Objectives

- Review historic treatments for hemorrhage
- Examine the current evidence and recommendations on:
  - Tourniquets and External Mechanical Devices
  - Topical Hemostatic Agents
  - Intravenous Hemostatic Agents
- Review Current Treatment Guidelines for Traumatic Hemorrhage:
  - Civilian
  - Military
- Use of Hemostatic Agents in Oklahoma

Extremity Hemorrhage

…from the historic US Military perspective:
Tourniquets in World War II
Wolff and Adkins.
US Army Medical Department 1945, 37:77-84

“We believe that the strap-and-buckle tourniquet in common use is ineffective in most instances under field conditions...it rarely controls bleeding no matter how tightly applied.”

Vietnam – 1960’s

Over 2500 deaths occurred in Vietnam secondary to hemorrhage from extremity wounds. These casualties had no other injuries.

Tourniquets in U.S Military Mid-1990s

- Old strap-and-buckle tourniquets were still being issued.
- Medics and corpsmen were being trained in courses where they were taught not to use them.
Tactical Combat Casualty Care in Special Operations

Military Medicine Supplement
August 1996

Trauma care guidelines customized for the battlefield

Factors That Might Have Changed Outcomes
(82 Fatalities – 12 Potentially Survivable)

- Hemostatic dressings/direct pressure (2)
- Faster CASEVAC or IV hemostatic agents (7)
- PRBCs on helos (2)
- Tourniquets (3)

U.S. Military Involvements & Massive Transfusion Management

- World War I: vascular collapse was thought to be caused by toxins
- World War II: plasma was the resuscitation fluid of choice; ATN was recognized as a consequence of hypovolemic shock
- Korea & Vietnam: concerns of ARDS in setting of fluid resuscitation
- Iraq & Afghanistan: MTP development and use of fresh whole blood

- Present Day: Hemostatic Agents
Tourniquets – Beekley et al
Journal of Trauma 2008

- 31st Combat Support Hospital in 2004
- 165 casualties with severe extremity trauma
- 67 with prehospital tourniquets; 98 without
- **7 DEATHS:** Four of the seven deaths were potentially preventable had an adequate prehospital tourniquet been placed

Potentially Preventable Deaths (232) in Iraq/Afghanistan

- CNS 9%
- MSOF 4%
- Airway 14%
- Hemorrhage 85%

From evaluation of 962 casualties, casualties could have more than 1 cause of death. (Kelly J., J Trauma 64:S21, 2008)

Survival with Emergency Tourniquets

- Tourniquets are saving lives on the battlefield
- 31 lives saved in 6 months by tourniquets
- Author estimates 2000 lives saved with tourniquets in this conflict up to that date (2009)
- No arms or legs lost because of tourniquet use
Preventable Death on the Battlefield: Iraq/Afghanistan

Eastridge 2012 Study:
- 4,596 U.S. deaths
- 87% pre-hospital deaths
- 24% of pre-hospital deaths were potentially survivable


Point of Wounding Care

Causes of preventable death on the battlefield today:
- Hemorrhage from extremity wounds
- Junctional hemorrhage (where an arm or leg joins the torso, such as in the groin area after a high traumatic amputation)
- Non-compressible hemorrhage (such as a gunshot wound to the abdomen)
- Tension pneumothorax
- Airway problems

Practical Use of Emergency Tourniquets to Stop Bleeding in Major Limb Trauma

- "The CAT is the best pre-hospital tourniquet."
- "The EMT is the best ED tourniquet."
- "Use improvised windlass tourniquets when scientifically validated tourniquets are unavailable."
“Some commercially available tourniquets do not reliably occlude arterial blood flow and may not be successful in preventing exsanguination in a trauma patient.”

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<th>Tourniquet Type</th>
<th>0%</th>
<th>20%</th>
<th>40%</th>
<th>60%</th>
<th>80%</th>
<th>100%</th>
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<td>Special Forces Tactical Tourniquet</td>
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<td>Emergency &amp; Military Tourniquet</td>
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<td>Self-Applied Tourniquet System (44%)</td>
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<td>One-Handed Tourniquet (22%)</td>
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<td>Mechanical Advantage Tourniquet (88%)</td>
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<td>Last Resort Tourniquet (67%)</td>
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Timing of Tourniquet Application:

- Pre-Hospital Tourniquet Application: 89% survival (78% in hospital.)
- Tourniquet Application BEFORE onset of shock: 96% survival (4% AFTER onset of shock.)

**TCCC Guidelines (2013)**

- Stop life-threatening external hemorrhage
- Direct casualty to administer self-aid
- Use Co-TCCC recommended tourniquet if anatomically amenable
- Apply proximal to bleeding sight, over the uniform, tighten, move to cover
Tactical Field & Evacuation Care

- Control life-threatening external hemorrhage with tourniquet (if anatomically amenable.) Apply directly to skin 2-3 inches above wound.
- Use Combat Gauze (hemostatic agent) for compressible hemorrhage not amenable to tourniquet use. Apply with direct pressure for at least 3 minutes.

Junctional Hemorrhage

These types of wounds are often caused by IEDs and may result in junctional hemorrhage.

Tactical Field & Evac Care, cont.

- If bleeding site is appropriate for use of a Co-TCCC-recommended junctional tourniquet, apply immediately when available. Use Combat Gauze with direct pressure while awaiting junctional tourniquet.
Tactical & Evac Care, cont.

- Reassess tourniquet placement and need.
- Expose wound, remove uniform, reapply directly to skin.
- Check for distal pulse. Tighten or apply second tourniquet (side by side) to eliminate pulse.
- Ensure all tourniquet sites are marked and timed.

Tactical Field Care & Evac, cont.

Tranexamic Acid

- If anticipated to need significant blood transfusion:
  - Hemorrhagic Shock or Severe Bleeding
  - Major Amputation(s)
  - Penetrating Torso Trauma
- Administer 1 gm TXA (in 100 ml NS or LR) ASAP < 3 hours after injury.
- Begin second infusion of 1 gm TXA after Hextend or other fluid treatment.

Hartford Consensus
2 April 2013

- Working group organized by American College of Surgeons Board of Regents and FBI
- In response to Sandy Hook shootings
- Excerpt from findings:

Life-threatening injuries in active shooter incidents such as those in Fort Hood, Tucson, and Aurora are similar to those encountered in combat settings. Military experience has shown that the number one cause of preventable death in victims of penetrating trauma is hemorrhage. Tactical Combat Casualty Care (TCCC) programs, when implemented with strong leadership support, have produced dramatic reductions in preventable death. Recognizing that active shooter incidents can occur in any community, the Hartford Consensus encourages the use of existing techniques and equipment, validated by over a decade of well-documented clinical evidence.
Management of External Hemorrhage

- Recommendations by Expert Panel of Civilian EMS Physicians
- After review of all available military and civilian literature

Tourniquets

- Recommendation #1:
  - “We recommend the use of tourniquets in the prehospital setting for the control of significant extremity hemorrhage if direct pressure is ineffective or impractical.”

Tourniquets (Remarks)

- Clear survival benefit
  - Consistent in large-scale clinical trials
- Direct Pressure may be ineffective
  - Major Arterial Injury
- Direct Pressure may be impractical
  - Limited Manpower
  - Unsecured Scene
  - Complex Extrication / Extraction
Tourniquets

- Recommendation #2:
  - "We suggest using commercially produced windlass, pneumatic, or ratcheting devices that have been demonstrated to occlude arterial flow."

Tourniquets

- Recommendation #3:
  - "We suggest against the use of narrow, elastic, or bungee-type devices."
Recommendation #4:

“We suggest that improvised tourniquets be applied only if no commercial device is available.”

“The Deckers’ neighbor, a sheriff’s deputy, was able to run over and use a belt as a tourniquet to stop Stephanie’s bleeding.”

Military experience

“Proven Effectiveness”

Non-commercial tourniquets

- Impede venous return only
- Inadequate arterial occlusion
- Worsening of hemorrhage

Boston Bombing Experience
Tourniquets

- Recommendation #5:
  - "We suggest against releasing a tourniquet that has been properly applied in the pre-hospital setting until the patient has reached definitive care."

Tourniquets (Remarks)

- "Relatively" Short Transport Time for most civilian EMS agencies
  - <6 hours is the generally accepted rule

- Prolonged Transport Times or Austere Environment?
  - Medical Control consultation required before tourniquet removal

Junctional Hemorrhage Devices

- No sufficient evidence to make recommendations

- Pending retrospective study from US military experience
Combat Ready Clamp (CRoC)

Abdominal Aortic & Junctional Tourniquet (AAJT)

SAM Junctional Tourniquet
Topical Hemostatic Agents

Recommendation 1:

“We suggest the use of topical hemostatic agents, in combination with direct pressure, for control of significant hemorrhage in the pre-hospital setting in anatomic areas where tourniquets cannot be applied and where sustained direct pressure alone is ineffective or impractical.”

Topical Hemostatic Agents (Remarks)

- Low volume of human data
- Consistent data from animal models demonstrating reduced hemorrhage when compared to standard gauze.
- Junctional hemorrhage and torso wounds may benefit from the combination of direct pressure and hemostatic dressings.

Recommendation #2:

“We suggest that topical hemostatic agents be delivered in a gauze form that supports wound packing.”
Topical Hemostatic
(Remarks)

- Military Experience
- Animal Studies
- Products that allow packing of the wound have superior hemorrhage control.
Topical Hemostatic Agents

Recommendation #3:
- "Only products determined effective and safe in a standardized laboratory injury model should be used."

Topical Hemostatic (Remarks)

- U.S. Army Institute for Surgical Research
  - Standardized large animal model for comparison of hemostatic dressings
  - All new products should be subject to this testing.

Additional Recommendations

- Tourniquets and topical hemostatic agents should be available to all pre-hospital personnel, including emergency medical responders.
Additional Research Needed

 Strong military data
 Minimal civilian research
 No data on special populations
  • Pediatrics
  • Elderly

New treatments for Hemorrhage

 Mechanical External Wound Closure
 IV Hemostatic Agents

iTClamp

 “Temporary Wound Closure”
“The iTClamp showed statistically significant improvement in survival, survival time, and estimated blood loss when compared to no treatment.”

PHARMACOLOGICAL AGENTS TO SUPPORT ANTI-COAGULATION

- Recombinant Activated Factor VII
- Prothrombin Complex Concentrate
- Antifibrinolytics
- Artificial Blood
**Recombinant Activated Factor VII**
- Hemostatic agent originally developed to treat Hemophilia
- Activates platelets at the site of injury
- Dosing widely variable (60-200 mcg/kg)
- Studies: Reduced the need for massive transfusion, but no reduction in mortality
- Thromboembolic complications
- 90 mcg/kg dose = $4,500

**Prothrombin Complex Concentrate**
- Factors II, VII, IX, and X
- Primarily used to reverse oral anticoagulant hemorrhage (intracranial and GI bleeding)
- No adequate studies in trauma
- Concerns for thromboembolism & DIC
- 1 dose = $1,000
Anti-Fibrinolytics

- Attenuates coagulopathy associated with hyperfibrinolysis
- Aprotinin
  - Renal & vascular complications, death
- Aminocaproic Acid
  - Used to reverse Heparin
  - Renal complications and Acute MI
- Tranexamic Acid
  - Initially used in elective surgery
  - No adequate studies (2010) until CRASH II

Artificial Blood

- “Alternative Oxygen Carriers”
  - Modified Hemoglobins
    - Polyheme
    - Hemopure
    - Perfluorocarbons
  - Short half life
  - Currently under study
  - Toxicity and lab interference unknown
**THE LANCET**

### Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

Findings 19396 patients were allocated to tranexamic acid and 19317 to placebo, of whom 9946 and 9942, respectively, were analysed. All-cause mortality was significantly reduced with tranexamic acid (2.3% [95% CI 1.8–2.9%]) versus placebo group (3.8% [95% CI 3.3–4.3%]; relative risk 0.61; 95% CI 0.50 to 0.73; p<0.0001). The risk of death due to bleeding was significantly reduced (28.7% [95% CI 23.5–34.1%]; relative risk 0.63; 95% CI 0.52 to 0.77; p<0.0001).

Interpretation Tranexamic acid safely reduced the risk of death in bleeding trauma patients in this study. On the basis of these results, tranexamic acid should be considered for use in bleeding trauma patients.
Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) Study

Jonathan J. Morris, MB, BCH, BAO; Joseph P. Duboe, MD; Todd E. Reamses, MD;
Mark J. Hyams, MD, FACS

Conclusions: The use of TXA with blood component-based resuscitation following combat injury results in improved measures of coagulopathy and survival, a benefit that is most prominent in patients requiring massive transfusion. Treatment with TXA should be implemented into clinical practice as part of a resuscitation strategy following severe wartime injury and hemorrhage.


Figure 2. Kaplan-Meier survival curve of the overall cohort, including patients receiving tranexamic acid (TXA) or no TXA. P < .001, Mantel-Cox log-rank test with 95% CI.

CRASH
Corticosteroids for the treatment of significant traumatic brain injury: an international randomized, double-blind placebo-controlled trial

- Traumatic Brain Injury Patients
- Effect on Death and Disability
- Study Dates: 12/1/2011 – 1/31/2017

AIM: "The CRASH-3 trial will provide reliable evidence about the effect of tranexamic acid on mortality and disability in patients with TBI. The effect of TXA on the risk of vascular occlusive events and seizures will also be assessed."
Tranexamic Acid (TXA)

- Practical Applications for Civilian EMS??

- In patients with the anticipated need for massive blood transfusion…

(i.e. blood loss internally or externally with signs of shock – tachycardia / hypotension)

External Hemorrhage

Penetrating Truncal Trauma
Blunt Truncal Trauma

TXA Cost
- Military $1.50 a dose
- Civilian $45-55 a dose
- Military considers shelf life in years
- Manufacturer likely doesn’t!
- Advised temps 59-86 degrees F
- Viewed very heat stable in Middle East

Initial TXA rollout in OK on 4/1/13
- Established in Massive Transfusion Protocols for Level I & II Trauma Centers
  - OU Medical Center
  - Saint Francis Hospital
  - Saint John Medical Center
Initial TXA rollout in OK on 4/1/13

- Tulsa Life Flight (first ever use of TXA by EMS in Oklahoma)
- EMSA
- Oklahoma City Fire
- Tulsa Fire
- Skiatook Fire
- Collinsville Fire

Preliminary Results (OKLA)

- Infrequent Use by TLF (very rare by EMSA)
- Vital Sign Parameters limit to the most severely injured (Low BP AND Fast HR)
- Small Sample Size
- High Mortality rate to date
  - Likely due to pre-existing injuries, inevitable outcome
- Large, multi-state study needed
Pediatric Tranexamic Acid

Tranexamic Acid:

- **Age:** Indicated for patients age 10 and above. 10-17 (pediatric dosing); 18 and above (adult dosing.)
- **Pediatric Dosing (age 10-17):** 15 mg/kg (up to 1 gm MAX) IVPB over 10 minutes.

Pediatric Tranexamic Acid

- Approved by Trauma Surgeons at OU and Saint Francis (Pediatric Trauma) in January 2015. Used in ED at SFH & OUMC.
- GOOD results so far (very few uses)

Final Thoughts

- Carry a Commercial Tourniquet (or several)... use them!
- Consider Combat Gauze
- Think about Tranexamic Acid
- Don’t let your patient die from internal or external hemorrhage!