Coagulation in perspective:
Blood management

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Objectives

To gain a basic understanding of the following:

1. Coagulation – components and processes
   – Why patients bleed.
2. Monitoring of coagulation – tests
   – Why patient is bleeding (or not)
   – May give clue as to why
3. Therapies to correct bleeding
   • Brings abnormal coagulation and testing together
Understanding why patients bleed (why patients need blood products)

• Requires understanding of hemostasis and coagulation
  – Impact of disease state
  – Impact of pharmacology (pre-op: antiplatelet, anti-thrombin, peri-op: heparin/protamine)
  – Impact of CPB/anesthesia fluid management
    • Hemodilution + fluid management
    • Temperature
    • Anticoagulation
    • CPB-induced systemic inflammatory response

Coagulation
Key Concepts

• Coagulation occurs on a continuum
Coagulation continuum

Drug treatments:
• Anticoagulants
• Antithrombotic
• Fibrinolytic

Blood products*

Drugs:
• Antifibrinolytics
• Reversal agents for anticoagulants

Thrombosis

Too much clotting
Interfere with blood flow
or tissue perfusion

Localized ischemia

Bleeding

Not enough clotting
Uninhibited blood flow
plus blood loss

Generalized ischemia

Key concepts

• Hemostasis occurs on a continuum
• Hemostasis is complex:
  – Blood flow
  – Right environment

Platelets

Cellular elements

Vascular function

Substrates

Vascular elements

Landing platform

Blood products

Flow

Vasculature
The reality

Complexity:
Difficult to describe
Difficult to measure
Difficult to pinpoint cause

Plasma components cascade #1 – coagulation

Important points:
1. EXTRINSIC = primary initiation
2. Intrinsic
   • Foreign surfaces
   • Support function...
3. Thrombin = regulatory point
4. Cofactors = Ca²⁺, Phospholipid
5. Measurement = PT, aPTT
   1. PT = extrinsic path
   2. PTT = intrinsic path

http://www.frca.co.uk/article.aspx?articleid=100096
Routine coagulation tests

Plasma-based tests
Clotting times (fibrin)
aPTT:
• Routine heparin therapy
• Coagulation factor deficits
• Normal range: 24-35 sec
PT/INR
• Coumadin therapy
• Coagulation factor deficits
• Normal range: 11-13 sec

Normal range: 150,000 – 450,000/mm³

Activated Clotting Time

• Whole blood test (POC)
• Intrinsic pathway (celite or kaolin activator)
• Normal range 100 to 130 seconds
Monitoring heparin anticoagulation

Medtronic HMS unit

<table>
<thead>
<tr>
<th>Test Cartridges Used</th>
<th>Optimized patient treatment using the HMS Plus System Includes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin Assay Cartridges</td>
<td>Measuring actual circulating heparin concentration</td>
</tr>
<tr>
<td>Heparin Dose Response (HDR)</td>
<td>Assessing patient's individual response to heparin</td>
</tr>
<tr>
<td>High Range ACT (HR-ACT)</td>
<td>ACT tests</td>
</tr>
</tbody>
</table>

Blood management

Presence of anticoagulant

- Monitor for presence: ACT, PT, PTT
- Reversal
  - Heparin – protamine
  - Coumadin – time; emergent – FFP
  - Direct thrombin inhibitors
    - Prothrombin complex concentrates (PCC)
    - Drugs...
Key concepts

• Hemostasis occurs on a continuum
• Hemostasis is complex
• Coagulation is more than the cascade model
  – Cell-based model

Cell-based coagulation monitoring

- Platelet number
- **Platelet function**
- Viscoelastic monitoring

Platelet function testing

<table>
<thead>
<tr>
<th>Name of test</th>
<th>Principle</th>
<th>Clinical applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet aggregometry</td>
<td>Platelet aggregation to a panel of agonists</td>
<td>Diagnosis of inherited and acquired platelet defects</td>
</tr>
<tr>
<td>PFA-100/200</td>
<td>High shear platelet adhesion and aggregation</td>
<td>Detection of inherited and acquired platelet defects, monitoring antithrombotic drugs</td>
</tr>
<tr>
<td>Flow cytometry</td>
<td>Measurement of platelet GP, secretion, MP, and activation markers by fluorescence</td>
<td>Diagnosis of platelet GP defects, platelet release, PMP, platelet activation markers, monitoring antithrombotic drugs</td>
</tr>
<tr>
<td>Impact</td>
<td>Measurement of platelet adhesion and aggregation under high shear</td>
<td>Detection of inherited and acquired platelet defects, monitoring antithrombotic drugs</td>
</tr>
<tr>
<td>Thrombelastography (TEG/ROTEM)</td>
<td>Monitoring rate and quality of clot formation</td>
<td>Prediction of surgical bleeding, aid to blood product usage, monitoring antithrombotic drugs</td>
</tr>
<tr>
<td>VerifyNow</td>
<td>Platelet aggregation</td>
<td>Monitoring antithrombotic drugs</td>
</tr>
<tr>
<td>Multiplate</td>
<td>Platelet aggregation</td>
<td>Monitoring antithrombotic drugs</td>
</tr>
<tr>
<td>VASP-P</td>
<td>Flow cytometry with phosphoprotein-phosphorylation</td>
<td>Monitoring P2Y12 receptor activity</td>
</tr>
<tr>
<td>Microparticles</td>
<td>Flow cytometry with calibrated beads</td>
<td>Platelet activation markers, intercellular communication</td>
</tr>
</tbody>
</table>

Key point!

If platelets do not stick:
   No location
   No “good” clot formation

Implications for: Platelet function vs. number
- Prior platelet activation
- Antiplatelet medications

Viscoelastic monitoring
   cell based model
Viscoelastic monitoring

Cell based model

Whole blood assays
- Clotting times
- Rate of clot formation
- Clot strength
- Lysis

Key concepts

- Hemostasis occurs on a continuum
- Hemostasis is complex
- Coagulation is MORE than cascade model
  - Cell-based model
- Clot formation is a threshold event related to thrombin generation
Thrombin generation

- **T1** = lag phase
- **T2** = maximum rate of TG
- **T3** = Peak [thrombin]
- **T4** = Total free thrombin (AUC)

Fibrin cross linking

Lateral aggregation

**TG** = thrombin generation, AUC = area under the curve = endogenous thrombin potential (ETP). From: Wolberg AS. Blood Rev. 2007.

Determining hemostatic capacity

Clot times (ACT, PT, PTT)

- Visco-elastic tests
- **Thrombin generation**

Cascade model explains this much

< 5% thrombin generated

**TG** = thrombin generation, AUC = area under the curve = endogenous thrombin potential (ETP). From: Wolberg AS. Blood Rev. 2007.
Thrombin and clot structure

<table>
<thead>
<tr>
<th>nM Thrombin</th>
<th>0.5</th>
<th>2.5</th>
<th>5.0</th>
<th>15</th>
<th>20</th>
</tr>
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- Low
- Thick
- Loose

- High
- Thin
- Tight

Key concepts

- Hemostasis occurs on a continuum
- Hemostasis is complex
- Coagulation is MORE than cascade model
  - Cell-based model
- Clot formation is a threshold event related to thrombin generation
- Clot quality determines protection from lysis
Clot quality and [thrombin]

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</tr>
</thead>
<tbody>
<tr>
<td>Fiber thickness</td>
<td>Thick</td>
<td>26120X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fiber weave</td>
<td>Loose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vulnerability to fibrinolysis</td>
<td>High</td>
<td></td>
<td></td>
<td></td>
<td>Low</td>
</tr>
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What are the requirements for formation of a perfect clot?

- Substrates for clot formation
  - Coagulation factors (plasma)
  - Cells (functional platelets)
- Appropriate location and conditions
  - Exposure to local activators (vascular wall)
  - Hemodynamics
- Protection from fibrinolysis
Why do patients bleed?  
Approaches to blood management

- Lack of sutures
- Presence of anticoagulant
- Reversal
- Factor deficiency or deficiencies
  - FFP, PCC
  - Avoid co-factor deficiencies (calcium)
  - Avoid loss – circuit, prime volume and type, CPB management, anesthesia!
  - Avoid loss (consumption) – pharmacology
    - Anticoagulants
    - Antifibrinolytics
  - Recycle the loss – hemoconcentration, recycle circuit volume after CPB
- Platelet deficiency (number or function)
  - Platelets
  - Avoid loss – circuit, prime volume and type, CPB management
  - Avoid loss (consumption/exhaustion) – ??
- Active fibrinolysis
  - Avoid – pharmacology (antifibrinolytics)
  - Maximize thrombin generation (FFP/PCC, platelets)
- Slow biochemical reaction time
  - Adequate warming

Tying coagulation-monitoring-treatment together

TRANSFUSION ALGORITHM
Blood management

Transfusion Algorithm

- Microvascular bleeding noted in surgical field
- Coagulation and platelet function tests run
- Fibrinogen <120-150 mg/dL
- Elevated PT and/or Elevated aPTT
- PLT<50-100K and/or FIB<15K and/or ADP<40K
- Activated Clotting Time (ACT) > baseline
- Proxamine
- Surgical bleed
- CRIO
- FFP
- PLT Transfusion

Fibrinogen

Elevated PT

Plt <50-100K

Activated Clotting Time (ACT) > baseline

Proxamine

Surgical Bleed

Cardiac Surgery Blood Transfusion Algorithm

- sponge weight < 10 g (or no sponge weight)
- sponge weight ≥ 10 g

No Blood Products

Normal POC test

Abnormal POC test