPPR)
  - Prolonged Clotting Times (unexplained) (MML 83097 profile = PROCT)
  - Other panels: Bleeding, Thrombosis, VWD, Factor Inhibitor (+ DIC, PltIt Fn - not MML; Mayo in-house only)

- Testing from Other Reference or Hospital Coagulation Laboratories
  - Lupus Anticoagulant (LA) test panel
  - Many specialized coag labs offer LA tests +/- panel: vary in panel content, reflexes & interpretive reporting
  - Prolonged/Abnormal PT/APTT test panel
    - Few labs offer -- varies in test content, reflexes, reporting
  - Mixing study (APTT, PT) +/- incubation → interpretation: available in many coag labs
PROCT / Prolonged Clot Time Profile (Mayo/MML #83097)

1. **Activated Partial Thromboplastin Time (APTT)**
   - Is result within normal range?
     - **YES** → **STOP** No additional APTT testing
     - **NO** → **APTT Mixing Test** (1:1 mix with normal plasma)

2. **Prothrombin Time (PT)**
   - Is result within normal range?
     - **YES** → **STOP** No additional PT testing
     - **NO** → **PT Mixing Test** (1:1 mix with normal plasma)

3. **Thrombin Time (TT)**
   - Is result within normal range?
     - **YES** → **STOP** No additional TT testing
     - **NO** → **Reptilase Time (RT)**

4. **Dilute Russell Viper Venom Time (DRVVT)**
   - Is result within normal range?
     - **YES** → **STOP** No additional DRVVT testing
     - **NO** → **DRVVT Mixing Test** (1:1 mix with normal plasma)

- **Does result correct sufficiently?**
  - **YES** → **Review all results. Additional clarification or testing needed?**
  - **NO** → **If indicated:**
    - Factor Assays: VIII, IX, XI, XII
    - If TT is normal: Perform platelet neutralization procedure (PNP)

- **If indicated:**
  - Factor Assays: II, V, VII, X

- **Interpretation of all results is performed**

- **Also performed:**
  - Fibrinogen
  - D-dimer
  - Soluble fibrin monomer
Questions & Discussion