Evaluation of the Bleeding Patient: Esoteric Tests

Dong Chen M.D., Ph.D.
Special Coagulation Laboratory
DISCLOSURE

• Relevant Financial Relationship(s)
  None
Objectives:

• Know the limitations of standard coagulation laboratory testing and indications of esoteric laboratory testing for diagnosing bleeding diatheses.

• Use an algorithmic approach to appropriately utilize esoteric testing.
A General Approach to Coagulation Esoteric Testing

- Patient’s Personal and Family Bleeding History
- Standard Coagulation Testing Results
- Select the Appropriate Esoteric Tests
Esoteric Tests to Discuss:

- Primary Fibrinolysis
- Platelet Disorders
- AVWS
- Molecular Testing
Esoteric Tests to Discuss:

- Primary Fibrinolysis
- AVWS
- Platelet Disorders
- Molecular Testing
Fibrin Clot and Fibrinolysis

- Fibrinogen
- FII-a
- Fibrin monomer
- XIII-a
- Fibrin clot
- t-PA/u-PA
- Plasminogen activator inhibitor-1 (PAI-1)
- Plasminogen
- α₂-antiplasmin (α₂-AP)
- Fibrin clot lysed
Aberrant Fibrinolysis

**Hereditary:** Fibrinolysis-related factor deficiency
- Deficiency of $\alpha_2$-antiplasmin
- Deficiency of Factor XIII
- Deficiency of PAI-1

**Secondary:** Aberrant expression of fibrinolysis proteins or activation of fibrinolysis
- Amyloidosis/lymphoma/myeloma
- Cancer (cavernous hemangioma)
- Liver disease
- Thrombolytic therapy
- Trauma or certain surgery

Hereditary Fibrinolysis Abnormality

<table>
<thead>
<tr>
<th>Protein</th>
<th>Prevalence of Congenital Deficiency</th>
<th>Bleeding Phenotype of Congenital Deficiency (first reported case)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha 2-antiplasmin</td>
<td>Few reported cases</td>
<td>Moderate to severe bleeding (Thromb Diath Haemorrh1969; 22: 251–62)</td>
</tr>
<tr>
<td>Factor XIII (FXIII)</td>
<td>1:1~5 million</td>
<td>Moderate to severe bleeding (delayed) (Thromb Diath Haemorrh. 1965;14:332-40)</td>
</tr>
<tr>
<td>Plasminogen activator Inhibitor-1 (PAI-1)</td>
<td>20 families reported</td>
<td>Moderate to severe bleeding (Blood 1997; 90:204–208)</td>
</tr>
</tbody>
</table>
Pattern of Standard Laboratory Testing Results

- Normal platelets
- Normal/slight shortening of clotting times: PT, aPTT or TT
- Normal coagulation factors or slightly ↓ fibrinogen
- ↑ D-dimer
- Negative soluble fibrin monomer complex (SFMC)
- **Screening test:** 5M urea or 1% monochloroacetic acid clot stability assay.
## Esoteric Testing Methods of Primary Fibrinolysis

<table>
<thead>
<tr>
<th>Protein (Cutoff for Bleeding)</th>
<th>Laboratory Tests</th>
</tr>
</thead>
</table>
| **FXIII** (<1%)              | **Antigen:** FXIII A and/or B subunit antigen level by ELISA  
**Activity:** Transglutamidase assay via ammonia release or biotinylated amine substrate incorporation into fibrinogen (chromogenic). |
| **a2-AP** (<10%)             | **Antigen:** Alpha 2-antiplasmin antigen by ELISA  
**Activity:**  
1. Plasmin amidolytic assay (chromogenic)  
2. Plasmin binding activity (ELISA like). |
| **PAI-1** (<3 ng/ml)         | **Antigen:** PAI-1 antigen by ELISA  
**Activity:**  
1. Residual t-PA/u-PA activity by plasmin amidolytic assay (chromogenic)  
2. t-PA or u-PA plasmin binding activity (ELISA like) |

## Acquired Primary Fibrinolysis vs. DIC

<table>
<thead>
<tr>
<th>Test</th>
<th>Primary Fibrinolysis</th>
<th>DIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td>Normal/decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>PT</td>
<td>Normal/slightly shortened</td>
<td>Prolonged</td>
</tr>
<tr>
<td>APTT</td>
<td>Normal/slightly shortened</td>
<td>Prolonged</td>
</tr>
<tr>
<td>Thrombin time (TT)</td>
<td>Normal</td>
<td>Prolonged</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Normal/slightly decreased</td>
<td>Decreased*</td>
</tr>
<tr>
<td>Coagulation Factors</td>
<td>Usually normal</td>
<td>Decreased*</td>
</tr>
<tr>
<td>Clot lysis time</td>
<td>Shortened</td>
<td>Shortened</td>
</tr>
<tr>
<td>Fibrin degradation products (FDP)</td>
<td>Normal or slightly increased</td>
<td>Increased</td>
</tr>
<tr>
<td>D-Dimer</td>
<td>Normal/increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Antithrombin III</td>
<td>Normal</td>
<td>Decreased*</td>
</tr>
<tr>
<td>Plasminogen</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>$\alpha_2$-Antiplasmin</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Erythrocyte morphology</td>
<td>Normal</td>
<td>Schistocytosis*</td>
</tr>
</tbody>
</table>
General Approaches to Esoteric Testing for Abnormal Fibrinolysis

- Distinct Bleeding Pattern and Concomitant Diseases
- Unremarkable Standard Coagulation Testing Results
  - ↑D-dimer and ↓clot lysis time
- Alpha 2-antiplasmin FXIII
  - PAI-1
  - (Antithrombin)
  - (Plasminogen)

(Antithrombin and plasminogen testing may assist the evaluation of acquired primary fibrinolysis.)
Esoteric Tests to Discuss:

- Primary Fibrinolysis
- Platelet Disorders
- AVWS
- Molecular Testing
### Acquired von Willebrand Syndrome (AVWS) Associated Diseases

<table>
<thead>
<tr>
<th>Pathophysiologic Category</th>
<th>Disease or Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Autoimmune: Antibodies to VWF</td>
<td>MGUS, lymphoma, autoimmune disorders</td>
</tr>
<tr>
<td>• Shear-induced VWF proteolysis (ADAMTS13)</td>
<td>AS/R; MS/R; VSD; LVAD; HOCM; PH</td>
</tr>
<tr>
<td>• Thrombocytosis</td>
<td>ET; and other MPNs.</td>
</tr>
<tr>
<td>• Aberrant VWF binding to tumor cells</td>
<td>Wilm’s tumor; certain plasma cell or lymphoproliferative disorders</td>
</tr>
<tr>
<td>• Decreased VWF synthesis</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>• Drug-related AVWS</td>
<td>Ciprofloxacin, valproic acid, hydroxyethyl starch, griseofulvin</td>
</tr>
</tbody>
</table>

AS/R: aortic stenosis/regurgitation; ET: essential thrombocythemia; MS/R: mitral valve stenosis/regurgitation; HOCM = hypertrophic obstructive cardiomyopathy; LVAD: left ventricular assist device; MGUS: Monoclonal Gammopathy; MPN = myeloproliferative neoplasms; PH: pulmonary hypertension; VSD: ventricular septal defect.
VWF:Activity/Antigen Ratio is Insensitive for Detecting AVWS with Subtle Loss of VWF HMWMs

<table>
<thead>
<tr>
<th></th>
<th>VWF:Ag (IU/dL)</th>
<th>VWF:RCo (IU/dL)</th>
<th>VWF:RCo/Ag Ratio (Cutoff: &lt;0.7)</th>
<th>VWF Multimer Electrophoresis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>105</td>
<td>96</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>LVAD Patient</td>
<td>231</td>
<td>220</td>
<td>0.95</td>
<td></td>
</tr>
<tr>
<td>Aortic Stenosis</td>
<td>147</td>
<td>112</td>
<td>0.76</td>
<td></td>
</tr>
<tr>
<td>Marked Thrombocytosis</td>
<td>57</td>
<td>52</td>
<td>0.91</td>
<td></td>
</tr>
</tbody>
</table>
ROC Curve of VWF:Lx/Ag and Rco/Ag Ratios for Detecting HMWM loss.

AUC=0.97

VWF:Lx/Ag=0.8
Sensitivity=88%
Specificity=92%

Mostly LVAD recipients

VWPR / von Willebrand Profile
Testing begins with:
- Coagulation Factor VIII Activity Assay, Plasma
- von Willebrand Factor Antigen, Plasma
- von Willebrand Factor Activity, Plasma

von Willebrand Factor (VWF) Antigen

- <55%
- 55%–200%

  Normal

von Willebrand Factor (VWF) Activity

- <55%
- 55%–200%

  Ristocetin Cofactor, Plasma

VWF Activity: VWF Antigen Ratio

- <0.8

von Willebrand Factor Multimer Analysis, Plasma

No evidence of von Willebrand disease. No further testing performed.

An interpretive report will be provided.
### Laboratory Features of AVWS in Patients with Mitral Regurgitation

<table>
<thead>
<tr>
<th>Laboratory Variables</th>
<th>Mild (N=14)</th>
<th>Moderate (N=14)</th>
<th>Severe (N=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regurgitation Volume (mL/beat)</td>
<td>&lt;30</td>
<td>30-59</td>
<td>≥60</td>
</tr>
<tr>
<td>Loss of VWF high molecular weight multimers</td>
<td>3 (21%)</td>
<td>8 (57%)</td>
<td>15 (79%)</td>
</tr>
<tr>
<td>Mitral Valve Replacement (N=17)</td>
<td></td>
<td></td>
<td>1 (6%)</td>
</tr>
</tbody>
</table>

General Approaches to VWF Multimer Testing

1. GI/Mucocutaneous Bleeding + Underlying Concomitant Diseases (e.g. Aortic stenosis, etc.)
2. Markedly Prolonged PFA-100 Normal VWF Antigen and Activity VWF:Activity/Antigen Ratio <0.8
3. VWF Multimer Analysis
Poster 2306

A Comparison of Von Willebrand Factor Indexes in Heartmate II Compared to Heartware Left Ventricular Assist Devices

Annual Meeting Program Information
Sunday, December 6, 2015, 6:00 PM-8:00 PM
Hall A (Orange County Convention Center)
Category: Disorders of Coagulation or Fibrinolysis

Session: 322. Disorders of Coagulation or Fibrinolysis: Poster II

Bhanu P Gupta, MD, MS*, Juan Leoni*, Parag Patel, MD*, Dong Chen, MD, PhD and Joseph Blackshear, MD*
Esoteric Tests to Discuss:

- Primary Fibrinolysis
- AVWS
- Platelet Disorders
- Molecular Testing
## Sensitivity of Detecting Dense Granule Deficiency by Routine Platelet Functional Tests

### 2012-2014 Demographics

<table>
<thead>
<tr>
<th></th>
<th>Total Subjects N = 10 Out of a total of 84 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female</td>
<td>6/4</td>
</tr>
<tr>
<td>Age at evaluation</td>
<td>Median 56.4 years</td>
</tr>
<tr>
<td></td>
<td>Range (10 days - 71.8 years)</td>
</tr>
</tbody>
</table>

### Bleeding Symptoms

<table>
<thead>
<tr>
<th>Bleeding Symptoms</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epistaxis</td>
<td>3</td>
</tr>
<tr>
<td>Bruising</td>
<td>7</td>
</tr>
<tr>
<td>Bleeding from superficial cuts</td>
<td>3</td>
</tr>
<tr>
<td>Oral bleed</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>3</td>
</tr>
<tr>
<td>Hematuria</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding with tooth extraction</td>
<td>2</td>
</tr>
<tr>
<td>Surgical bleeding</td>
<td>4</td>
</tr>
<tr>
<td>Menorrhagia</td>
<td>4</td>
</tr>
<tr>
<td>Hematoma/ Hemarthrosis</td>
<td>1</td>
</tr>
<tr>
<td>Intracranial bleed</td>
<td>1</td>
</tr>
</tbody>
</table>

### Laboratory Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td>197.5x10⁹/L (Range 27-389 x10⁹/L)</td>
</tr>
<tr>
<td>Median dense granule</td>
<td>0.7 (n=10, 0-1.1) normal range ≥1.2</td>
</tr>
</tbody>
</table>

---

Clinical and Laboratory Features of Patients with Platelet Dense Granule Deficiency: A Single Institution Experience

Platelet Transmission Electron Microscopy (PTEM)

• Whole Mount
  • Dense granules

• Platelet Thin Section
  • Alpha granules
  • Other platelet ultrastructure
Establishment of Platelet Transmission Electron Microscopic Tests

Dr. James G. White, Regents’ Professor of the University of Minnesota

Whole Mount Platelet Transmission Electron Microscopy (WM-PTEM)

Platelet Rich Plasma

Normal Control

Dense Granules
- Hermansky-Pudlak Syndrome
- Wiskott-Aldrich Syndrome
- Chédiak-Higashi Syndrome
- Jacobson-Paris Trousseau Syndrome
- Storage Pool Deficiency NOS
Communication with Patients

Normal Donor

Hermansky Pudlak Syndrome
Dense Granule Counting Criteria and Examples

- **TEM setting**
  - Electron microscope magnification is set at x1500
  - At least 100 platelets are counted

- **The features of true dense granules**
  - **Typical dense granules** (A-2,3,5,6,8; B-1,2):
    - Uniformly dense/dark texture
    - Perfectly round with sharp contour
    - > 50 nm in diameter
  - **Variants**
    - Tails or processes (A-4)
    - Rings or baskets
    - Hairy and fine processes from the dense core

- **The features of false dense granules**
  - **Alpha granules:** large, mostly irregular and less dense granules (A-1, 7,12,10)
  - Clusters or chains of small irregular-shaped particles (B-5,6,7,8)
  - Very small (< 50 nm) and pale dots (A-9,11;B-3)
  - Other nonspecific dirt or debris

Normal Reference Range of Platelet Dense Bodies


≥ 1.2 dense bodies/platelet

(n=111)
Thin Section Platelet Transmission Electron Microscopy (TS-PTEM)

Normal Donor

Gray Platelet Syndrome
General Approaches to Platelet Transmission

Electron Microscopy (PTEM)

- Persistent Mucocutaneous Bleeding with a Family Bleeding History and/or Thrombocytopenia
- Normal/Unusual Abnormal Platelet Function Testing Results
  - No VWD
- PTEM Testing
Flow Cytometry is the Test of Choice for Confirming Platelet Surface Receptor Deficiencies

- Reduced response to collagen
- Glanzmann thrombasthenia
- Bernard-Soulier syndrome
- Reduced response to collagen
- TXA2, ADP receptors
CD41 expression level (\%) = \frac{\text{Sample CD41 MFI}}{\text{Median of Normal donor CD41 MFI}}

MFI: Mean fluorescent intensity
Mayo Clinic Normal Range Studies  
Platelet Glycoprotein Expression

<table>
<thead>
<tr>
<th>Glycoprotein</th>
<th>Alternative Name</th>
<th>Normal Range 95% CI</th>
<th>Disease If Deficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP IIb</td>
<td>CD41</td>
<td>≥70%</td>
<td>Glanzmann thrombasthenia</td>
</tr>
<tr>
<td>GP IIIa</td>
<td>CD61</td>
<td>≥70%</td>
<td></td>
</tr>
<tr>
<td>GP Ib-α</td>
<td>CD42b</td>
<td>≥70%</td>
<td>Bernard Soulier syndrome</td>
</tr>
<tr>
<td>GP IX</td>
<td>CD42a</td>
<td>≥70%</td>
<td></td>
</tr>
<tr>
<td>GP Ia</td>
<td>CD49b</td>
<td>≥60%</td>
<td>Collagen receptor deficiency</td>
</tr>
<tr>
<td>GP VI (n=70)</td>
<td>GP6</td>
<td>≥70%</td>
<td></td>
</tr>
</tbody>
</table>

n=112; age:18-76 years
Persistent Mucocutaneous Bleeding with a Family Bleeding History and/or Thrombocytopenia

Abnormal and Distinct Platelet Aggregation Results

Confirmatory Test for Platelet Surface Receptor Deficiency by Flow Cytometry

General Approaches to Platelet Glycoprotein Flow Cytometry Testing
Poster 1061

Value of Platelet Esoteric Testing in Laboratory Diagnosis of Platelet Disorders: A Single Center Experience

Disorders of Platelet Number or Function
Program: Oral and Poster Abstracts
Session: 311. Disorders of Platelet Number or Function: Poster I
Saturday, December 5, 2015, 5:30 PM-7:30 PM
Hall A, Level 2 (Orange County Convention Center)

Juliana Perez Botero, MD, Deepti M. Warad, M.B.B.S., Rong He, MD, Rajiv K. Pruthi, MBBS and Dong Chen, MD, PhD
Esoteric Tests to Discuss:

- Primary Fibrinolysis
- Platelet Disorders
- AVWS
- Molecular Testing
Missing Obvious Standard Laboratory Phenotypes

<table>
<thead>
<tr>
<th>Syndromic Congenital Platelet Disorders</th>
<th>Frequency (reported families)</th>
<th>Inheritance</th>
<th>Gene (Chromosome)</th>
<th>Phenotypic Tests</th>
<th>Other Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wiskott-Aldrich syndrome</td>
<td>&gt;100</td>
<td>XL</td>
<td>WAS (Xp11)</td>
<td>Low MPV</td>
<td>Immune deficiency</td>
</tr>
<tr>
<td>X-linked thrombocytopenia</td>
<td>&gt;100</td>
<td>XL</td>
<td>WAS (Xp11)</td>
<td>Low MPV</td>
<td>Mild immune deficiency</td>
</tr>
<tr>
<td>MYH9-related disease</td>
<td>&gt;100</td>
<td>AD</td>
<td>MYH9 (22q12-13)</td>
<td>Smear PTEM</td>
<td>Cataracts, nephropathy, deafness</td>
</tr>
<tr>
<td>Paris-Trousseau/Jacobsen syndrome</td>
<td>&gt;100</td>
<td>AD</td>
<td>FLI-1 del(11q23)</td>
<td>PTEM</td>
<td>Cardiac and facial defect</td>
</tr>
<tr>
<td>Thrombocytopenia with absent Radii</td>
<td>&gt;50</td>
<td>AR</td>
<td>RBM8A (1q21.1)</td>
<td>Clinical</td>
<td>Bilateral radial aplasia</td>
</tr>
<tr>
<td>GATA-1-related disease</td>
<td>&gt;10</td>
<td>XL</td>
<td>GATA1 (Xp11)</td>
<td>PTEM</td>
<td>Hemolytic anemia, MDS, or hemoglobinopathy</td>
</tr>
<tr>
<td>Congenital thrombocytopenia with radio-ulnar synostosis</td>
<td>&lt;10</td>
<td>AD</td>
<td>HOXA11 (7p14-15)</td>
<td>Clinical</td>
<td>Aplastic anemia</td>
</tr>
<tr>
<td>Thrombocytopenia with sitosterolemia</td>
<td>&lt;10</td>
<td>AR</td>
<td>ABCG5/8 (2p21)</td>
<td>Clinical</td>
<td>Tendon xanthomas, atherosclerosis</td>
</tr>
<tr>
<td>FLNA-related thrombocytopenia</td>
<td>&lt;10</td>
<td>XL</td>
<td>FLNA (Xq28)</td>
<td>Clinical</td>
<td>Periventricular nodular heterotopia</td>
</tr>
<tr>
<td>York platelet syndrome</td>
<td>&lt;10</td>
<td>AD</td>
<td>STIM1 (11p15.5)</td>
<td>PTEM</td>
<td>Neuromyopathy</td>
</tr>
</tbody>
</table>
## Non-syndromic Congenital Platelet Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Frequency (reported families)</th>
<th>Inheritance</th>
<th>Gene (Chromosome)</th>
<th>Phenotypic Tests</th>
<th>Important Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bernard-Soulier syndrome</td>
<td>&gt;100</td>
<td>AR/AD</td>
<td>GP1BA (17p13)</td>
<td>Smear LTA Flow</td>
<td>Giant platelets</td>
</tr>
<tr>
<td>Biallelic/monoallelic</td>
<td></td>
<td></td>
<td>GP1BB (22q11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>GP9 (3q21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital amegakaryocytic thrombocytopenia</td>
<td>&gt;100</td>
<td>AR</td>
<td>MPL (1p34)</td>
<td>BM Bx</td>
<td>Megakaryocytic aplasia</td>
</tr>
<tr>
<td>Familial platelet disorder and predisposition to AML</td>
<td>&gt;50</td>
<td>AD</td>
<td>RUNX1 (21q22)</td>
<td>Clinical</td>
<td>MDS/AML risk</td>
</tr>
<tr>
<td>Gray platelet syndrome</td>
<td>&gt;10</td>
<td>AR</td>
<td>NBEAL2 (3p21.1)</td>
<td>PTEM</td>
<td>Myelofibrosis and splenomegaly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>GFI1B (9q34.13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANKRD26-related thrombocytopenia</td>
<td>&gt;10</td>
<td>AD</td>
<td>ANKRD26 (10p2)</td>
<td>Clinical</td>
<td>MDS/AML risk</td>
</tr>
<tr>
<td>ITGA2B/B3-related thrombocytopenia</td>
<td>&gt;10</td>
<td>XL</td>
<td>ITGA2B/B3 (17q21.31/32)</td>
<td>Flow cytometry</td>
<td>Large platelets</td>
</tr>
<tr>
<td>TUBB1-related thrombocytopenia</td>
<td>&lt;10</td>
<td>AD</td>
<td>TUBB1 (6p21.3)</td>
<td>PTEM</td>
<td>Giant platelets</td>
</tr>
<tr>
<td>CYCS-related thrombocytopenia (THC4)</td>
<td>&lt;10</td>
<td>AR</td>
<td>CYCS (7p153)</td>
<td>Clinical</td>
<td>Normal Platelets and no bleeding</td>
</tr>
</tbody>
</table>

**Important Features**
- Giant platelets
- Megakaryocytic aplasia
- MDS/AML risk
- Myelofibrosis and splenomegaly
- Normal Platelets and no bleeding
General Approaches to Platelet Molecular Testing

- Persistent Mucocutaneous Bleeding with a Family Bleeding History and/or Thrombocytopenia
- Normal/Unusual Abnormal Standard and Esoteric Testing Results
- No VWD

Clinical Phenotype ➔ Laboratory Phenotype ➔ Genotype

Targeted Genetic Testing
Platelet Transmission Electron Microscopy and Flow Cytometry in the Diagnosis of Congenital/Hereditary Qualitative or Quantitative Platelet Disorders

Juliana Perez Botero, MD1, Laynalee K Cardel, MT2*, Aneel A. Ashrani, MBBS, MSc1,2, John A. Heit, MD2,3, Rong He, MD2, C Christopher Hook, MD1,2, Robert D McBane II, MD2,3*, Animesh Pardanani, MBBS, PhD2,4, Deepti M. Warad, M.B.B.S.2,5, Waldemar E Wysokinski, MD, PhD2,3*, Vilmarie Rodriguez, MD5, William L. Nichols Jr., M.D.2,4, Rajiv K. Pruthi, MBBS1,2, Dong Chen, MD, PhD2 and Mrinal M Patnaik, MBBS1,2

1Division of Hematology, Mayo Clinic, Rochester, MN
2Division of Hematopathology, Special Coagulation Laboratory, Mayo Clinic, Rochester, MN
3Division of Cardiovascular Diseases, Department of Medicine, Mayo Clinic, Rochester, MN
4Division of Hematology, Department of Medicine, Mayo Clinic, Rochester, MN
5Division of Pediatric Hematology and Oncology, Mayo Clinic, Rochester, MN
Esoteric Tests Discussed:

- Primary Fibrinolysis
- AVWS
- Platelet Disorders
- Molecular Testing
A General Approach to Coagulation Esoteric Testing

1. Patient’s Personal and Family Bleeding History
2. Standard Coagulation Testing Results
3. Select the Appropriate Esoteric Tests
Thank You

Questions & Discussion