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FOR: JONATHAN WOODSON, M.D., ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

SUBJECT: Battlefield Medical Research, Development, Training and Evaluation Priorities, 2012-08

EXECUTIVE SUMMARY

The Defense Health Board (DHB) submitted a report to the Assistant Secretary of Defense (Health Affairs) (ASD(HA)) on June 14, 2011 with a list of high-priority battlefield medical research, development, test and evaluation (RDT&E) issues relating to battlefield trauma care. The report advised the Department to endorse the issues and forward them to the Armed Services Biomedical Research and Evaluation Management Committee and Service Surgeons General as high priority RDT&E efforts for improving battlefield trauma care. This report contains an updated and abbreviated list of the highest priority battlefield medical RDT&E issues. The DHB recommends that the ASD(HA) forward to the Deputy Assistant Secretary of Defense (Force Health Protection and Readiness) and Service Surgeons General for consideration.

BACKGROUND

The importance of prehospital care for our combat wounded was highlighted by a presentation at the May 2012 Committee on Tactical Combat Casualty Care (CoTCCC) meeting by COL Brian Eastridge, a committee member and Joint Trauma System representative. COL Eastridge conducted a 10-year analysis on the causes of death in U.S. combat fatalities. He noted that:

1) Approximately 25 percent of combat fatalities occurred in casualties with potentially survivable injuries;

2) Almost 90 percent of combat fatalities occur in the prehospital phase of care; and

3) Approximately 50 percent of casualties who die after admission to a medical treatment facility were suffering from essentially irreversible hemorrhagic shock present at the time of admission.

These findings highlight the critical importance of prehospital care in ensuring that our combat wounded have the best possible chance of survival.

METHODOLOGY

The TCCC Guidelines are a set of evidence-based trauma care guidelines customized for use in the prehospital combat setting. TCCC is currently used in training for medics by all Services in the Department of Defense (DoD) and by many U.S. coalition partners. The CoTCCC, a work

group of the DHB's Trauma and Injury Subcommittee, performs a quarterly review of current evidence demonstrating the successes and shortcomings of the TCCC Guidelines, and considers proposed updates and revisions. The CoTCCC utilizes available evidence and defines areas requiring additional research to fill critical knowledge gaps that may substantially benefit combat casualty care.

As part of this process, the CoTCCC evaluates evidence gaps relating to battlefield trauma care. While randomized controlled trials are not feasible on the battlefield, animal model studies, civilian trauma studies and retrospective reviews of combat casualty data may inform decisions. During its May 2012 meeting, the CoTCCC reviewed existing information gaps in battlefield trauma care and recommended a list of more than fifty battlefield RDT&E priorities. The Trauma and Injury Subcommittee subsequently revised and approved this list of priorities for DHB review. The Subcommittee presented the list to the DHB on June 25, 2012, during which the Board deliberated and accepted the Subcommittee's proposal, and requested that the Subcommittee shorten the list to the absolute highest priorities. The CoTCCC met on August 16, 2012 and discussed which battlefield trauma care research efforts should be considered as the highest priority. Work Group members considered the following factors when voting on the items that they felt were most important:

- Will conducting this research help to identify the causes of preventable death on the battlefield?
- How likely is it that the outcomes of this research will reduce the incidence of preventable death on the battlefield?
- Will conducting this research help identify ways to reduce long-term disability for casualties?
- Is the research question applicable to prehospital care providers?
- What methods or tools are currently available to address the problem we are proposing to address in the research question?
- How long would it take?
- How much would it cost?

The Work Group provided a list of the priority items to the Subcommitee. On November 8, 2012, the Subcommitee held a teleconference to review the list and determine the final top ten. This list was presented to the Board in an open public session on November 26, 2012.

DELIBERATIONS

The Board extensively deliberated the Subcommittee's findings and recommendations when the list of priorities was inititally presented on June 25, 2012. The result of their initial deliberations is the complete list of significant battlefield medical RDT&E priorities included at Attachment A. Once this list was refined by the CoTCCC and Trauma and Injury Subcommittee, Board member Dr. Donald Jenkins presented the revised list on behalf of the Subcommittee. The Board members briefly discussed each of the ten items proposed and concurred that these items should be considered the most important. Members expressed that the Department should use this list to guide the prioritization of prospective clinical research. They voted unanimously to accept the list provided by the Subcommittee as a Board recommended list of top priorities.

FINDINGS

Battlefield trauma research conducted to support the U.S. military should focus on issues that possess the greatest potential benefit for U.S. casualties. Since the greatest percentage of fatalities occur during the prehospital phase of care, this should be an area of increased research emphasis. The items contained on the list below represent the priorities that the Board believes offer the greatest return on investment for Combat Casualty Care RDT&E.

1. Unit-based prehospital trauma registries

At present, the documentation of in-theater trauma care is inconsistent, incomplete and often not transferred to either unit-based prehospital trauma registries (such as that pioneered by the 75th Ranger Regiment) or a trauma system registry, such as the Joint Theater Trauma Registry (JTTR). Improved methods to document pre-hospital care are essential. Further, command attention is vital to this aspect of combat trauma care and would help ensure our troops continue to receive the best possible battlefield trauma care.

2. FDA-approved freeze-dried blood products (such as plasma and platelets)

Freeze dried plasma (FDP) was identified at the 2010 U.S. Army Institute of Surgical Research (USAISR)-Medical Research and Materiel Command Fluid Resuscitation Conference as the most promising near-term fluid for damage control resuscitation in circumstances when Special Operations Forces medics or other combat medical personnel must care for a casualty in a remote location where evacuation may be delayed for several hours or days. FDP was encouraged as a top research priority among the subject matter experts at this conference. The Food and Drug Administration (FDA) has not yet approved any dried plasma product and the Special Operations community is currently pursuing a French FDP product as an interim solution.

The importance of platelets as well as plasma in hemostatic resuscitation has recently been documented.[1,2] Similar to plasma, storage requirements limit the ability of platelets to be fielded forward of fixed medical treatment facilities.[3] Since trauma-related hemorrhage remains the leading cause of preventable death in combat casualties,[4] optimizing hemorrhage control and managing hemorrhagic shock offer the greatest potential to avoid preventable death from combat injuries. Most combat fatalities occur before the casualty reaches a medical treatment facility. Obtaining an FDA-approved freeze-dried platelet product along with evidence of a survival benefit from the product would enable this potentially lifesaving treatment modality to be used in the pre-hospital phase of combat casualty care.

3. Clinicopathological review of every U.S. combat fatality, including preventable death analyses from combat units

It is challenging to determine optimal processes to reduce the incidence of potentially survivable fatalities on the battlefield without adequate data. A study conducted by Holcomb examined the causes of death among SOF during the Global War on Terror (GWOT) between 2001 and 2004, and a similar study conducted by Kelly compared injury severity and causes of death during OIF

and OEF from 2003 to 2004, with those during 2006.[5,6] Information obtained from autopsy records for fatalities in the current conflicts could assist in determining the causes of death and which deaths were potentially preventable. This information may then be used to guide battlefield trauma care process improvement efforts.

Published studies of preventable deaths in specific combat units[5,7] have enabled U.S. military medical personnel to make targeted improvements in prehospital trauma care. Especially since equipment is not standardized and training varies, analyses of each fatality provides an opportunity to identify whether this lack of standardization results in any additional fatalities. Studies examining these issues would enable Line combat leaders to take appropriate actions to improve trauma care in their units or Service.

4. Development and testing of non-compressible torso and junctional hemorrhage control devices

Combat trauma data indicate that hemorrhage caused by junctional injuries is now a significant cause of preventable death on the battlefield.[8] In 2011, the DHB recommended the Combat Ready Clamp™ (CRoC) be approved for use in casualties with junctional hemorrhage. The CRoC is designed to decrease hemorrhage by applying direct or indirect pressure on the arterial supply in the inguinal region. Additional studies are needed to better define the indications for this device and its optimal use in combat casualties. Furthermore, ongoing safety and efficacy studies should be performed, as those conducted have been limited to cadaver studies using a sample size.

The Abdominal Aortic Tourniquet™ is a second type of hemorrhage control device that compresses proximal vascular supply. Recently approved by the FDA, it is intended to provide hemorrhage control by compressing the aorta immediately distal to the renal arteries, reducing blood flow to distal abdominal, pelvic and lower extremity vessels. It may help stop hemorrhage in an otherwise noncompressible area. Efficacy studies should be conducted on this and similar devices in human patients or an appropriate animal model.

5. Optimized airway devices and training

Current options for airway management in the battlefield trauma care setting include the nasopharyngeal airway, chin-lift/jaw-thrust positioning, sit-up-and lean-forward positioning, endotracheal intubation, supraglottic airways and surgical airways. Other airway technology options might be developed that would expand the options available to battlefield medical care providers for managing difficult airways in austere settings. Potential new technology solutions should be developed and evaluated for casualties with airway trauma. These devices should be small, light, rugged, simple and be easy to use by Emergency Medical Technician-Basic level providers with minimal training time.

CoTCCC member LTC Robert Mabry reported that combat medics have a 33 percent failure rate in performing prehospital surgical airways.[9] The battlefield is a uniquely disadvantageous environment in which to perform an emergency surgical procedure; additionally, combat medical personnel are generally inexperienced in performing surgical airways. Further research is

needed to identify techniques and technology that will better equip combat medical providers with the best possible skills and devices to perform emergency surgical airways.

6. Optimal fluid resuscitation for casualties with Traumatic Brain Injury and shock

Fluid resuscitation in casualties with traumatic brain injury (TBI) is complicated by concerns about raising blood pressure to ensure adequate cerebral perfusion without causing increased hemodilutional coagulopathy, increased intracranial pressure, and increased hydrostatic pressure at areas of vascular injuries (which could increase blood loss from a site of unrepaired vascular injury). There is a need for studies investigating optimal resuscitation strategies for casualties who have TBI and are in, or at risk for, hemorrhagic shock. Both blood component therapy and asanguinous fluid resuscitation should be studied, but the greatest evidence gap is the effects of asanguinous fluids on patients with TBI.

7. Training and evaluation methods for TCCC skills

Combat medical personnel must often perform lifesaving interventions in the very challenging battlefield environment. It is imperative that the training methodology used to teach these skills to combat medics, corpsmen, and pararescuemen be optimized and based on proven methods. Possible training modalities for these skills include lectures, simulation devices, cadavers, field laboratories, simulated combat scenarios and live tissue training. The optimal mix of training modalities has not been well-documented or established. Pressure exists from animal rights groups for the abandonment of live tissue training. However, there is no definitive data indicating that alternative methods of training sufficiently arm medics and other TCCC practitioners with an acceptable level of skill and readiness for the battlefield.

It is imperative that combat medical personnel be as well prepared as possible to perform lifesaving interventions. Many simulation devices are available to help achieve this goal, but limited data document the relative efficacy of various commercially available simulation technologies. As the Department faces pressure to increase simulation training, studies are needed to fill this information gap, especially for such procedures as surgical airways, supraglottic airways, intraosseous infusion devices, hemorrhage control interventions, and needle decompression.

8. Impact of TCCC interventions in preventing Post Traumatic Stress Disorder and TBI, including the role of analgesia in preventing PTSD

Incidences of TBI and post-traumatic stress disorder (PTSD) among combat casualties have increased significantly in recent years,[10] making this an issue of utmost imporance to the Department. Simultaneously, several studies demonstrate the value of TCCC in reducing combat fatality rates and improving outcomes for casualties sustaining combat injuries. However, there is a gap in the evidence base regarding the effectiveness of TCCC interventions in preventing PTSD and TBI, and the impact of those interventions on the long-term outcomes of those with TBI or PTSD.

In a retrospective study using data from the JTTR, Holbrook and colleagues noted an association between administration of morphine analgesia and decreased incidence of PTSD.[11] In this study, analgesia was provided at a Level I or Level II medical treatment facility (MTF). Transport time from point of injury to administration of morphine upon arrival at the MTF was one hour or less in 71 percent of patients. Of the patients that received morphine, 98 percent received it intravenously. Given the retrospective nature of the study, there is a need for prospective studies on this topic to determine whether there is a causal relationship between IV morphine analgesia administration and decreased risk of PTSD, as well as whether this link holds true for other forms of analgesia.

9. Combat casualty care monitoring devices

Improved monitoring techniques that provide rapid, reliable and actionable information about a casualty's status are of great value for combat medics. These data are even more useful if they are: 1) shown or able to be shown in a trending display so that the medic may see temporal patterns of the vital sign(s) being monitored; and 2) able to be downloaded or printed in order to be preserved as part of a casualty's prehospital care documentation. Furthermore, there is continued interest in identifying optimal monitoring methods that would detect casualties who need, or will soon need, lifesaving interventions. Such monitors would help efforts to avoid preventable death. Tissue oxygenation is one physiological parameter that may have value both as a predictor for cardiovascular collapse and as a guide to resuscitation efforts. This parameter reflects central venous oxygenation and should be evaluated for use in monitoring combat casualties in the prehospital setting.

10. Impact of Tactical Evacuation provider level and skill sets on survival (prospective studies)

Transporting casualties who have serious injuries requires appropriate timing and resources. A critical care gap currently exists between transport from forward surgical/resuscitative care and more definitive care. Optimal casualty outcomes may be influnced by Tactical Evacuation (TACEVAC) provider expertise and available resources. There are at least three models of evacuation platform staffing in use in the United States Central Command (USCENTCOM) Area of Operations at present: the MERT model, which usually includes an emergency medicine consultant; U.S. air ambulance platforms with flight paramedics; and, U.S. air ambulance platforms with Army combat medics (68 Whiskeys). There is a need for prospective studies to determine the optimal TACEVAC staffing model.

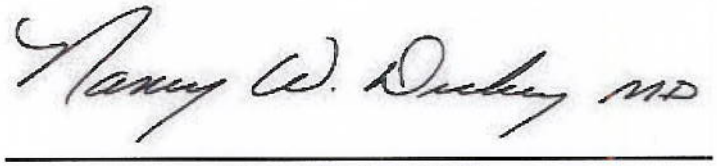
SUBJECT: Battlefield Medical Research, Development, Training and Evaluation Priorities, 2012-08

RECOMMENDATIONS

The Board advises the Department to endorse the following medical RDT&E issues and forward them to the Deputy Assistant Secretary of Defense (Force Health Protection and Readiness) and Service Surgeons General for consideration as high priority RDT&E efforts that will improve battlefield trauma care. The Board recommends the Department track the research regarding these priority issues and provide regular updates concerning their status to the DHB.

1. Unit-based prehospital trauma registries
2. FDA-approved freeze-dried blood products (such as plasma and platelets)
3. Clinicopathological review of every U.S. combat fatality, including preventable death analyses from combat units
4. Development and testing of non-compressible torso and junctional hemorrhage control devices
5. Optimized airway devices and training
6. Optimal fluid resuscitation for casualties with TBI and shock
7. Training and evaluation methods for TCCC skills
8. Impact of TCCC interventions in preventing PTSD and TBI, including the role of analgesia in preventing PTSD
9. Combat casualty care monitoring devices
10. Impact of TACEVAC provider level and skill sets on survival (prospective studies)

FOR THE DEFENSE HEALTH BOARD:



Nancy Dickey, M.D.
DHB President

ATTACHMENTS

A. List of Additional Battlefield Medical RDT&E Priorities

WORKS CITED

1. Holcomb J, Spinella P. Optimal use of Blood in Trauma Patients. *Biologicals* 2010; Epub ahead of print.

2. Cap A, Spinella P, Borgman M, et al. Timing and Location of Blood Product Transfusion and Outcomes in Massively Transfused Combat Casualties. *J Trauma Acute Care Surg* 2012;**73**:S89-S94.

3. Joshi NV, Raftis JB, Lucking AJ, et al. Lyophilised Reconstituted Human PlateletsIncrease Thrombus Formation in a Clinical Ex Vivo Model of Deep Arterial Injury. *Thrombosis and Hemostasis* 2012; **108**:1-7.

4. Eastridge BJ, Costanzo G, Jenkins D, et al. Impact of Joint Theater Trauma System Initiatives on Battlefield Injury Outcomes. *Annals of Surgery* 2009; **198**(6):852-7.

5. Holcomb JB, McMullin NR, Pearse L, et al. Causes of Death in U.S. Special Operations Forces in the Global War on Terrorism (2001-2004). *Annals of Surgery* 2007; **245**(6):986-991.

6. Kelly JF, Ritenour AE, McLaughlin DF, et al. Injury Severity and Causes of Death From Operation Iraqi Freedom and Operation Enduring Freedom: 2003-2004 Versus 2006. *Journal of Trauma* 2007; **64**(2):S21-7.

7. Kotwal RS, Montgomery HR, Mabry RL, et.al. Eliminating Preventable Death on the Battlefield. *Archives of Surgery* 2011; **146**: 1350-1358.

8. Report of the Army Dismounted Complex Blast Injury Task Force, 18 June 2011. Dismounted Complex Blast Injury Task Force. Available at: http://www.armymedicine.army.mil/reports/DCBI%20Task%20Force%20Report%20(Redacted%20Final).pdf.

9. Mabry RL. An Analysis of Battlefield Cricothyroidotomy in Iraq and Afghanistan. *J Spec Oper Med* 2012; **12**(1): 17-23.

10. Fischer, H. U.S. Military Casualty Statistics: Operation New Dawn, Operation Iraqi Freedom, Operation Enduring Freedom. Congressiona Research Service 7-5700. September 28, 2010.

11. Holbrook TL, Galarneau MR, Dye JL, et. al. Morphine use after combat injury in Iraq and incidence of post-traumatic stress disorder. *NEJM* 2010; **362**: 110-117.

ADDITIONAL REFERENCES

Arishita GI, Vayer JS, and RF Bellamy. Cervical Spine Immobilization of Penetrating Neck Wounds in a Hostile Environment. *Journal of Trauma* 1989; **29**(3): 332-7.

Barkana Y, Stein M, Scope A, et al. Prehospital Stabilization of the Cervical Spine for Penetrating Injuries of the Neck – Is It Necessary. *Injury* 2000; **31**(5): 305-9.

Bartolacci RA, Munford BJ, Lee A, et al. Air Medical Scene Response to Blunt Trauma: Effect on Early Survival. *Med J Aust* 1998; **169**: 612-6.

Belmont PJ Jr., Schoenfeld AJ, and G. Goodman. Epidemiology of Combat Wounds in Operation Iraqi Freedom and Operation Enduring Freedom: Orthopaedic Burden of Disease. *Journal of Surgical Orthopaedic Advances* 2010; **19**(1): 2-7.

Bilukha OO, Brennan M, and M. Anderson. Injuries and Deaths from Landmines and Unexploded Ordnance in Afghanistan, 2002-2006. *JAMA* 2007; **298**: 516-8.

Butler FK Tactical Combat Casualty Care: Update 2009. *Journal of Trauma* 2010; Suppl 1:S10-3.

Coats T, Roberts I, and H Shakur. Antifibrinolytic Drugs for Acute Traumatic Injury. *Cochrane Database System Review* 2011; 19(1):CD004896.

Comstock S, Pannell D, Talbot M, et al: Spinal injuries after improvised explosive device incidents: implications for tactical combat casualty care. *J Trauma* 2011; **71**: S413-S417.

Curry N, Hopewell S, Doree C, et al. The Acute Management of Trauma Hemorrhage: A Systematic Review of Randomized Controlled Trials *Critical Care* 2011; **15**(2): R92.

Deal VT, McDowell D, Benson P, et al. Tactical Combat Casualty Care February 2010 Direct from the Battlefield: TCCC Lessons Learned in Iraq and Afghanistan, *J Spec Oper Med* 2010; **10**(3): 77-119.

Eastridge BJ, Wade CE, Spott MA, et al. Utilizing a Trauma Systems Approach to Benchmark and Improve Combat Casualty Care. *Journal of Trauma* 2010; **69**(Suppl 1): S5-9.

Eastridge BJ, Costanzo G, Jenkins D, et al. Impact of Joint Theater Trauma System Initiatives on Battlefield Injury Outcomes. *Annals of Surgery* 2009; **198**(6): 852-7.

Garner A. The Role of Physician Staffing of Helicopter Emergency Medical Services in Prehospital Trauma Response. *Emerg Med Australas* 2004; **16**: 318-23.

Garner A, Rashford S, Lee A, et al. Addition of Physicians to Paramedic Helicopter Services Decreases Blunt Trauma Mortality. *Aust N Z J Surg* 1999; **69**: 697-701.

Gerhardt RT, De Lorenzo RA, Oliver J, Holcomb JB, and JA Pfaff. Out-of-Hospital Combat Casualty Care in the Current War in Iraq. *Ann Emerg Med* 2009; **53**: 169-74.

Gruen RL and B Mitra. Tranexamic Acid for Trauma. *The Lancet* 2011; **377**(9771): 1052-4.

Guerriero C, Cairns J, Perel P, et al. Cost-Effectiveness Analysis of Administering Tranexamic Avid to Bleeding Trauma Patients Using Evidence from the CRASH-2 Trial. *PLoS One* 2011; **6**(5): e18987.

Holcomb J, Spinella P: Optimal use of blood in trauma patients. *Biologicals* 2010; Epub ahead of print.

Holcomb JB, McManus JG, Kerr ST, et al. Needle Versus Tube Thoracostomy in a Swine Model of Traumatic Tension Hemopneumothorax. *Prehospital Emergency Care* 2009; **13**(1):18-27.

Holcomb JB, Stansbury LG, Champion HR, et al Understanding Combat Casualty Care Statistics. *J Trauma 2006;* **60**(2):397-401.

Jenkins DW Jr, McKinney MK, Szpak MW, et al. Veres Needle in the Plural Space. *South Med J* 1983; **76**(11): 1383-5.

Kang DG and RA Lehman, Jr. Spine Immobilization: Prehospitalization to Final Destination. *Journal of Surgical Orthopaedic Advances* 2011; **20**(1):2-7.

Kelly JF, Ritenour AE, McLaughlin DF, et al. Injury Severity and Causes of Death From Operation Iraqi Freedom and Operation Enduring Freedom: 2003-2004 Versus 2006. *J Trauma* 2007; **64**(2): S21-7.

Kheirabadi BS, Scherer MA, Estep JS, et al. Determination of Efficacy of New Hemostatic Dressings in a Model of Extremity Arterial Hemorrhage in Swine. *J Trauma* 2009; **67**: 450-60.

Kragh JF Jr, Walters TJ, Baer DG, et al. Survival with emergency tourniquet use to stop bleeding in major limb trauma. *Ann Surg* 2009; **249**: 1-7.

Kragh JF, Walters TJ, Baer DG, et. al. Practical use of emergency tourniquets to stop bleeding in major limb trauma. *J Trauma* 2008; **64**: S38-S50

Levy JH. Antifibrinolytic Therapy: New Data and New Concepts. *Lancet* 2010; 376:3-4.

Ling GS, Rhee P, and JM Ecklund. Surgical Innovations Arising from the Iraq and Afghanistan Wars. *Annu Rev Med* 2010; 61:457-68.

Littlejohn LF, Devlin JJ, Kircher SS, et al. Comparison of Celox-A, ChitoFlex, WoundStat, and Combat Gauze Hemostatic Agents versus Standard Gauze Dressing in Control of Hemorrhage in a Swine Model of Penetrating Trauma. *Acad Emerg Med* 2011; **18**(4): 340-50.

Mitra B, Fitzgerald M, Cameron PA, et al. Tranexamic Acid for Trauma. *The Lancet* 2010; **376**(9746): 1049.

Morrison CA, Carrick MM, Norman MA, et al. Hypotensive Resuscitation Strategy Reduces Transfusion Requirements and Severe Postoperative Coagulopathy in Trauma Patients with Hemorrhagic Shock: Preliminary Results of a Randomized Controlled Trial. *J Trauma* 2011; **70**: 652-63.

Perkins JG, Cap AP, Weiss BM, et al. Massive Transfusion and Nonsurgical Hemostatic Agents. *Critical Care Medicine* 2008; **36**(7 Suppl): S325-39.

Ramasamy A, Midwinter M, Mahoney P, et al. Learning the Lessons from Conflict: Pre-Hospital Cervical Spine Stabilization following Ballistic Neck Trauma. *Injury* 2009; **40**(12): 1342-5.

Schoenfeld AJ, Goodman GP and PJ Belmont, Jr. Characterization of Combat-Related Spinal Injuries Sustained by a U.S. Army Brigade Combat Team During Operation Iraqi Freedom *The Spine Journal* 2010 [Epub ahead of print].

Shuja F, Finkelstein RA, Fukudome E, et al. Development and Testing of Low Volume Hyperoncotic, Hyperosmotic Spray-Dried Plasma for the Treatment of Trauma-Associated Coagulopathy. *J Trauma* 2011; **70**: 664-71.

Stuke L, Pons P. Guy J, et al: Prehospital spine immobilization for penetrating trauma-review and recommendations from the prehospital trauma life support executive committee. *J Trauma* 2011; **71**: 763-770.

Sydenham E. Thousands of Lives Could Be Saved Using Tansexamic Acid for Patients with Bleeding Trauma. *Injury Prevention* 2011; May 5 [Epub ahead of print].

Taber KH, Warden DL, and RA Hurley. Blast-Related Traumatic Brain Injury: What is Known? *J Neuropsychiatry Clin Neurosci* 2006; **18**:141-5.

Tobin JM, Via DK, and T Carter. Tactical Evacuation: Extending Critical Care on Rotary Wing Platforms to Forward Surgical Facilities. *Military Medicine* 2011; **176**(1):4.

Vandromme MJ, Griffin RL, Kerby JD, et al. Identifying Risk for Massive Transfusion in the relatively Normotensive Patient: Utility of the Prehospital Shock Index. *Journal of Trauma* 2011; **70**: 384-90.

Wang HE, Mann NC, Mears G, et al. Out-of-Hospital Airway Management in the United States. *Resuscitation* 2011; **82**: 378-85.

Warner KJ, Copass MK, and EM Bulger. Paramedic Use of Needle Thoracostomy in the Prehospital Environment. *Prehospital Emergency Care* 2008; **12**(2): 162-8.

Waxman S, Beekley A, Morey A, et al. Penetrating Trauma to the External Genitalia in Operation Iraqi Freedom. *Int J Impot Res* 2009; **21**: 145–8.

Yeguiayan JM, Rosencher N, and M Freysz. Tranexamic Acid for Trauma. *Lancet* 2010; **376**(9746): 1050-1.

ATTACHMENT A. List of Battlefield Medical RDT&E Priorities (unordered)

Unit-based prehospital trauma registries
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asanguinous fluid resuscitation should be studied, but the greatest evidence gap is the effects of asanguinous fluids on patients with TBI.

Training and evaluation methods for TCCC skills

Combat medical personnel must often perform lifesaving interventions in the very challenging battlefield environment. It is imperative that the training methodology used to teach these skills to combat medics, corpsmen, and pararescuemen be optimized and based on proven methods. Possible training modalities for these skills include lectures, simulation devices, cadavers, field laboratories, simulated combat scenarios and live tissue training. The optimal mix of training modalities has not been well-documented or established. Pressure exists from animal rights groups for the abandonment of live tissue training. However, there is no definitive data indicating that alternative methods of training sufficiently arm medics and other TCCC practitioners with an acceptable level of skill and readiness for the battlefield.

It is imperative that combat medical personnel be as well prepared as possible to perform lifesaving interventions. Many simulation devices are available to help achieve this goal, but limited data document the relative efficacy of various commercially available simulation technologies. As the Department faces pressure to increase simulation training, studies are needed to fill this information gap, especially for such procedures as surgical airways, supraglottic airways, intraosseous infusion devices, hemorrhage control interventions, and needle decompression.

Impact of TCCC interventions in preventing Post Traumatic Stress Disorder and TBI, including the role of analgesia in preventing PTSD

Incidences of TBI and post-traumatic stress disorder (PTSD) among combat casualties have increased significantly in recent years,[10] making this an issue of utmost imporance to the Department. Simultaneously, several studies demonstrate the value of TCCC in reducing combat fatality rates and improving outcomes for casualties sustaining combat injuries. However, there is a gap in the evidence base regarding the impact of TCCC interventions in preventing PTSD and TBI, and differences in outcomes of those with TBI or PTSD.

In a retrospective study using data from the JTTR, Holbrook and colleagues noted an association between administration of morphine analgesia and decreased incidence of PTSD.[11] In this study, analgesia was provided at a Level I or Level II medical treatment facility (MTF). Transport time from point of injury to administration of morphine upon arrival at the MTF was one hour or less in 71 percent of patients. Of the patients that received morphine, 98 percent received it intravenously. Given the retrospective nature of the study, there is a need for prospective studies on this topic to determine whether there is a causal relationship between IV morphine analgesia administration and decreased risk of PTSD, as well as whether this link holds true for other forms of analgesia.

Combat casualty care monitoring devices

Improved monitoring techniques that provide rapid, reliable and actionable information about a casualty's status are of great value for combat medics. These data are even more useful if they are: 1) shown or able to be shown in a trending display so that the medic may see temporal patterns of the vital sign(s) being monitored; and 2) able to be downloaded or printed in order to

be preserved as part of a casualty's prehospital care documentation. Furthermore, there is continued interest in identifying optimal monitoring methods that would detect casualties who need, or will soon need, lifesaving interventions. Such monitors would help efforts to avoid preventable death. Tissue oxygenation is one physiological parameter that may have value both as a predictor for cardiovascular collapse and as a guide to resuscitation efforts. This parameter reflects central venous oxygenation and should be evaluated for use in monitoring combat casualties in the prehospital setting.

Impact of Tactical Evacuation provider level and skill sets on survival (prospective studies)
Transporting casualties who have serious injuries requires appropriate timing and resources. A critical care gap currently exists between transport from forward surgical/resuscitative care and more definitive care. Optimal casualty outcomes may be influnced by Tactical Evacuation (TACEVAC) provider expertise and available resources. There are at least three models of evacuation platform staffing in use in the United States Central Command (USCENTCOM) Area of Operations at present: the MERT model, which usually includes an emergency medicine consultant; U.S. air ambulance platforms with flight paramedics; and, U.S. air ambulance platforms with Army combat medics (68 Whiskeys). There is a need for prospective studies to determine the optimal TACEVAC staffing model.

Non-Compressible Hemorrhage Control

Critical Plasma Components for Treatment of Non-Compressible Hemorrhage with Supporting Studies

The DHB recently recommended tranexamic acid (TXA) for use in combat casualties with hemorrhagic shock or at significant risk for developing hemorrhagic shock, based on the survival benefits documented in the CRASH-2 subgroup analysis and the MATTERS study.[12, 13, 14, 15] Other plasma components may also be beneficial in promoting hemostasis and improving survival when used alone or in conjunction with TXA. Additional research is needed to: better define which plasma components may be advantageous; determine their optimal use in conjunction with other aspects of resuscitative therapy; and quantify any improvements in survival rates that are potentially associated with their use.

Oxygen-Carrying Resuscitation Fluids

Several published papers question the benefit of prehospital asangiunous fluids in trauma patients.[16, 17, 18] In contrast, blood component therapy in a balanced 1:1 ratio of plasma and packed red blood cells has been shown to increase survival in patients with significant hemorrhage and require massive transfusion.[19] Oxygen-carrying resuscitation fluids, especially when used in conjunction with FDP, might provide a survival benefit over crystalloids and colloids. Possibilities might include the next generation of hemoglobin-based oxygen carriers or perfluorocarbons. Products and supporting studies should be pursued to determine any survival benefit.

Whole Blood Substitute for Resuscitation from Hemorrhagic Shock

Optimal prehospital resuscitation fluids should replicate as closely as possible both the oxygen-carrying capability of whole blood or packed red blood cells, as well as the hemostasic benefit produced by clotting components found in liquid plasma or FDP. The development of a whole blood substitute with these dual features that can reproduce the lifesaving ability of either whole

blood or 1:1 resuscitation, which is also suitable for battlefield use by combat medical personnel, is the "Holy Grail" of fluid resuscitation research.

Improved Battlefield Analgesia

Opioid Analgesia and Mortality

Narcotic analgesic medications continue to be the standard of care for battlefield analgesia. However, these medications carry the risk of cardiorespiratory depression. Hemorrhagic shock continues to be the leading cause of potentially preventable death among combat casualties. In a casualty with or at risk for hemorrhagic shock, narcotic analgesics may result in a worsening of hemodynamic status and ultimately in death. This risk may be greater when the narcotic is given intramuscularly (IM) and the onset of analgesia is delayed, possibly resulting in additional doses to relieve ongoing pain. There are no published studies comparing the relative safety of IM morphine, intravenous (IV) morphine, oral transmuscoal fentanyl citrate (OTFC) and ketamine in the prehospital management of combat casualties. This data would enable medics to make more informed decisions regarding battlefield analgesia. Specifically, a study is needed to evaluate the relationship between opioid analgesics and survival using casualty data from the Joint Theater Trauma Registry (JTTR) in matched injury severity score cohorts. Subgroup data analyses should include incidence reporting of any uncontrolled hemorrhage and shock, as well as the type and route of administration of the provided opioid.

Transdermal Lidocaine for Analgesia in Combat Trauma

Narcotic analgesics can cause cardiorespiratory depression, which is especially problematic in casualties who are potentially at risk for hemorrhagic shock. Ketamine does not cause cardiac or respiratory depression, but may be associated with dysphoric reactions or other adervse events. Transdermal lidocaine is an alternative option for battlefield analgesia. Lidocaine works locally, blocking pain impulses from the site of pain or injury. Five percent lidocaine patches are approved by the FDA for the treatment of post-herpetic neuralgia. Lidocaine patches were reported to reduce the pain associated with rib fractures.[20] This agent and possibly other transdermal agents should be evaluated for use in battlefield pain management.

Pre-Hospital Care Documentation and Databasing

Voice-Activated Medical Recording Devices

Documentation of battlefield trauma care continues to be inconsistent, as noted in a number of published reports.[7, 21, 22] While the 75th Ranger Regiment has had success with a medic-designed TCCC card, an analysis of alternatives is needed to determine whether other documentation methodologies may improve prehospital care documentation and better enable both accurate descriptions of care rendered and enhanced process improvement efforts. One option that should be considered is a voice-activated recording device that can be attached to the helmet. The time-stamped voice file could be forwarded to support personnel after combat action for incorporation in both the patient's electronic medical record and the JTTR.

Hemostatic Dressing Studies

Comparison Testing of Celox™ Gauze, Combat Gauze™, ChitoGauze,™ and the Modified Rapid Deployment Hemostat

New hemostatic agents/dressings have become available since Combat Gauze™ was introduced several years ago and recommended for use in TCCC. Although there have been favorable

reports from both pre-hospital and in-hospital use of Combat Gauze™, it would be useful to study new agents in comparison to Combat Gauze™ using the consensus bleeding model developed at USAISR to gain an understanding of their relative efficacy and safety.

Multiple Fragmentation Wound Hemostatic Dressing with Supporting Studies
The majority of casualties currently received at Level III facilities in the Afghanistan Theater of Operations have blast injuries from improvised explosive devices (IEDs) or rocket-propelled grenades (RPGs). These individuals often have shrapnel wounding patterns with multiple entry wounds that may span both extremities and torso. Hemostatic options designed for this type of wounding pattern should be evaluated for use in combat casualties.

Hemostatic Dressings for Large Battlefield Soft Tissue Injuries Casualties with Supporting Studies
As noted above, the majority of casualties currently being admitted to Level III facilities in the Afghanistan Theater of Operations have incurred IED or RPG blast injuries. These individuals often have devastating injuries that may include wounds with very large soft tissue defects. Hemostatic dressings designed for this type of wounding pattern should be evaluated for use in combat casualties.

Negative Pressure Hemostatic Dressing System with Supporting Studies
Preliminary studies at USAISR demonstrate that the application of negative pressure may be a useful adjunct in promoting hemostasis. Negative pressure could potentially be applied by a portable device or through use of wall suction. Studies to further evaluate the efficacy and utility of this technique are needed.

Hemostatic Strategies and Agents for Coagulopathic Casualties
For all of the wound types noted above, testing for newly developed hemostatic agents proposed for combat care use is done using animal hemorrhage models with a high incidence of mortality in the untreated control groups. Agents are selected based on superior performance in efficacy trials and a lack of reported adverse effects in safety trials. A recent in-theater study demonstrated that many combat casualties are coagulopathic at the time of admission to Role III facilities and that coagulopathy is associated with increased mortality.[23] Future laboratory evaluations of proposed hemostatic agents should include efficacy studies in coagulopathic casualties, and employ models with extensive soft tissue injuries as well as focal vascular injuries.

Strategies for Lowering Intracranial Pressure during Prehospital Care
The Board recently reviewed strategies for managing TBI in TCCC and providedseveral recommendations to the Department. One area in which additional studies are needed is in the area of prehospital measures undertaken to mitigate increases in intracranial pressure (ICP) in casualties with impending cerebral herniation. Studies are needed that would outline device effectiveness in lowering ICP and document improvements in casualty outcome from lowered ICP.

Comparative Chest Seal Studies
The TCCC Guidelines recommend occlusive dressings for the treatment of open pneumothoraces resulting from combat wounds ("sucking chest wounds"). Although a number of chest seals are commercially available, data are limited to support the relative merits of one model versus another. Comparative chest seal studies should review the following important features: size, ease of handling, quality of adhesion to a bleeding chest wound and the effectiveness of incorporating a valve in the seal design to decrease the potential for tension pneumothorax onset following application.

Medic Resiliency Studies
Combat medics treating their wounded teammates on the battlefield are required to perform lifesaving interventions on individuals with devastating wounds. During the course of repeated combat deployments, medics, corpsmen and pararescueman may have numerous exposures to casualties with overwhelming injuries, many which may have resulted in fatalities. This may place these individuals at high risk for PTSD. Studies are needed to define the extent of this disorder among combat medical personnel and to evaluate potential treatment interventions.

Prehospital Strategies to Lower Extremity Osteomyelitis Incidence
Osteomyelitis from combat wounds that include extremity bony injuries may worsen a casualty's disability and prolong recovery. Measures designed to prevent this type of infection are needed. Additional studies are needed to define what prehospital interventions may be undertaken to successfully reduce the incidence of osteomyelitis.

The Effect of Gender on Survival in Combat Casualties
Women are generally found to have a more favorable outcome following traumatic injury than men. One recent study found that this survival advantage is inverted in U.S. casualties from Iraq and Afghanistan.2[4] This issue should be more fully researched and reasons sought for any observed decrease in the probability of survival among female casualties.

TCCC Curriculum Translations for Partner Nations
Many coalition partner nations now use the TCCC Guidelines to train their forces in managing combat trauma on the battlefield. In addition, many countries who are or may become strategic partners with the U.S,. are interested in obtaining TCCC training. As updates to the TCCC Guidelines and curriculum are implemented to reflect future changes in best practices for battlefield trauma care, these changes should be translated into the languages of all the nations with which the U.S. is engaged in strategic partnerships or training relationships.

Field Handheld Diagnostic Imaging Capablities
A small, multi-use, durable device that would improve the ability of combat medics to diagnose specific life-threatening conditions such as tension pneumothorax, hemothorax, expanding intracranial hemorrhagic lesions and abdominal bleeding might facilitate more timely and appropriate prehospital interventions. This tool should be capable of recording, transmitting and downloading diagnostic findings and would enable more precise diagnoses and treatments to be provided during prehospital trauma care.

WORKS CITED:

1. Holcomb J, Spinella P. Optimal use of Blood in Trauma Patients. *Biologicals* 2010; Epub ahead of print.

2. Cap A, Spinella P, Borgman M, et al. Timing and Location of Blood Product Transfusion and Outcomes in Massively Transfused Combat Casualties. *J Trauma Acute Care Surg* 2012;**73**:S89-S94.

3. Joshi NV, Raftis JB, Lucking AJ, et al. Lyophilised Reconstituted Human PlateletsIncrease Thrombus Formation in a Clinical Ex Vivo Model of Deep Arterial Injury. *Thrombosis and Hemostasis* 2012; **108**:1-7.

4. Eastridge BJ, Costanzo G, Jenkins D, et al. Impact of Joint Theater Trauma System Initiatives on Battlefield Injury Outcomes. *Annals of Surgery* 2009; **198**(6):852-7.

5. Holcomb JB, McMullin NR, Pearse L, et al. Causes of Death in U.S. Special Operations Forces in the Global War on Terrorism (2001-2004). *Annals of Surgery* 2007; **245**(6):986-991.

6. Kelly JF, Ritenour AE, McLaughlin DF, et al. Injury Severity and Causes of Death From Operation Iraqi Freedom and Operation Enduring Freedom: 2003-2004 Versus 2006. *Journal of Trauma* 2007; **64**(2):S21-7.

7. Kotwal RS, Montgomery HR, Mabry RL, et.al. Eliminating Preventable Death on the Battlefield. *Archives of Surgery* 2011; **146**: 1350-1358.

8. Report of the Army Dismounted Complex Blast Injury Task Force, 18 June 2011. Dismounted Complex Blast Injury Task Force. Available at: http://www.armymedicine.army.mil/reports/DCBI%20Task%20Force%20Report%20(Redacted%20Final).pdf.

9. Mabry RL. An Analysis of Battlefield Cricothyroidotomy in Iraq and Afghanistan. *J Spec Oper Med* 2012; **12**(1): 17-23.

10. Fischer, H. U.S. Military Casualty Statistics: Operation New Dawn, Operation Iraqi Freedom, Operation Enduring Freedom. Congressiona Research Service 7-5700. September 28, 2010.

11. Holbrook TL, Galarneau MR, Dye JL, et. al. Morphine use after combat injury in Iraq and incidence of post-traumatic stress disorder. *NEJM* 2010; **362**: 110-117.

12. CRASH-2 Collaborators, Roberts I, Shakur H, et al. The Importance of Early Treatment with Tranexamic Acid in Bleeding Trauma Patients: An Exploratory Analysis of the CRASH-2 Randomized Controlled Trial. *Lancet* 2011; 377(9771): 1096-101, 1101.e1-2.

13. CRASH-2 Trial Collaborators, Shakur H, Roberts I, et al. Effects of Tranexamic Acid on Death, Vascular Occlusive Events, and Blood Transfusion in Trauma Patients with Significant Hemorrhage. *Lancet* 2010; **376**(9734): 23-32.

14. CRASH-2 Trial Collaborators. Improving the Evidence Base for Trauma Care: Progress in the International CRASH-2 Trial. *PLoS Clinical Trials* 2006; **1**(6):e30.

15. Morrison JJ, Dubose JJ, Rasmussen TE, et al. Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) Study. *Arch Surg* 2012; **142**(2): 113-9.

16. Bickell WH, Wall MJ, Pepe PE, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. *NEJM* 1994; **331**: 1105-1109.

17. Haut ER, Kalish BT, Cotton BA, et al: Prehospital Intravenous Fluid Administration is Associated With Higher Mortality in Trauma Patients: A National Trauma Data Bank Analysis. *Ann Surg* 2011; **253**: 371-377.

18. Ley E, Clond M, Srour M, et al: Emergency department crystalloid resuscitation of 1.5 L or more is associated with increased mortality in elderly and non-elderly trauma patients. *J Trauma* 2011;**70**: 398-400.

19. Borgman MA, Spinella PC, Perkins JG, et. al. The ratio of blood products transfused in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007; **63**: 805-813.

20. Zink KA, Mayberry JC, Peck EG, et. al. Lidocaine patches reduce pain in trauma patients with rib fractures. *Am Surg* 2011; **77**: 438-442.

21. Therien SP, Nesbitt ME, Duran-Stanton AM et. al. Prehospital Medical Documentation in the Joint Theater trauma Regeistry: A Retrospective Study. *J Trauma* 2011; **71**(1): S103-8.

22. O'Connell KM, Littleton-Kearney MT, Bridges E, et. al. Evaluating the Joint Theater Trauma Registry as a Data Source to Benchmark Casualty Care. *Military Medicine* 2012; **177**(5): 546-552.

23. Niles SE, McLaughlin DF, Perkins JG, et. al. Increased Mortality Associated with the Early Coagulopathy of Trauma in Combat Casualties. *J Trauma* 2008; **64**(6): 1459-65.

24. Cross JD, Johnson AE, Wenke JC, et. Al. Mortality in female war veterans of Operations Enduring Freedom and Iraqi Freedom. *Clin Orthop Relat Res* 2011; E-pub 10 March 2011.