Disclosures

• None
Objectives

• Discuss coagulopathy related to trauma
• Review novel topical hemostatic agents
• Review data for tourniquets
Background

• Hemorrhage is the second leading cause of death in trauma
• Hemorrhage is the lead cause of preventable death in trauma
Prevalence of Uncontrolled Bleeding

<table>
<thead>
<tr>
<th>Surgical Discipline</th>
<th>Uncontrolled Bleeding Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>5%–7% Post-op(^1)</td>
</tr>
<tr>
<td>General</td>
<td>1.9% Laparoscopic cholecystectomy(^2)</td>
</tr>
<tr>
<td>Obstetric</td>
<td>3.9% (vaginal); 6.4% (cesarean)(^3,4)</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>2%–6.3% Hip/knee arthroplasty(^5-7)</td>
</tr>
<tr>
<td>Urologic</td>
<td>4%–8% TURP(^8); 3.3%–9.9% URL(^9)</td>
</tr>
<tr>
<td>Trauma</td>
<td>30%–40%(^10,11)</td>
</tr>
</tbody>
</table>

Hemostasis
“Life in the Balance”

Bleeding to Death
- Trauma
- Major Surgery
- Hemophilia

Clotting to Death
- Stroke
- MI
- Thrombosis

The Hemorrhaging Patient

- The Basics
  - Direct Pressure, splint fractures
  - Rapid Transport, Minimize fluids
  - Tourniquets (stay tuned)
Reducing Fractures Stops Bleeding
Open Book Pelvis Fracture
Resuscitating the Bleeding Patient

- Lethal Triad of Trauma
  - Hypothermia < 34
  - Acidosis < 7.1
  - Coagulopathy > 2

\[\{\text{98\% Mortality (w/o damage control)}\}\]
Addressing Coagulopathy

• Blood-based resuscitation
  – Military reports
  – Minimize crystalloid
  – Rapid transport to FST for blood based therapy

• Permissive hypotension
  – SBP 80-90 mmHg for penetrating trauma
  – SBP 120 mmHg for head injury
Table 4. Total Volumes of Fluids Administered to Patients with Penetrating Torso Injuries, According to Treatment Group.*

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>IMMEDIATE RESUSCITATION (N = 309)</th>
<th>DELAYED RESUSCITATION (N = 289)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before arrival at the hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ringer’s acetate (ml)</td>
<td>870±667</td>
<td>92±309</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Trauma center</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ringer’s acetate (ml)</td>
<td>1608±1201</td>
<td>283±722</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Packed red cells (ml)</td>
<td>133±393</td>
<td>11±88</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 5. Outcome of Patients with Penetrating Torso Injuries, According to Treatment Group.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>IMMEDIATE RESUSCITATION</th>
<th>DELAYED RESUSCITATION</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival to discharge — no. of patients/total patients (%)</td>
<td>193/309 (62)*</td>
<td>203/289 (70)†</td>
<td>0.04</td>
</tr>
<tr>
<td>Estimated intraoperative blood loss — ml‡</td>
<td>3127±4937</td>
<td>2555±3546</td>
<td>0.11</td>
</tr>
<tr>
<td>Length of hospital stay — days§</td>
<td>14±24</td>
<td>11±19</td>
<td>0.006</td>
</tr>
<tr>
<td>Length of ICU stay — days§</td>
<td>8±16</td>
<td>7±11</td>
<td>0.30</td>
</tr>
</tbody>
</table>

NEJM 1994; 331 (17): 1105-9
Damage Control Resuscitation: Directly Addressing the Early Coagulopathy of Trauma

John B. Holcomb, MD, FACS, Don Jenkins, MD, FACS, Peter Rhee, MD, FACS, Jay Johannisman, MD, FS, FACS, Peter Mahoney, FRCA, RAMC, Sumeru Mehta, MD, E. Darrin Cox, MD, FACS, Michael J. Gehrke, MD, Greg J. Beilman, MD, FACS, Martin Schreiber, MD, FACS, Stephen F. Flaherty, MD, FACS, Kurt W. Grathwohl, MD, Phillip C. Spinella, MD, Jeremy G. Perkins, MD, Alec C. Beekley, MD, FACS, Neil R. McMullin, MD, Myung S. Park, MD, FACS, Ernest A. Gonzalez, MD, FACS, Charles E. Wade, PhD, Michael A. Dubick, PhD, C. William Schwab, MD, FACS, Fred A. Moore, MD, FACS, Howard R. Champion, FRCS, David B. Hoyt, MD, FACS, and John R. Hess, MD, MPH, FACP

“Prolongation of the PT is the sentinel event...and occurs early in the operation”

J Trauma 2003
Fresh Frozen Plasma Should be Given Earlier to Patients Requiring Massive Transfusion

Ernest A. Gonzalez, MD, Frederick A. Moore, MD, John B. Holcomb, MD, Charles C. Miller, PhD, Rosemary A. Kozar, MD, PhD, S. Rob Todd, MD, Christine S. Cocanour, MD, Bjorn C. Balldin, MD, and Bruce A. McKinley, PhD

2007; 62:112
Topical Agents

WOUNDSTAT

QuikClot ACS
Advanced Clotting Sponge
Temporary Traumatic Wound Treatment
To Stop Moderate-to-Severe Bleeding
By Promoting Rapid Coagulation

For Emergency External Use
Do not eat

- See Directions On Back -
Topical Agents

• Mechanical only
  – Gauze – matrix for clot formation
• Mechanical and inherent hemostatic capability
  – Tissue factor activators
  – Induce Hypercoagulable State
Topical Agents

• Characteristics:
  – Stop large arterial vessel bleeding < 3 minutes
  – No need to mix/reconstitute
  – Light weight
  – Long/indefinite shelf life in extreme setting
  – Safe/no infectious concerns
  – Inexpensive
Mechanisms

• Mucoadhesive agents
  – Chitosan based: Celox, HemCon
  – Plug the hole
• Factor concentrates
  – QuikClot
  – Create a hypercoagulable environment
• Procoagulant supplementation
  – Dressing with imbedded procoagulant factors

• All require 3-5 minute hold
• All must be removed (non-absorbable)
Mucoadhesive Agents
HemCon/Chitoflex/Celox

- Chitosan based product that adheres to the bleeding surface and seals it
  - Supposed to work in coagulopathy because it plugs the hole
  - Must be in firm contact with the bleeding surface
- Bacteriostatic
Celox: Heparinized Porcine Model

Hemostasis Following Heparinization and Femoral Artery Injury Using No Compression or 1 Minute Compression

- No Hemostasis Despite Compression
- Hemostasis after Further 1 min Compression
- Immediate Hemostasis, No Compression

Not published
Factor Concentrates
QuikClot

• Zeolite (volcanic rock)
  – Absorbs water to make the local area hypercoagulable
  – Poor outcome in coagulopathic patient
Table 3 Post-Injury Effects of Control (gauze) and QuikClot Treatments

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gauze</th>
<th>QuikClot</th>
<th>( p ) Value of Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-treatment blood loss (ml)</td>
<td>5338 ± 806</td>
<td>1397 ± 806</td>
<td>(&lt;0.01)</td>
</tr>
<tr>
<td>Resuscitation fluid used (ml)</td>
<td>9686 ± 1260</td>
<td>5574 ± 1260</td>
<td>(0.04)</td>
</tr>
<tr>
<td>Peak temperature at tissue interface (°C)</td>
<td>37.5 ± 0.01</td>
<td>93.3 ± 10.5</td>
<td>(&lt;0.01)</td>
</tr>
<tr>
<td>Survival</td>
<td>1/8</td>
<td>7/8</td>
<td>(&lt;0.01)</td>
</tr>
<tr>
<td>(12%)</td>
<td>(88%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival time (min)</td>
<td>44.5 ± 3.6</td>
<td>58.3 ± 1.8</td>
<td>(&lt;0.01)</td>
</tr>
</tbody>
</table>
Hemostatic Dressings

Quick-Clot
Procoagulant Supplement
Combat Gauze

• Woven gauze impregnated with Kaolin
  – Activates clotting process
  – Must be in dense contact with bleeding surface
    • Hold for 3-5 minutes
  – May not be effective in coagulopathic patient
Evidence/Trials

• No prospective studies
• Retrospective, uncontrolled data
• Animal data
In Vitro Effects of Topical Agents on Coagulation

Fig. 7. The average thrombograms of pig blood after treatment with different hemostatic agents. Two milliliter of blood samples were mixed with 9 mg of each agent and assayed after addition of calcium chloride. The agents were compared with a known contact pathway activators (Celite) and untreated blood (control).

Kheirabadi et al. J Trauma 2009; 66:316-328
Comparison of Various Topical Hemostatics

Animal Studies

Kheirabadi et al. J Trauma 2009; 66:316-328
Liver Injury Model

In the control and QuikClot ACS+ animals that survived to reoperation, removal of the packs led to immediate rebleeding, severe enough that repacking would have been necessary in all cases. In the Celox arm, however, all but one animal had successful removal of packs and excess hemostatic agent without the need for repacking.

Tourniquets
Tourniquets

• **SAVE LIVES!!**

• Max time 120 minutes

• Risk factors for injury
  – Injury/Shock
  – Age
  – Vascular disease
Tourniquet

• Use a wide, smooth material
• Apply to the thickest part of the extremity
• Tighten to the pressure needed to make the extremity pulseless
• Mark the time that the tourniquet was applied
  – Do NOT cover the extremity
### TABLE 2. Indications for Tourniquet Use in Emergency Medical Services (EMS) and other Prehospital Settings

<table>
<thead>
<tr>
<th>Amputation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to stop bleeding with pressure dressing(s)</td>
</tr>
<tr>
<td>Injury does not allow control of bleeding with pressure dressing(s)</td>
</tr>
<tr>
<td>Significant&lt;sup&gt;a&lt;/sup&gt; extremity hemorrhage in the face of any or all of:</td>
</tr>
<tr>
<td>Need for airway management</td>
</tr>
<tr>
<td>Need for breathing support</td>
</tr>
<tr>
<td>Circulatory shock</td>
</tr>
<tr>
<td>Need for other emergent interventions or assessment</td>
</tr>
<tr>
<td>Bleeding from multiple locations</td>
</tr>
<tr>
<td>Impaled foreign body with ongoing extremity bleeding</td>
</tr>
<tr>
<td>Under fire or other dangerous situation for responding caregivers</td>
</tr>
<tr>
<td>Total darkness or other adverse environmental factors</td>
</tr>
<tr>
<td>Mass casualty event&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Significant extremity hemorrhage

<sup>b</sup> Mass casualty event
# Tourniquet Use

**Table 1. Potential Complications of Use of Tourniquets**

<table>
<thead>
<tr>
<th>Local</th>
<th>Systemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative swelling and stiffness</td>
<td>Increased central venous pressure</td>
</tr>
<tr>
<td>Delay in recovery of muscle power</td>
<td>Arterial hypertension</td>
</tr>
<tr>
<td>Compression neuropraxia</td>
<td>Cardiorespiratory decompensation</td>
</tr>
<tr>
<td>Wound hematoma</td>
<td>Cerebral infarction</td>
</tr>
<tr>
<td>Wound infection</td>
<td>Alterations in acid-base balance</td>
</tr>
<tr>
<td>Direct vascular injury</td>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>Bone and soft-tissue necrosis</td>
<td>Deep venous thrombosis</td>
</tr>
<tr>
<td>Compartment syndrome</td>
<td>Tourniquet pain</td>
</tr>
<tr>
<td></td>
<td>Systemic inflammatory response</td>
</tr>
<tr>
<td></td>
<td>syndrome (^a)</td>
</tr>
<tr>
<td></td>
<td>Fibrinolysis (^b)</td>
</tr>
</tbody>
</table>

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Conclusion

• 1. Minimize coagulopathy
  – Minimize fluids
  – Rapid transport to trauma center

• 2. Minimize bleeding
  – Permissive hypotension
  – Tourniquet use
  – Rapid transport to trauma center

• 3. Novel Hemostatic agents
  – Celox and Combat Gauze appear to be the best
Podcast On Topical Hemostatics

• http://www.east.org/resources/traumacast-detail/28