Shear Stress and Arterial Thrombosis: Mechanism And Significance For Vascular Devices And Reconstructions

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Disclosures

- Employment
  - Staff Vascular Surgeon – Cleveland Clinic Foundation
  - Endologix – Chief Medical Officer
- Consultant
  - Intact Vascular
  - ROX Medical
  - BioConnect Systems

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  - Original researcher on SSIPA
  - Much of this presentation based on his work and instruction
- "Discovery" of this phenomenon in clinical vascular care an output of medical device development

Catastrophe – Flooded River
Does not “dam itself off”

Catastrophe – Trauma
Blood “dams” unrestricted hemorrhage
A MIRACLE- The “PLATELET PLUG”

Venous vs. Arterial Thrombus

- Flow
  - Venous – stasis
  - Arterial – high flow
- Histology
  - Venous – “red” clot; platelet poor/fibrin erythrocyte rich
  - Arterial – “white” clot; platelet rich
Paradoxes of Arterial thrombosis

1. Platelet aggregation studies with stasis (Virchow's triad paradigm)
2. Platelet concentration is small
   Transport should take months to occlude
3. Reported platelet bonding rate is too slow
   GP Ib/vWF ~ 0.1 - 30 sec
   Activation, GP IIb/IIIa ~ minutes
4. Bond strength too weak
   Shear forces should rip off thrombus

Occlusive thrombus should not occur
Heart attacks and strokes do not exist!
We should all bleed to death!

Shear-induced unfolding triggers adhesion of von Willebrand factor fibers

Multivalent Bonding

<table>
<thead>
<tr>
<th>Shear Stress</th>
<th>Force (pN)</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>170</td>
<td>2</td>
</tr>
<tr>
<td>400</td>
<td>1,700</td>
<td>17</td>
</tr>
<tr>
<td>4,000</td>
<td>17,000</td>
<td>170</td>
</tr>
</tbody>
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Bonding Kinetics

- Aggregation - **SUPER** fast
- <10 microseconds (milliseconds)
- Multivalent bonding occurs simultaneously with 40 nm spacing \(\rightarrow\) "Velcro" effect

Shear rises with stenosis
Shear up 50% with roughness

In Vitro Flow Experiments: Polyester Graft
- Compared thrombus generation characteristics with five polyester woven fabrics in 4-mm tubes (high and low shear based on CFD models)
- Results
  - High Fluid Shear Experiment ~500-600 dyne/cm²
  - All fabric types exhibited large amounts of thrombus formation
  - Low Fluid Shear Experiment ~30-50 dyne/cm²
  - All fabric types exhibited minimal or no thrombus formation
- No performance difference was observed between the five different graft materials in either the High or Low Shear Models

SSIPA in Clinical Vascular Texts – “Missing in Action”
- Rutherford’s “Vascular Surgery”
  - “shear stress induced platelet aggregation” not in index
  - No mention of platelet function in context of shear stress
  - Shear stress only noted as modulator of vessel diameter
  - No mention of “shear stress” in description of platelet physiology
  - Arterial thromboses recognized as “platelet rich” but no mechanism cited

Medical Literature Search: 1995-2010
“Shear stress-induced platelet aggregation”
1.8 million articles

“Key Issues”
- Affect of hemodynamics on platelet biology just starting to be explored
- Growing appreciation of high shear in amplification, kinetics and magnitude of platelet aggregation
- Current antiplatelet therapies do not target these mechanisms

Implications in Clinical Vascular Care
- Endografts: Implicated in multiple endografts thrombotic complications
- Carotid: primary disease, post-CEA “White Clot”, filter design
- Graft Occlusion: prosthetic and autogenous
- AV graft / fistula failure
- MI’s, CVA’s, etc.
- Tailoring anti-platelet therapy
“Take Home” Message

- High Shear = Hemorrhage
- Invokes highly evolved mechanism to prevent exsanguination