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SUBJECT: Prehospital Use of Ketamine in Battlefield Analgesia 2012-03

INTRODUCTION

The Tactical Combat Casualty Care (TCCC) Guidelines are a set of trauma care guidelines customized for use in the pre-hospital combat setting. The Guidelines identify three stages of care: (1) care under fire; (2) tactical field care; and (3) tactical evacuation care (TACEVAC). TCCC is currently used in training for medics by all Services in the Department of Defense (DoD) and by many U.S. coalition partners.^{1,2} The Committee on Tactical Combat Casualty Care (CoTCCC), a work group of the Defense Health Board (DHB) 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.^{1,2}

BACKGROUND

The TCCC Guidelines currently outline the same pain management strategy for both tactical field care and TACEVAC settings. The plan dictates self-administration of Mobic or Tylenol for casualties who are able to continue fighting. If unable to fight, the TCCC Guidelines recommend oral transmucosal fentanyl citrate (OTFC) when Intravenous (IV)/Intraosseous(IO) access may not be obtained, and Morphine sulfate when IV/IO access may be obtained. The current TCCC Guidelines may be found at Attachment A.

On June 14, 2011, the DHB issued a recommendation for DoD battlefield trauma research, development, test and evaluation priorities which included the benefits and risks of using ketamine for pre-hospital analgesia. At the November 14, 2011 DHB meeting, Dr. John Gandy provided an informational briefing regarding the proposed addition of ketamine to the TCCC Guidelines as a battlefield analgesic. On November 15, 2011, the CoTCCC received a more detailed briefing from Dr. Gandy, as well as a briefing from Dr. Christopher Maani, Chief of Anesthesia at the U.S. Army Institute of Surgical Research and Burn Center and Brooke Army Medical Center. On November 15, 2011, changes were made to the proposed amendment. These changes were approved by the CoTCCC and on the following day, after additional edits, by the Trauma and Injury Subcommittee.

The Board deliberated the findings and recommended changes to the TCCC Guidelines on February 21, 2012 during open session in San Antonio, Texas. The Board amended the recommendations to include a restriction for the use of ketamine in casualties with suspected traumatic brain injury (TBI) or penetrating globe injury. With the addition of a restriction against using ketamine for these casualties, the members voted unanimously to forward the recommendation to the ASD(HA). This report presents the Board's recommendation that ketamine be added to the TCCC Guidelines as an alternative to morphine, along with the

available evidence for this proposed addition. The majority of the data regarding ketamine use are limited to either pediatric populations and/or ketamine used in combination with other drugs. There are few studies (level B evidence) that address the sole use of ketamine, as an analgesic, in adult populations. Numerous studies suggest ketamine is effective and safe in pediatric patients, and when administered in conjunction with other analgesics/anesthetics. Additionally, many anecdotal reports regarding ketamine use in austere environments including tactical field settings suggest that it is safe and effective in managing pain and fills a gap in tactical field analgesia.

FINDINGS

Morphine: the Slipping Gold Standard in TCCC Pain Management

In a review article describing pain management in operational settings, Wedmore, et. al. described opiate analgesia as the most effective pain management drug class for severe pain.³ Although intramuscular morphine has received criticism, due to Service fielding decisions, it remains the most commonly used analgesic. Morphine offers easy administration (via auto injector, intramuscularly) and a well-known side effect profile. A recent observational study involving 696 deployed U.S. military personnel without serious TBI suggested that the early provision of IV morphine analgesia at Level I or Level 2 Medical Treatment Facilities was associated with lower rates of post-traumatic stress disorder (PTSD). Sixty one percent of those diagnosed with PTSD had received morphine (in early resuscitation) while 76 percent of those who were not diagnosed with PTSD had received morphine. Data regarding other analgesic modalities that may have been employed were not available.⁴ Although this study had significant limitations, when considered along with a small retrospective study suggesting a correlation between ketamine used intraoperatively for burn patients and a decreased incidence of PTSD, the theme of effective pain remediation and lower rates of PTSD persists.⁵

In the Military Advanced Regional Anesthesia and Analgesia Handbook, the authors describe the undisputable success of opioids, such as morphine, for treating pain in the field but note their potential for life-threatening side effects. The authors also state that previous conflicts have resulted in a high incidence of morphine addiction in soldiers.⁶ Historically, morphine on the battlefield has been administered as an intramuscular (IM) injection, limiting its effectiveness due to delayed onset. Current opinion reflects that the IV administration of morphine is advantageous for relieving acute and severe pain as it provides quick relief and is easier to titrate, thus reducing the risk of overdose in individuals with severe pain.^{7, 8}

Morphine, like all opioid analgesics, has a narrow therapeutic window and a number of significant side effects. Morphine may cause hypotension which could increase the risk of death in casualties with severe hemorrhage. This may be a significant risk considering that hemorrhage is the most common cause of preventable death in the Iraq and Afghanistan conflicts.⁹ TBI is often considered the signature injury of the current conflict. Morphine may also increase intracranial pressure, which may exacerbate TBI.^{6, 10} Acute respiratory depression, excessive sedation and nausea, are all well-known side effects of opioids with profound operational implications.¹¹ In addition to these acute issues, opioid adverse side effects may inhibit recovery and rehabilitation.¹²

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In an ongoing survey of combat medical personnel being conducted by the Naval Operational Medical Lessons Center, respondents indicate that IM morphine is the most commonly used battlefield analgesic, but rated it less effective than either IV morphine or ketamine at providing fast pain relief.¹³ This pattern of use is largely because few combat units (except for Special Operations units) have provided OTFC or ketamine as analgesic options for their combat medics and corpsmen. Additionally, anecdotal reports in operational settings describe individuals with severe pain refractory to morphine that responded quickly following administration of ketamine.³

Ketamine: A New Alternative to Conventional Battlefield Analgesia

Ketamine hydrochloride was first used in humans as a dissociative anesthetic in 1965.^{14, 15, 16} Ketamine is highly lipid soluble; as such, clinical effects present within one minute of administration when given intravenously and within five minutes when given intramuscularly.¹⁷ It has been used extensively in acute care medicine, and has a reportedly low frequency of serious adverse effects in doses used for analgesia.^{17, 18, 19, 20, 21} Ketamine is known for its hemodynamic stability, advantageous airway and respiratory properties, low cost, broad range of clinical applications, ease of storage, and excellent therapeutic index.^{22, 23} A particular benefit for the use of ketamine on the battlefield or in a TACEVAC setting is that when administered in small (analgesic) doses it does not generally impair airway maintenance or spontaneous respirations and increases blood pressure and heart rate.^{16, 21, 24, 25} Ketamine's wide therapeutic window^{15, 26, 27} makes it the anesthetic of choice in austere or resource poor environments where monitoring equipment may be rudimentary or absent and a single operator provides the anesthetic and monitors the patient.^{15, 27}

According to Dr. Maani, Ketamine offers additional tactical benefits, including:

- Minimal impact on medic carrying capacity
- Useful in a mass casualty scenario when conventional analgesia/anesthesia and individual monitoring would not be plausible
- Ability to withstand environmental extremes

Ketamine may be administered via a variety of routes to include oral, rectal, intranasal, IM, IO, and IV. A Cochrane Review examined perioperative ketamine use for acute postoperative pain. This meta-analysis included randomized controlled trials in which ketamine was administered in addition to a basic analgesic (such as morphine or a non-steroidal anti-inflammatory drug) as well as trials that employed the same analgesics without ketamine. The authors concluded that perioperative subanesthetic doses of ketamine reduced rescue analgesia requirements, pain intensity, or both. It also found that ketamine reduced morphine consumption and that adverse effects were mild or absent.²⁸

At higher doses, the utility of ketamine is limited by undesirable psychomimetic effects (such as excessive sedation, cognitive dysfunction, hallucinations and nightmares).¹² Dr. Maani notes that, although uncommon, ketamine may cause secretions, nausea/vomiting, headache, dizziness or blurred vision, a cataleptic state, and sedation with potential recall (memory loss) problems. Subanesthetic (low)-dose ketamine has demonstrated significant analgesic efficacy without these side effects. In fact, low-dose ketamine has rarely been associated with adverse effects.¹² In a

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2009 review of analgesic options for pain relief on the battlefield, Black and McManus noted that “ketamine in subanesthetic doses is an almost ideal analgesic because of its profound pain relief, its potentiation of opioids, its role in preventing opioid hyperalgesia, and its large margin of safety.”²⁹

The two primary side effects associated with ketamine are laryngospasm and emergence reactions. In two large trials conducted in emergency departments, the risk of laryngospasm in children, who are recognized to have a higher incidence of laryngospasm than adults, was 0.4 percent and 0.07 percent.^{30, 31} The frequency of respiratory compromise following procedural sedation and analgesia with ketamine was lower than that seen in other analgesics, including fentanyl.³¹ Anecdotal reports suggest that given the larger diameter of the adult airway, simple airway repositioning is sufficient to relieve airway compromise following ketamine administration. Although uncommon and generally associated with higher (anesthetic) doses, providers administering ketamine should anticipate emergence reactions. The risk-benefit ratio may shift toward the use of other analgesic agents for older individuals.³² By inhibiting reuptake of catecholamines, the resulting increased heart rate and blood pressure are accompanied by increased myocardial oxygen consumption. This may be a problem in those with underlying coronary artery disease.³² In one of the largest studies of adults (n=70) receiving ketamine in an emergency department, the investigators specifically noted the absence of any evidence of ischemic cardiac events, despite that the study population included geriatric patients (as old as 68 years).³³ Recent evidence suggests that low-dose ketamine may serve as an effective adjuvant to opioids, anesthetics, and other analgesic agents.^{12, 24, 34}

Bringing Ketamine to the Battlefield

In polytrauma casualties, relieving the pain from a fractured femur with opiates may be lethal due to cardiorespiratory depression if the casualty also had unrecognized internal bleeding and/or pulmonary injury. Ketamine offers prehospital providers the ability to relieve pain without the potential adverse effects of opioids, such as hypotension and respiratory depression.

A review paper by non-anesthesiologists describing ketamine analgesia in field settings offers a number of operational considerations. Although the preservation of spontaneous respirations with complete analgesia is unparalleled, military providers must be aware of potential side effects following ketamine administration that may impact operational success. For example, following ketamine administration, individuals may make spontaneous utterances and purposeless motions. The Food and Drug Administration (FDA) approved package insert and Hazardous Substances Data Bank include a special note stating that emergence reactions occur in approximately 12 percent of patients.^{35, 36} Although this generally occurs when higher doses are provided, if operational security mandates strict noise discipline then alternatives should be considered. Furthermore, emergence reactions may require the use of active restraint by multiple care-takers.³⁷

Anecdotal reports from CoTCCC members indicate that ketamine has been used successfully on the battlefield for analgesia, primarily by Special Operations Forces. Additionally, Wedmore et. al. provide several anecdotal accounts of effective pain management using ketamine in varied combat environments.³ Members also note that protocols for ketamine use are available in the

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Military Advanced Regional Anesthesia and Analgesia Handbook, U.S. Special Operations Command Tactical Trauma Protocols (since 2008), Army Ranger Medic Protocols (since 2010), and the Pararescue Procedures Handbook. Additionally, the Fourth Edition of the Army Ranger Medic Handbook, due to be released later this year, will include ketamine.

Ketamine has traditionally been contraindicated in patients with head injury due to a belief that it may increase intracranial pressure (ICP).³⁸ The FDA approved package insert also notes that an increase in intracranial cerebrospinal fluid pressure has been reported after administration of ketamine and advises extreme caution when using ketamine in patients with increased ICP.³⁵ In vitro and animal studies suggest that ketamine may in fact have neuroprotective properties due to it being an *N*-methyl-*D*-aspartate antagonist.^{38, 39, 40, 41} Additionally, recent studies suggest that ketamine may be safe for brain injured patients.^{38, 42, 43, 44, 45} However, these studies had small sample sizes and primarily examined ketamine administration in combination with other anesthetics or sedatives. Because many of these ketamine studies are limited to procedural sedation in pediatric populations and none address ketamine use in pre-hospital, austere environments, the generalizability to tactical settings is limited. The consensus opinion of the Board members who are subject matter experts in neurosurgery and neurotrauma reaffirmed that the quality of the studies suggesting that ketamine can be used safely in those with head injury is insufficient and that these results are not generalizable to casualties with head injuries. The DHB concludes that this literature contains low-level evidence that may not be applicable, and recommends that until large randomized controlled trials examining the use of ketamine alone demonstrate that ketamine does not increase ICP, ketamine should not be used in patients with significant TBI (penetrating brain injury or head injury with altered level of consciousness).

Ketamine may increase intraocular pressure (IOP).⁴⁶ Overall, the evidence base is limited and conflicting regarding the safety of ketamine in patients with eye injuries. A recent unpublished study of ketamine administered to children that was presented at the 2011 American Academy of Pediatrics conference concluded that ketamine did not cause a significant elevation in IOP when measured by non-ophthalmologists and could therefore be used safely in patients with suspected eye injury.⁴⁷ However, this study had a small sample size, was not peer reviewed, and is not representative of the deployed military population. Furthermore, the majority of studies of the effects of ketamine on IOP have included only children or animals and evidence of an effect on IOP is conflicting. Limited evidence is available regarding the effects of ketamine on IOP in adults. DHB consensus opinion derived from ophthalmology subject matter expert opinion (DHB member) notes that patients with glaucoma or acute globe injuries to the eye should not receive ketamine because of the risk associated with increased IOP. As such, the DHB recommends that ketamine is not used on patients with suspected penetrating eye injury.

The CoTCCC has reviewed the skill sets for TCCC providers on February 7-8, 2012 and recommended that ketamine should only be administered by combat medics or combat paramedics (to include Special Operations Force Advanced Tactical Practitioners, critical care flight paramedics, and Air Force pararescuemen). Consistent with the current recommendation for administration of morphine and OTFC, ketamine is not recommended for use by all combatants or combat lifesavers.

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The initial analgesic doses for ketamine recommended for adults in Auerbach's Wilderness Medicine, a standard text for medical practice in austere environments, are 50-75 mg IM and 15-30 mg IV.⁴⁸ This text notes that even at small parenteral doses, ketamine can provide profound analgesia. Other sources recommend 0.44 to 1 mg/kg IM or 0.2-0.5 mg/kg IV.^{3, 49, 50} As the dose-related effect of ketamine transitions from analgesia to anesthesia, nystagmus emerges as a side effect of ketamine.⁴⁶ As such, the DHB recommends that nystagmus is used as the end point indicator for ketamine dosage.

CONCLUSION

Ketamine offers a useful addition to the combat medic's options for battlefield pain management. Adding ketamine to the TCCC Guidelines would enhance the combat medic's ability to adequately control pain in tactical settings without the risk of opioid-induced hypotension and respiratory depression. Should these recommendations be included in the TCCC Guidelines, those responsible for developing and maintaining the TCCC curriculum should include additional information regarding the common side effects and contraindications to using ketamine.

RECOMMENDATIONS

The Board recommends DoD incorporate the following text, allowing ketamine to be used for analgesia, into the TCCC Tactical Field Care and Tactical Evacuation Care Guidelines (addition is represented below by underlining):

12. Provide analgesia as necessary.

NOTE: Ketamine must not be used if the casualty has suspected penetrating eye injury or significant TBI (evidenced by penetrating brain injury or head injury with altered level of consciousness).

a. Able to fight:

These medications should be carried by the combatant and self-administered as soon as possible after the wound is sustained.

- Mobic, 15 mg PO once a day
- Tylenol, 650-mg bilayer caplet, 2 PO every 8 hours

b. Unable to fight:

Note: Have naloxone readily available whenever administering opiates.

- Does not otherwise require IV/IO access
- Oral transmucosal fentanyl citrate (OTFC), 800 µg transbucally
- Recommend taping lozenge-on-a-stick to casualty's finger as an added safety measure
- Reassess in 15 minutes
- Add second lozenge, in other cheek, as necessary to control severe pain
- Monitor for respiratory depression

OR

-Ketamine 50-100mg IM

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-Repeat dose every 30 minutes to 1 hour as necessary to control severe pain or until the casualty develops nystagmus (rhythmic eye movement back and forth)

OR

-Ketamine 50 mg intranasal (using nasal atomizer device)

-Repeat dose every 30 minutes to 1 hour as necessary to control severe pain or until the casualty develops nystagmus

- IV or IO access obtained:

- Morphine sulfate, 5 mg IV/IO

- Reassess in 10 minutes.

- Repeat dose every 10 minutes as necessary to control severe pain.

- Monitor for respiratory depression

OR

-Ketamine 20 mg slow IV/IO push over 1 minute

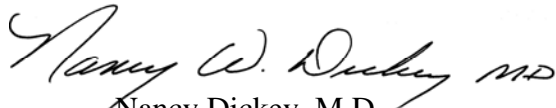
- Reassess in 5-10 minutes.


- Repeat dose every 5-10 minutes as necessary to control severe pain or until the casualty develops nystagmus

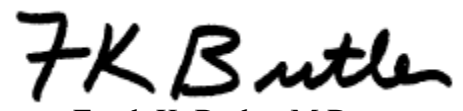
-Continue to monitor for respiratory depression and agitation

- Promethazine, 25 mg IV/IM/IO every 6 hours as needed for nausea or for synergistic analgesic effect

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WORKS CITED:

1. Butler FK, Giebner SD, McSwain N, et al., eds. *Prehospital Trauma Life Support Manual: Military Version*. 7th ed. St. Louis: Mosby; 2010.
2. Eastridge BJ, Mabry RL, Blackbourne LH, et. al. We Don't Know What We Don't Know: Prehospital Data in Combat Casualty Care. *The United States Army Medical Department Journal* 2011; April-June: 11-14.
3. Wedmore IS, et. al. Pain Management in the Wilderness and Operational Setting. *Emerg Med Clin N Am* 2005; **23**: 585-601.
4. Holbrook TL, Galarneau MR, Dye JL et. al. Morphine Use after Combat Injury in Iraq and Post-Traumatic Stress Disorder. *N Engl J Med* 2010; **362**: 110-117.
5. McGhee LL, Maani CV, Garza TH, et. al. The Correlation Between Ketamine and Post-Traumatic Stress Disorder in Burned Service Members. *J Trauma* 2008; **64**(2 Suppl): S195-S198.
6. Buckenmaier C, Bleckner L. Military Advanced Regional Anesthesia and Analgesia Handbook, Chapter 26: Acute Pain Management in the Field. Office of the Surgeon General, Department of the Army, United States of America. 2008. P. 95-99.
7. Butler FK, Hagmann J, Butler EG. Tactical Combat Casualty Care in Special Operations. *Military Medicine* 1996; **161**(Suppl 1): 3-16.
8. Butler FK, Smith DJ, Eds. Tactical Management of Diving in Special Operations. Undersea and Hyperbaric Medical Society, 46th Workshop. April 30, 1996, Anchorage Alaska.
9. 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* 2008; **64**: S21-S27.
10. Morphine. Hazardous Substances Data Bank, a database of the National Library of Medicine's TOXNET System. Report downloaded February 5, 2012. Available at: <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>.
11. Jennings PA, Cameron P, Bernard S, et. al. Morphine and Ketamine Is Superior to Morphine Alone for Out-of-Hospital Trauma Analgesia: A Randomized Controlled Trial. *Annals of Emergency Medicine* 2012; Jan 11 [Epub ahead of print].
12. Buvanendran A, Kroin J. Multimodal Analgesia for Controlling Acute Postoperative Pain. *Current Opinion in Anesthesiology* 2009; **22**:588-593.
13. Naval Operational Medical Lessons Learned Center. Combat Medical Personnel Evaluation of Battlefield Trauma Care Equipment Initial Report. November 2011.

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14. Domino EF, Chodoff P, Corssen G. Pharmacologic Effects of CI-581. A New Dissociative Anesthetic in Man. *Clin Pharmacol Ther* 1965; **6**: 279-91.
15. Strayer RJ, Nelson LS. Adverse Events Associated with Ketamine for Procedural Sedation in Adults. *Am J Emerg Med* 2008; **26**: 985-1028.
16. Visser E, Schug SA. The Role of Ketamine in Pain Management. *Biomedicine & Pharmacotherapy* 2006; **60**: 341-348.
17. Alonso-Serra HM, Weslet K for the National Association of EMS Physicians Standards and Clinical Practices Committee. Position Paper: Prehospital Pain Management. *Prehospital Emergency Care* 2003; **7**(4): 482-488.
18. Jennings PA, Cameron P, Bernard S. Ketamine as an Analgesic in the Pre-hospital Setting: A Systematic Review. *Acta Anaesth Scand*. 2011; **55**: 638-643.
19. Cherry DA, Plummer JL, Gourlay GK et. al. Ketamine as an Adjunct to Morphine in the Treatment of Pain. *Pain* 1995; **62**: 119-121.
20. Howes MC. Ketamine for Paediatric Sedation/Analgesia in the Emergency Department. *Emerg. Care J*. 2004; **21**: 275-280.
21. Porter K. Ketamine in Prehospital Care. *Emerg Med J*. 2004; **21**: 351-354.
22. U.S. Army Aeromedical Research Laboratory Warfighter Performance and Health Division Report, Comparison of the Effects of Ketamine and Morphine on the Performance of Representative Military Tasks, USAARL Report No. 2010-17, August 2010.
23. Craven R. Ketamine. *Anaesthesia* 2007; **62** (Suppl. 1): 48-53.
24. Subramaniam K, Subramaniam B, Steinbrook R. Ketamine as Adjuvant Analgesic to Opioids: A Quantitative and Qualitative Systematic Review. *Anaesth Analg* 2004; **99**: 482-495.
25. White PF, Way WL, Trevor A. Ketamine-Its Pharmacology and Therapeutic Uses. *Anesthesiology* 1982; **56**: 119-136.
26. Green SM, Clark R, Hostetler MA, et. al. Inadvertent Ketamine Overdose in Children: Clinical Manifestations and Outcome. *Ann Emerg Med* 1999; **34**: 492-497.
27. Green SM, Clem KJ, Rothrock SG. Ketamine Safety Profile in Developing World: Survey of Practitioners. *Acad Emerg Med* 1996; **3**: 598-604.
28. Bell RF, Dahl JB, Moore RA et. al. Perioperative Ketamine for Acute Postoperative Pain. Cochrane Database of Systematic Reviews 2006, Issue 1. Art No.: CD004603.

SUBJECT: Prehospital Use of Ketamine in Battlefield Analgesia 2012-03

29. Black IH, McManus J. Pain Management in Current Combat Operations. *Prehospital Emergency Care* 2009; **13**(2): 223-227.
30. Green SM, Rothrock SG, Lynch EL, et. al. Intramuscular Ketamine for Pediatric Sedation in the Emergency Department: Safety Profile with 1,022 Cases. *Ann Emerg Med* 1998; **31**: 688-697.
31. Roback MG, et. al. Adverse Events Associated with Procedural Sedation in a Pediatric Emergency Department: A Comparison of Common Parenteral Drugs. *Acad Emerg Med* 2005; **12**: 508-513.
32. Green SM, Li J. Ketamine in Adults: What Emergency Physicians Need to Know about Patient Selection and Emergence Reactions. *Academic Emergency Medicine* 2000; **7**(3): 278-281.
33. Chudnofsky CR, Weber JE, Stroyanoff PJ et. al. A Combination of Midazolam and Ketamine for Procedural Sedation and Analgesia in Adult Emergency Department Patients. *Acad Emerg Med* 2000; **7**: 228-235.
34. Schmid RL, Sandler AN, Katz J. Use and Efficacy of Low-Dose Ketamine in the Management of Acute Postoperative Pain: A Review of Current Techniques and Outcomes. *Pain* 1999; **82**: 111-125.
35. Ketamine Hydrochloride Injection Package Insert.
http://www.bionichepharma.com/pdf/Ketamine_Package_Insert.pdf. Accessed February 29, 2012.
36. Ketamine. Hazardous Substances Data Bank, a database of the National Library of Medicine's TOXNET System. Report downloaded March 7, 2012. Available at:
<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>.
37. Guldner GT, Petinaux B, Clemens P, et. al. Ketamine for Procedural Sedation and Analgesia by Nonanesthesiologists in the Field: A Review for Military Health Care Providers. *Military Medicine* 2006; **171**(6): 484-490.
38. Filanovsky Y, Miller P, Kao J. Myth: Ketamine Should Not Be Used as an Induction Agent for Intubation in Patients with Head Injury. *CJEM* 2010; **12**(2): 154-157.
39. Shapira Y, Artru AA, Lam AM. Ketamine Decreases Cerebral Infarct Volume and Improves Neurological Outcome Following Experimental Head Trauma in Rats. *J Neurosurg Anesthesiol* 1992; **4**: 231-240.
40. Shapira Y, et. al. Therapeutic Time Window and Dose Response of the Beneficial Effects of Ketamine in Experimental Head Injury. *Stroke* 1994; **25**: 231-240.

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41. Hoffman WE, et. al. Ketamine Decreases Plasma Catecholamines and Improves Outcome from Incomplete Cerebral Ischemia in Rats. *Anesthesiology* 1992; **76**: 755-762.
42. Hughes S. BET 3: Is Ketamine a Viable Induction Agent for the Trauma Patient with Potential Brain Injury. *Emerg Med J* 2011; **28**(12): 1076-1077.
43. Bar-Joseph, et. al. Effectiveness of Ketamine in Decreasing Intracranial Pressure in Children with Intracranial Hypertension. *J Neurosurg Pediatr* 2009; **4**(1): 40-46.
44. Albanese J et. al. Ketamine Decreases Intracranial Pressure and Electroencephalographic Activity in Traumatic Brain Injury Patients During Propofol Sedation. *Anesthesiology* 1997; **87**(6): 1328-1334.
45. Mayberg TS, et. al. Ketamine Does Not Increase Cerebral Blood Flow Velocity of Intracranial Pressure during Isoflurane/Nitrous Oxide Anesthesia in Patients Undergoing Craniotomy. *Anesth Analg* 1995; **81**:84-89.
46. Ketamine Side Effects. <http://www.drugs.com/sfx/ketamine-side-effects.html>. Accessed 7 February 2012.
47. Halstead SM, Deakyne S, Bajaj L, et. al. The Effect of Ketamine on Intraocular Pressure in Pediatric Patients during Procedural Sedation. Abstract presented at 2011 American Academy of Pediatrics conference.
48. Coleman SD, Gaeta RR: Principles of Pain Management. In: Auerbach PS: Wilderness Medicine; Sixth Edition. Elsevier: Mosby, Philadelphia; 2012: 354-362.
49. Bennet RC, Stewart RC. Ketamine. In: Paris SM, Stewart RD, Eds. Pain Management in Emergency Medicine. Norwalk (CT): Appleton & Lange; 1988. p. 295-310.
50. Sadove MS, Shulman M, Hatano S, et. al. Analgesic Effects of Ketamine Administered in Subdissociative Doses. *Anaesth Analg* 1971; **50**(3): 452-457.

**ATTACHMENT A:
TACTICAL COMBAT CASUALTY CARE
GUIDELINES**

Tactical Combat Casualty Care Guidelines

1 November 2010

* All changes to the guidelines made since those published in the 2010 Seventh Edition of the PHTLS Manual are shown in **bold text**. The new material on fluid resuscitation is shown in **red text**.

Basic Management Plan for Care Under Fire

1. Return fire and take cover.
2. Direct or expect casualty to remain engaged as a combatant if appropriate.
3. Direct casualty to move to cover and apply self-aid if able.
4. Try to keep the casualty from sustaining additional wounds.
5. Casualties should be extricated from burning vehicles or buildings and moved to places of relative safety. Do what is necessary to stop the burning process.
6. Airway management is generally best deferred until the Tactical Field Care phase.
7. Stop *life-threatening* external hemorrhage if tactically feasible:
 - Direct casualty to control hemorrhage by self-aid if able.
 - Use a CoTCCC-recommended tourniquet for hemorrhage that is anatomically amenable to tourniquet application.
 - Apply the tourniquet proximal to the bleeding site, over the uniform, tighten, and move the casualty to cover.

Basic Management Plan for Tactical Field Care

1. Casualties with an altered mental status should be disarmed immediately.
2. Airway Management
 - a. Unconscious casualty without airway obstruction:
 - Chin lift or jaw thrust maneuver
 - Nasopharyngeal airway
 - Place casualty in the recovery position
 - b. Casualty with airway obstruction or impending airway obstruction:
 - Chin lift or jaw thrust maneuver
 - Nasopharyngeal airway
 - Allow casualty to assume any position that best protects the airway, to include sitting up.
 - Place unconscious casualty in the recovery position.
 - If previous measures unsuccessful:
 - Surgical cricothyroidotomy (with lidocaine if conscious)
3. Breathing
 - a. In a casualty with progressive respiratory distress and known or suspected torso trauma, consider a tension pneumothorax and decompress the chest on the side of the injury with a 14-gauge, 3.25 inch needle/catheter unit inserted in the second intercostal space at the midclavicular line. Ensure that the needle entry into the chest is not medial to the nipple line and is not directed towards the heart.
 - b. All open and/or sucking chest wounds should be treated by immediately applying an occlusive material to cover the defect and securing it in place. Monitor the casualty for the potential development of a subsequent tension pneumothorax.
4. Bleeding
 - a. Assess for unrecognized hemorrhage and control all sources of bleeding. If not already done, use a CoTCCC-recommended tourniquet to control life-threatening external hemorrhage that is anatomically amenable to tourniquet application or for any traumatic amputation. Apply directly to the skin 2-3 inches above wound.
 - b. For compressible hemorrhage not amenable to tourniquet use or as an adjunct to tourniquet removal (if evacuation time is anticipated to be longer than two hours), use Combat Gauze as the hemostatic agent of choice. Combat Gauze should be applied with at least 3 minutes of direct pressure. Before releasing any tourniquet on a casualty who has been resuscitated for

hemorrhagic shock, ensure a positive response to resuscitation efforts (i.e., a peripheral pulse normal in character and normal mentation if there is no traumatic brain injury (TBI)).

- c. Reassess prior tourniquet application. Expose wound and determine if tourniquet is needed. If so, move tourniquet from over uniform and apply directly to skin 2-3 inches above wound. If a tourniquet is not needed, use other techniques to control bleeding.
- d. When time and the tactical situation permit, a distal pulse check should be accomplished. If a distal pulse is still present, consider additional tightening of the tourniquet or the use of a second tourniquet, side by side and proximal to the first, to eliminate the distal pulse.
- e. Expose and clearly mark all tourniquet sites with the time of tourniquet application. Use an indelible marker.

5. Intravenous (IV) access

- Start an 18-gauge IV or saline lock if indicated.
- If resuscitation is required and IV access is not obtainable, use the intraosseous (IO) route.

6. Fluid resuscitation

Assess for hemorrhagic shock; altered mental status (in the absence of head injury) and weak or absent peripheral pulses are the best field indicators of shock.

- a. If not in shock:
 - No IV fluids necessary
 - PO fluids permissible if conscious and can swallow
- b. If in shock:
 - Hextend, 500-mL IV bolus
 - Repeat once after 30 minutes if still in shock.
 - No more than 1000 mL of Hextend
- c. Continued efforts to resuscitate must be weighed against logistical and tactical considerations and the risk of incurring further casualties.

d. If a casualty with an altered mental status due to suspected TBI has a weak or absent peripheral pulse, resuscitate as necessary to maintain a palpable radial pulse.

7. Prevention of hypothermia

- a. Minimize casualty's exposure to the elements. Keep protective gear on or with the casualty if feasible.
- b. Replace wet clothing with dry if possible. **Get the casualty onto an insulated surface as soon as possible.**
- c. **Apply the Ready-Heat Blanket from the Hypothermia Prevention and Management Kit (HPMK) to the casualty's torso (not directly on the skin) and cover the casualty with the Heat-Reflective Shell**

(HRS).

d. If an HRS is not available, the previously recommended combination of the Blizzard Survival Blanket and the Ready Heat blanket may also be used.

e. If the items mentioned above are not available, use dry blankets, poncho liners, sleeping bags, or anything that will retain heat and keep the casualty dry.

f. Warm fluids are preferred if IV fluids are required.

8. Penetrating Eye Trauma

If a penetrating eye injury is noted or suspected:

- a) Perform a rapid field test of visual acuity.
- b) Cover the eye with a rigid eye shield (NOT a pressure patch.)
- c) Ensure that the 400 mg moxifloxacin tablet in the combat pill pack is taken if possible and that IV/IM antibiotics are given as outlined below if oral moxifloxacin cannot be taken.

9. Monitoring

Pulse oximetry should be available as an adjunct to clinical monitoring.

Readings may be misleading in the settings of shock or marked hypothermia.

10. Inspect and dress known wounds.

11. Check for additional wounds.

12. Provide analgesia as necessary.

a. Able to fight:

These medications should be carried by the combatant and self-administered as soon as possible after the wound is sustained.

- Mobic, 15 mg PO once a day
- Tylenol, 650-mg bilayer caplet, 2 PO every 8 hours

b. Unable to fight:

Note: Have naloxone readily available whenever administering opiates.

- Does not otherwise require IV/IO access
 - Oral transmucosal fentanyl citrate (OTFC), 800 ug transbuccally
 - Recommend taping lozenge-on-a-stick to casualty's finger as an added safety measure
 - Reassess in 15 minutes
 - Add second lozenge, in other cheek, as necessary to control severe pain.
 - Monitor for respiratory depression.
- IV or IO access obtained:
 - Morphine sulfate, 5 mg IV/IO
 - Reassess in 10 minutes.

- Repeat dose every 10 minutes as necessary to control severe pain.
- Monitor for respiratory depression
- Promethazine, 25 mg IV/IM/IO every 6 hours as needed for nausea or for synergistic analgesic effect

13. Splint fractures and recheck pulse.

14. Antibiotics: recommended for all open combat wounds

- a. If able to take PO:
 - Moxifloxacin, 400 mg PO one a day
- b. If unable to take PO (shock, unconsciousness):
 - Cefotetan, 2 g IV (slow push over 3-5 minutes) or IM every 12 hours
 - or
 - Ertapenem, 1 g IV/IM once a day

15. Burns

- a. Facial burns, especially those that occur in closed spaces, may be associated with inhalation injury. Aggressively monitor airway status and oxygen saturation in such patients and consider early surgical airway for respiratory distress or oxygen desaturation.
- b. Estimate total body surface area (TBSA) burned to the nearest 10% using the Rule of Nines.
- c. Cover the burn area with dry, sterile dressings. For extensive burns (>20%), consider placing the casualty in the Blizzard Survival Blanket in the Hypothermia Prevention Kit in order to both cover the burned areas and prevent hypothermia.
- d. Fluid resuscitation (USAISR Rule of Ten)
 - If burns are greater than 20% of Total Body Surface Area, fluid resuscitation should be initiated as soon as IV/IO access is established. Resuscitation should be initiated with Lactated Ringer's, normal saline, or Hextend. If Hextend is used, no more than 1000 ml should be given, followed by Lactated Ringer's or normal saline as needed.
 - Initial IV/IO fluid rate is calculated as %TBSA x 10cc/hr for adults weighing 40- 80 kg.
 - For every 10 kg ABOVE 80 kg, increase initial rate by 100 ml/hr.
 - If hemorrhagic shock is also present, resuscitation for hemorrhagic shock takes precedence over resuscitation for burn shock. Administer IV/IO fluids per the TCCC Guidelines in Section 6.
- e. Analgesia in accordance with the TCCC Guidelines in Section 12 may be administered to treat burn pain.
- f. Prehospital antibiotic therapy is not indicated solely for burns, but antibiotics should be given per the TCCC guidelines in Section 14 if indicated to prevent infection in penetrating wounds.

- g. All TCCC interventions can be performed on or through burned skin in a burn casualty.
- 16. Communicate with the casualty if possible.
 - Encourage; reassure
 - Explain care
- 17. Cardiopulmonary resuscitation (CPR)
Resuscitation on the battlefield for victims of blast or penetrating trauma who have no pulse, no ventilations, and no other signs of life will not be successful and should not be attempted.
- 18. Documentation of Care
Document clinical assessments, treatments rendered, and changes in the casualty's status on a TCCC Casualty Card. Forward this information with the casualty to the next level of care.

Basic Management Plan for Tactical Evacuation Care

* The term "Tactical Evacuation" includes both Casualty Evacuation (CASEVAC) and Medical Evacuation (MEDEVAC) as defined in Joint Publication 4-02.

1. Airway Management

- a. Unconscious casualty without airway obstruction:
 - Chin lift or jaw thrust maneuver
 - Nasopharyngeal airway
 - Place casualty in the recovery position
- b. Casualty with airway obstruction or impending airway obstruction:
 - Chin lift or jaw thrust maneuver
 - Nasopharyngeal airway
 - Allow casualty to assume any position that best protects the airway, to include sitting up.
 - Place unconscious casualty in the recovery position.
 - If above measures unsuccessful:
 - Laryngeal Mask Airway (LMA)/intubating LMA or
 - Combitube or
 - Endotracheal intubation or
 - Surgical cricothyroidotomy (with lidocaine if conscious).
- c. Spinal immobilization is not necessary for casualties with penetrating trauma.

2. Breathing

- a. In a casualty with progressive respiratory distress and known or suspected torso trauma, consider a tension pneumothorax and decompress the chest on the side of the injury with a 14-gauge, 3.25 inch needle/catheter unit inserted in the second intercostal space at the midclavicular line. Ensure that the needle entry into the chest is not medial to the nipple line and is not directed towards the heart.
- b. Consider chest tube insertion if no improvement and/or long transport is anticipated.
- c. Most combat casualties do not require supplemental oxygen, but administration of oxygen may be of benefit for the following types of casualties:
 - Low oxygen saturation by pulse oximetry
 - Injuries associated with impaired oxygenation
 - Unconscious casualty
 - Casualty with TBI (maintain oxygen saturation > 90%)
 - Casualty in shock
 - Casualty at altitude
- d. All open and/or sucking chest wounds should be treated by immediately applying an occlusive material to cover the defect

and securing it in place. Monitor the casualty for the potential development of a subsequent tension pneumothorax.

3. Bleeding

- a. Assess for unrecognized hemorrhage and control all sources of bleeding. If not already done, use a CoTCCC-recommended tourniquet to control life-threatening external hemorrhage that is anatomically amenable to tourniquet application or for any traumatic amputation. Apply directly to the skin 2-3 inches above wound.
- b. For compressible hemorrhage not amenable to tourniquet use or as an adjunct to tourniquet removal (if evacuation time is anticipated to be longer than two hours), use Combat Gauze as the hemostatic agent of choice. Combat Gauze should be applied with at least 3 minutes of direct pressure. Before releasing any tourniquet on a casualty who has been resuscitated for hemorrhagic shock, ensure a positive response to resuscitation efforts (i.e., a peripheral pulse normal in character and normal mentation if there is no TBI.)
- c. Reassess prior tourniquet application. Expose wound and determine if tourniquet is needed. If so, move tourniquet from over uniform and apply directly to skin 2-3 inches above wound. If a tourniquet is not needed, use other techniques to control bleeding.
- d. When time and the tactical situation permit, a distal pulse check should be accomplished. If a distal pulse is still present, consider additional tightening of the tourniquet or the use of a second tourniquet, side by side and proximal to the first, to eliminate the distal pulse.
- e. Expose and clearly mark all tourniquet sites with the time of tourniquet application. Use an indelible marker.

4. Intravenous (IV) access

- a. Reassess need for IV access.
 - If indicated, start an 18-gauge IV or saline lock
 - If resuscitation is required and IV access is not obtainable, use intraosseous (IO) route.

5. Fluid resuscitation

Reassess for hemorrhagic shock (altered mental status in the absence of brain injury and/or change in pulse character.) **If BP monitoring is available, maintain target systolic BP 80-90 mmHg.**

- a. If not in shock:
 - No IV fluids necessary.
 - PO fluids permissible if conscious and can swallow.
- b. If in shock and blood products are not available:**
 - Hextend 500-mL IV bolus
 - Repeat after 30 minutes if still in shock.

- **Continue resuscitation with Hextend or crystalloid solution as needed to maintain target BP or clinical improvement.**
- c. **If in shock and blood products are available under an approved command or theater protocol:**
 - **Resuscitate with 2 units of plasma followed by packed red blood cells (PRBCs) in a 1:1 ratio. If blood component therapy is not available, transfuse fresh whole blood. Continue resuscitation as needed to maintain target BP or clinical improvement.**
- d. **If a casualty with an altered mental status due to suspected TBI has a weak or absent peripheral pulse, resuscitate as necessary to maintain a palpable radial pulse. If BP monitoring is available, maintain target systolic BP of at least 90 mmHg.**

6. Prevention of hypothermia

- a. Minimize casualty's exposure to the elements. Keep protective gear on or with the casualty if feasible.
- b. Replace wet clothing with dry if possible. **Get the casualty onto an insulated surface as soon as possible.**
- c. **Apply the Ready-Heat Blanket from the Hypothermia Prevention and Management Kit (HPMK) to the casualty's torso (not directly on the skin) and cover the casualty with the Heat-Reflective Shell (HRS).**
- d. **If an HRS is not available, the previously recommended combination of the Blizzard Survival Blanket and the Ready Heat blanket may also be used.**
- e. If the items mentioned above are not available, use poncho liners, sleeping bags, or anything that will retain heat and keep the casualty dry.
- f. **Use a portable fluid warmer capable of warming all IV fluids including blood products.**
- g. Protect the casualty from wind if doors must be kept open.

7. Penetrating Eye Trauma

If a penetrating eye injury is noted or suspected:

- a) Perform a rapid field test of visual acuity.
- b) Cover the eye with a rigid eye shield (NOT a pressure patch).
- c) Ensure that the 400 mg moxifloxacin tablet in the combat pill pack is taken if possible and that IV/IM antibiotics are given as outlined below if oral moxifloxacin cannot be taken.

8. Monitoring

Institute pulse oximetry and other electronic monitoring of vital signs, if indicated.

9. Inspect and dress known wounds if not already done.

10. Check for additional wounds.

11. Provide analgesia as necessary.

a. Able to fight:

- Mobic, 15 mg PO once a day
- Tylenol, 650-mg bilayered caplet, 2 PO every 8 hours

b. Unable to fight:

Note: Have naloxone readily available whenever administering opiates.

- Does not otherwise require IV/IO access:

- Oral transmucosal fentanyl citrate (OTFC) 800 ug transbuccally

- Recommend taping lozenge-on-a-stick to casualty's finger as an added safety measure.
- Reassess in 15 minutes.
- Add second lozenge, in other cheek, as necessary to control severe pain.
- Monitor for respiratory depression.

- IV or IO access obtained:

- Morphine sulfate, 5 mg IV/IO

- Reassess in 10 minutes
- Repeat dose every 10 minutes as necessary to control severe pain.
- Monitor for respiratory depression.

- Promethazine, 25 mg IV/IM/IO every 6 hours as needed for nausea or for synergistic analgesic effect.

12. Reassess fractures and recheck pulses.

13. Antibiotics: recommended for all open combat wounds

a. If able to take PO:

- Moxifloxacin, 400 mg PO once a day

b. If unable to take PO (shock, unconsciousness):

- Cefotetan, 2 g IV (slow push over 3-5 minutes) or IM every 12 hours,

or

- Ertapenem, 1 g IV/IM once a day

14. Burns

a. Facial burns, especially those that occur in closed spaces, may be associated with inhalation injury. Aggressively monitor airway status and oxygen saturation in such patients and consider early surgical airway for respiratory distress or oxygen desaturation.

b. Estimate total body surface area (TBSA) burned to the nearest 10% using the Rule of Nines.

- c. Cover the burn area with dry, sterile dressings. For extensive burns (>20%), consider placing the casualty in the Blizzard Survival Blanket in the Hypothermia Prevention Kit in order to both cover the burned areas and prevent hypothermia.
- d. Fluid resuscitation (USAISR Rule of Ten)
 - If burns are greater than 20% of Total Body Surface Area, fluid resuscitation should be initiated as soon as IV/IO access is established. Resuscitation should be initiated with Lactated Ringer's, normal saline, or Hextend. If Hextend is used, no more than 1000 ml should be given, followed by Lactated Ringer's or normal saline as needed.
 - Initial IV/IO fluid rate is calculated as %TBSA x 10cc/hr for adults weighing 40-80 kg.
 - For every 10 kg ABOVE 80 kg, increase initial rate by 100 ml/hr.
 - If hemorrhagic shock is also present, resuscitation for hemorrhagic shock takes precedence over resuscitation for burn shock.
Administer IV/IO fluids per the TCCC Guidelines in Section 5.
- e. Analgesia in accordance with TCCC Guidelines in Section 11 may be administered to treat burn pain.
- f. Prehospital antibiotic therapy is not indicated solely for burns, but antibiotics should be given per TCCC guidelines in Section 13 if indicated to prevent infection in penetrating wounds.
- g. All TCCC interventions can be performed on or through burned skin in a burn casualty.
- h. Burn patients are particularly susceptible to hypothermia. Extra emphasis should be placed on barrier heat loss prevention methods and IV fluid warming in this phase.

15. The Pneumatic Antishock Garment (PASG) may be useful for stabilizing pelvic fractures and controlling pelvic and abdominal bleeding. Application and extended use must be carefully monitored. The PASG is contraindicated for casualties with thoracic or brain injuries.

16. Documentation of Care

Document clinical assessments, treatments rendered, and changes in casualty's status on a TCCC Casualty Card. Forward this information with the casualty to the next level of care.