

JOINT TRAUMA SYSTEM CLINICAL PRACTICE GUIDELINE (JTS CPG)



Pain, Anxiety and Delirium (CPG ID: 29)

This CPG will delineate specific treatment guidelines for pain, anxiety and delirium (PAD) between Role 1, Role 2, Role 3 and higher echelons of care, with an emphasis on Role 3.

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SUMMARY OF CARE

1. Pain is universally present in combat casualties and an obligatory part of trauma care.
2. Adequate pain control is an essential part of care from point of injury to Continental US (CONUS) care; it has been shown to reduce the development of chronic pain syndromes and reduce the incidence of post-traumatic stress disorder
3. Prior to escalating any treatment for pain, consider other potential physiologic etiologies.
4. Orders for the treatment of pain and anxiety should include set goals and the minimum amount of medication necessary to achieve the goals should be used.
5. The Acute Pain Service (APS) should be established and be an integral part of casualty care starting at the theater hospital (Role 3 care).
6. The primary mission of the APS is the provision of effective pain control as well as the treatment and prevention of anxiety and delirium in any injured patient. Standardized and validated scoring systems should be used (see appendices) for assessment and to guide therapies.
7. An APS should include a tracking system that lists all patients on the acute pain service, their injuries and therapeutic interventions along with treatment plan comments.
8. Refer to [Table 1 in Appendix A](#) for overall pharmacologic treatment guidelines for PAD.
9. See [Appendix G](#) for a sample order set including medication options and dosing.
10. Intermittent dosing of analgesics and anxiolytics should be instituted prior to continuous dosing and continuous drips should be stopped daily to obtain a reliable physical examination and to perform a spontaneous breathing trial in ventilated patients who are potential candidates for extubation.
11. In casualties with injuries that predispose them to compartment syndrome, the decision to use regional anesthesia must be carefully considered if the patients have not previously undergone fasciotomies. Regional anesthesia must be closely monitored in order to not mask a compartment syndrome.

GOALS

This CPG provides an evidenced based framework for the management of pain, agitation/anxiety and delirium (PAD) in injured combat casualties. It is a moral, medical, and operational imperative to provide state of the art pain services to combat casualties, in so forth reducing the incidence of chronic pain syndromes, PTSD, and long-term narcotic dependency. This process begins at the point of injury and Role 1 facility. As the casualty moves along the care continuum, pain and anxiety must continue to be addressed with the increasing capabilities inherent to the Medical Treatment Facility (MTF). In this CPG, emphasis is placed on Role 3 care, as this is the first MTF that typically is equipped with robust treatment options. Optimal analgesia is a team effort and should be coordinated by the trauma surgeon, the acute pain service consultant, and the critical care consultant in conjunction with the bedside nurse who ultimately delivers therapy and monitors the adequacy of it. This CPG will address the need for an Acute Pain Service (APS) at Role 3 care.¹⁻³ The APS will be introduced as a necessary adjunct to the Trauma Team. This multidisciplinary collaboration will assess analgesia needs throughout Role 3 care based on injury complexity, trauma burden, risks for coagulopathy / thromboembolic events, anticipated number of surgical procedures, evacuation plan, logistical constraints, and practitioner expertise. It is also important to recognize that pain control should be optimized as a priority over sedation and that the principle of “analgo-sedation” (e.g. analgesia based sedation) is a viable solution for critically injured casualties.⁴

This CPG will also delineate specific treatment guidelines between Role 1, Role 2, Role 3 and higher echelons of care. Role 1 care guidelines are incorporated from the Department of Defense Committee on Tactical Combat Casualty Care recommendations.

BACKGROUND

Pain is universally present in combat casualties. Ensuring that critically injured patients are treated for PAD is an essential in the acute setting but also for prevention of the potential long-term consequences when they are not addressed appropriately. Beginning with point of injury (Tactical Combat Casualty Care) and continuing through the increasing echelons of care, active management of PAD, encompassing prevention, assessment, and treatment are medically and morally imperative. Given the magnitude of injury burden in our combat casualty population, surgical and life-sustaining treatment priorities may conflict, take precedent or overshadow the assessment and active management of PAD. Guidelines should be established understanding that sound clinical judgment, logistic and personnel constraints, and the operational context may dictate the use of other methods. Adequate early pain control to reduce posttraumatic stress disorder and ongoing pain control is an obligatory part of trauma care. The stress response involves a well-established sequence of physiologic and molecular events that include fever, tachycardia, tachypnea, hypertension, gastrointestinal ileus, hypercoagulability, protein catabolism, immunosuppression, among other undesirable consequences that delay or prevent a wounded warrior's full rehabilitation and recovery.^{5,6} Effective pain management requires coordination of all medical providers from the point of injury throughout the echelons of care and the medical evacuation system.

Pain is frequently accompanied by anxiety and delirium in critically injured patients and the medications utilized to treat these conditions may paradoxically prolong or even exacerbate them. A multimodal approach to pain control can reduce the total dosage and duration of narcotics required, minimize or even eliminate complications associated with narcotics and reduce narcotic dependence.⁷ Adjuncts such as acetaminophen, ketamine, non-steroidal anti-inflammatory drugs (NSAIDs), continuous peripheral nerve infusions, and continuous epidural infusions greatly increase patient safety and the effectiveness of narcotics while reducing the side effects.

TEAM-BASED MULTIMODAL APPROACH

1. The adoption of a team-based multimodal approach to the management of pain, anxiety and delirium most feasibly commences at the level of Role 3 care and should be continued throughout Role IV and subsequent CONUS care. This multimodal management includes the establishment of an acute pain service (APS) at starting at the Role 3 and continuing for the duration of the casualty's care. The physician on the team who has the most, and preferentially extensive, experience in pain management should direct the APS. At the Role 3, the APS is staffed from existing Combat Support Hospital (CSH) assets and should include a physician (usually anesthesiologist) pain consultant, chief pain nurse, and ward pain nurse champions.^{1,8,9}
2. The APS personnel should interact directly and frequently with the primary treating service, typically led by a trauma surgeon and/or intensivist. This is best accomplished by including the APS in daily rounds led by the primary trauma team and by incorporating the assessment and plan for pain management as a mandatory component of patient rounds. If it is not feasible to incorporate the APS into trauma rounds, then the APS is responsible for daily pain rounds, pain management consults, and reports to the trauma team leader
3. The APS should be available to all patients that are admitted to the Role 3 theater hospital. The primary mission of the APS is the provision of effective pain control as well as the treatment and prevention of

anxiety and delirium in any injured patient. There are standardized and validated scoring systems for the assessment of PAD; including the:

- DoD/VA Pain Rating Scale ([Appendix B](#) and [Appendix C](#))
 - Richmond Agitation Sedation Scale (RASS) ([Appendix D](#))
 - Confusion Assessment Method (CAM) ([Appendix E](#))
4. The Defense and Veterans Pain Rating Scale (DVPRS) and supplemental questions have undergone, and continue to undergo, validation studies.¹⁰ The DVPRS should be used to assess pain, the RASS score should be used to assess anxiety, and the CAM should be used to assess the presence of delirium. Consider potential surgical and medical causes of increased pain and anxiety prior to treating.
 5. The APS should consist of an interdisciplinary team of physicians, nurses and pharmacists and should be available 24/7. In addition to participating in daily trauma rounds, they should be responsible for coordinating pain management plans with the validating flight surgeon, medical evacuation team and the receiving MTF. Additionally it should include a tracking and PI system that follows all patients on the service listing their injuries, therapeutic interventions and care plan; this should be electronically maintained along the continuum of care.
 6. To facilitate implementation and utilization of the APS a ‘pain cart’ with all of the needed supplies for regional anesthesia should be stocked in the anesthesia area. The regional anesthesia area should have immediate access to ACLS medications and intralipid. An ultrasound machine should be available for the APS and anesthesia use to facilitate regional blocks. APS order sets can be utilized and should include pain management goals using the minimum amount of medication in order to achieve patient comfort. The goal for patients with delirium is to achieve a delirium free state as measured by the CAM.
 - See [Appendix G](#) for a sample order set including medication options and dosing.
 - See Table 1 in [Appendix A](#) for a summary list of recommendations.

PREVENTION

PAIN

Pain, as a product of trauma, cannot be prevented, per se, but there are many mechanisms for minimizing and managing pain. This begins with interrupting the mechanism and treating the injury, which are beyond the scope of this CPG; however, an essential part of long-term pain control is early and adequate intervention at the point of injury.^{1,11-13} Pain recognition and assessment should be a routine part of combat casualty management followed by prompt intervention. Early interventions are essential to prevent the psychological and biochemical consequences of pain and pain related phenomenon, and to reduce the risk of chronic pain syndrome.⁴ Orders for the treatment of pain and anxiety should include set goals and the minimum amount of medication necessary to achieve the goals should be used. The goals are determined by the need to achieve patient comfort and safety.

ANXIETY AND DELIRIUM

Similarly, the prevention of anxiety, agitation and delirium begin with recognition. All combat casualties are at risk for anxiety, which they may attempt to conceal or not disclose. As with pain prevention, management of the underlying etiology, including pain, hypoxia, metabolic abnormalities, and medications effects are essential principals. Disorientation to place and time as a result of unconsciousness, sedation, and loss of awareness that results from hospitalization contribute to PAD. This can be prevented with frequent and systemic efforts at reorientation and maintenance of normal sleep patterns.⁴

Interventions to promote healthy, REM sleep include exposure to bright light or sunlight during normal daytime hours and enforced darkness during normal night time hours. Orders should be written for scheduled periods of minimal or no disruption during normal sleep hours and patients be allowed to use earplugs during sleep to minimize noise disruption. Conversely, patients should be provided with hearing aids or eye glasses, as needed, to combat sensory deprivation. Victims of close proximity blast exposure should be presumed to have some degree of hearing loss and undergo an audiology evaluation. Intermittent dosing of analgesics and anxiolytics should be instituted prior to continuous dosing. Patients who require dosing more frequently than every 2 hours should be placed on continuous dosing titrated to their goal.

Efforts to prevent delirium in critically injured patients include Awakening and Breathing Coordination (ABC), non-pharmacologic Delirium (D) interventions, and early Exercise (E) and mobility. The ABCDE's should be incorporated into treatment care plans for all ICU patients starting no later than the Role 3.^{4,14} Propofol is an option for short term sedation in acutely agitated patients. It has rapid onset and it is also cleared rapidly. Propofol has been associated with hypotension which may be related to intravascular depletion. It is dissolved in a 10% lipid solution which should be accounted for when calculating calorie requirements. Propofol is an excellent drug for ICU patients scheduled to undergo CCATT missions. When used for transport, Propofol should only be administered to intubated patients.

Spontaneous Breathing Trials (SBT) should be performed daily. Physical and occupational therapy (PT/OT) should be initiated as soon as possible or at minimum 72 hours after intubation.^{14,15}

There is insufficient evidence that prophylactic administration of antipsychotics to the general ICU population prevents delirium and, therefore, we make no recommendation for it.¹⁶ Benzodiazepines, although potentially useful for control of agitation, may increase delirium and should be avoided or minimized in patients experiencing or at increased risk for delirium.

EVALUATION OF PAIN

Some level of pain is present in all combat casualties. While the pain may be initially masked by the intensity of the situation, the combat medic or when the patient reaches the first level of care should assess the level of pain. Seriously injured patients who are not intubated should be assessed every 1-4 hours for the presence of pain. All patients who are intubated need to be continuously monitored for adequate analgesia. Signs of inadequate pain control in the intubated patient include tachycardia, hypertension and agitation. However – it is imperative that other causes be excluded such as early compartment syndrome, missed injuries, or impending physiologic decline. If the patient is appropriately communicative then using the then DoD/VA Pain Rating Scale (DVPRS) and Supplemental Questions as quantifiers can facilitate evaluation and trends.^{3,10} All combat casualties will have a pain score recorded on admission to a Echelon III facility and as part of routine care while in the intensive care unit.

EVALUATION OF AGITATION AND DELIRIUM

The assessment of anxiety, agitation, delirium as well as pain can be complicated by the presence of traumatic brain injury (TBI). TBI, in addition to overall injury burden, and therapeutic interventions can affect the evaluation for agitation as well as impede an accurate neurologic assessment. Moderate to severe TBI patients are at particularly high risk for having atypical and/or paradoxical reactions to both sedating and stimulating agents.^{17,18} In addition, the reactions to individual agents and their overall impact on the TBI patient in terms of pain, alertness, agitation, anxiety, and delirium may change drastically over relatively short periods of time as their injury and cognitive status evolves. The Richmond Agitation Sedation Scale (RASS), and the Confusion Assessment Method (CAM) tools to help with the evaluation; they are included as Appendices D and E.

TREATMENT OF PAIN: GENERAL INFORMATION

As previously stated pain is a universal symptom of the combat injured patient and must be managed early and effectively. Adequate early pain control has been shown to reduce post-traumatic stress disorder and ongoing pain control is an obligatory part of trauma care. Inadequate treatment results in undesirable consequences that delay or prevent a wounded warrior's full rehabilitation and recovery.

With regards to specific opioid medications, any opioid available can be titrated to equal effectiveness for achieving desired pain control. This CPG is going to emphasize the use of Ketamine throughout the deployed continuum of care. Ketamine is a very effective analgesic either by itself or as an adjunct to opioid analgesia and can be used to reduce the total narcotic burden.^{19,20} Ketamine, in parenteral doses of 0.15-0.3 mg/kg, has been shown to reduce pain scores, total narcotic use, and need for rescue medication when used with morphine for acute pain control.²⁰

ROLE 1 TREATMENT OF PAIN

The Role I pain treatment guidelines described here are adopted directly from the most recent protocols developed by the Department of Defense's Committee on Tactical Combat Casualty Care, available online. The most current guidelines, with full course material and supporting documentation, is available through a Common Access Card enabled webpage from the Military Health System (https://mhs.health.mil/References/REF_TCCC.cshtml).

Additionally, the *Journal of the Special Operations Medical Association* maintains free access to the current protocols (<https://www.jsomonline.org/TCCC.html>).^{21,22} See [Appendix G](#) for a sample order set including medication options and dosing.

Analgesia on the battlefield should generally be achieved using one of three options, per the TCCC triple analgesia protocol. This is an abbreviated presentation of that protocol. The detailed description can be obtained via websites described above.

- **Option 1**, for mild to moderate pain when the casualty is still able to fight should include the TCCC Combat pill pack with acetaminophen and meloxicam given simultaneously.
- **Option 2**, for moderate to severe pain when the casualty is not in shock or respiratory distress, and the casualty is not at significant risk of developing either condition, should include oral transmucosal fentanyl citrate (OTFC) 800 ug. Naloxone (0.4 mg IV or IM) should be available when using opioid analgesics.
- **Option 3**, for moderate to severe pain when the casualty is in hemorrhagic shock or respiratory distress or the casualty is at significant risk of developing either condition, should include ketamine 50 mg IM or IN or ketamine 20 mg slow IV or IO. Ketamine doses can be repeated every 30 minutes for IM or IN and every 20 minutes for IV or IO administration.

Casualties should be disarmed after being given OTFC and always disarmed after receiving ketamine. Documentation of a mental status exam using the AVPU method should be performed prior to and after administering opioids or ketamine, and recorded on the TCCC Card (DD Form 1380, JUN 2014). Ketamine may be a useful adjunct to reduce the amount of opioids required to provide effective pain relief. It is safe to give ketamine to a casualty who has previously received morphine or OTFC. IV Ketamine should be given over 1 minute.

ROLE 2 TREATMENT OF PAIN

Damage Control Surgery is provided at Role 2. An anesthesiologist and/or certified registered nurse anesthetist will be on staff and in conjunction with the surgeons, will be responsible for perioperative pain management. Role 2's differ in their capability with some consisting of a single operating room bed and a single post-operative ICU bed while others have attached Emergency Care and Post-Operative Holding Capacity.

In the more austere Role 2, pain should be managed with intravenous opioids and ketamine titrated as needed to provide adequate pain control; if dysphoric symptoms emerge with ketamine, then a small amount of benzodiazepine should be administered.

More robust Role 2's will have additional personnel, equipment, and supplies available. At these locations, the capability might exist for peripheral nerve blocks, which could be performed by the anesthesia provider or by the orthopedic surgeon assigned to the unit. Infusion pumps may also be available for continuous opioid infusions in critically injured patients, with dosage titrated as needed to provide adequate pain control. Patients on infusions require close monitoring in an ICU setting. Some of these more robust Role 2's with attached ward holding may have Patient Controlled Analgesia (PCA) pumps that can be used by patients to manage their pain. Pain should be adequately controlled prior to starting PCA; the patient can then use the PCA for self-dosing as needed for pain. Starting dose for PCA's are as follows:

1. Morphine PCA in adults is 1-3 mg with 10-20 minute lockout
2. Hydromorphone PCA in adults is 0.1-0.3 mg with 10-20 minute lockout
3. Fentanyl PCA is 15-25 mcg with 10-20 minute lockout.

Patients on PCA require monitoring by nursing staff. Naloxone must be available to treat respiratory distress that may occur secondary to opioids.

ROLE 3 TREATMENT OF PAIN

Regional anesthesia procedures should be performed in a monitored setting where nursing staff is available to help with patient care and provide appropriate recovery services for the patients. The Acute Pain Service (discussed extensively above) should maintain and provide input for standing orders to include:

- Continuous epidural and peripheral nerve catheter infusion and single injection epidural or intrathecal narcotics.
- Intravenous patient controlled analgesia (PCA) Orders. Fentanyl, hydromorphone, and morphine are the narcotic agents of choice. (Meperidine (Demerol) is not an approved compound for repeated PCA dosing as the metabolite normeperidine reduces the seizure threshold.)

Low dose ketamine infusions have profound analgesic effects with very minimal side effects. The anti-inflammatory effects of ketamine may also attenuate the systemic inflammatory response seen in trauma.^{13,23,24} Ketamine binds the NMDA receptor and in addition to having direct analgesic properties, it also decreases the total dose of narcotics that is needed for adjuvant pain control. Ketamine infusions should be made as follows:

- 250 mg of Ketamine in 250 ml of normal saline.
- For patients who are 70 kg or greater and less than 60 years old, start infusions at 10 mg per hour in the setting of acute and neuropathic pain.
- Patients > 60 year old or <70kg should receive 100 micrograms/kg/hour of ketamine in the setting of acute or neuropathic pain.

- Custom orders may be titrated by the attending anesthesiologist or critical care physician

EPIDURAL CATHETERS

Neuraxial analgesia can be a very effective pain treatment in the injured warfighter, but special care must be taken to ensure that it is provided safely. Standard preservative free local anesthetics include ropivacaine and bupivacaine. The standard medication for aeromedical evacuation is 0.2% ropivacaine with sufficient volume for 3 days. Patients should be on stable doses of infusions prior to AE transportation. The risk/benefit of epidural placement must be considered in the injured combat casualty who is also at risk for venous thromboembolic events. While all antiplatelet and anticoagulant medications increase the risk of bleeding, low molecular weight heparin (LMWH) use in patients undergoing epidural anesthesia greatly increases the risk of epidural hematoma, which can lead to paralysis. The acute pain service should maintain and provide input for standing orders to include:

Given that our patients are transported through a spectrum of care and across thousands of miles, the implementation of regional anesthesia should be integrated throughout the trauma system and must be safe and effective. An anesthesia provider is responsible for the initial placement and dosing of an epidural catheter. Only members of the Acute Pain Service can change the dosing or infusion rate.

1. All catheters should receive a 3 ml test dose of local anesthetic containing at least 1:400,000 epinephrine.
2. Low molecular weight heparin (LMWH) use in patients undergoing epidural anesthesia increases the risk of spinal or epidural hematoma, which may cause long term or permanent paralysis. We recommend against the use of LMWH in AE patients given the increased motion of delivery catheters during patient transport and resulting increased risk for spinal & epidural hematoma formation.
3. Prophylactic LMWH dosing should be held for 12 hours prior to placement of an epidural catheter.
4. Therapeutic dosing should be held for 24 hours prior to placement of epidural catheters.
5. Administration of LMWH should be delayed for 2 hours after catheter removal.
6. The maximum recommended prophylactic dose of LMWH with an epidural catheter in place is 40 mg SQ daily.
7. Twice daily dosing of LMWH is not recommended for patients with indwelling epidural catheters.
8. The initial dose of once daily prophylactic LMWH should not be given until 6-8 hours after catheter placement. Subsequent daily doses should start 24 hrs after this first dose.
9. These recommendations are consistent with the most recent ASRA (American Society of Regional Anesthesia) guidelines for the prevention of epidural hematoma.

[Appendix F](#) is a summary of American Society of Regional Anesthesia guidelines as they relate to use of LMWH in combat casualties. The ASRA guidelines were originally developed for use of LMWH in the perioperative course.

Additionally, these recommendations change on a frequent basis. <https://www.asra.com/> should be consulted for the most current recommendations.

PERIPHERAL NERVE CATHETERS

1. All catheters should undergo a local anesthetic test dose containing 1:400,000 epinephrine.
2. For patients undergoing deep plexus or peripheral block, we recommend that recommendations regarding neuraxial techniques be similarly applied.
3. Each patient should have no more than two catheters and the total dose of 0.2% Ropivacaine should not exceed 20 ml per hour.
4. Regional anesthesia patients should be recovered by standard post anesthesia care unit (PACU) criteria.

Patients with epidurals and peripheral nerve blocks should be held in recovery until they meet standard discharge criteria from PACU and ICU. Patients with peripheral nerve blocks and epidural catheters that have met discharge criteria from ICU and PACU may be managed on the floor. Any patient with an epidural catheter or peripheral nerve block must be closely monitored for signs or symptoms of compartment syndrome (see below). No narcotics will be added to the peripheral nerve block or epidural infusions given the ongoing revision of validation for air transport by the United States Air Force (USAF).

TREATMENT OF ANXIETY AND AGITATION

Given the nature of combat injuries and the environment of care, both agitation and anxiety can be expected and should be preemptively managed. In a patient with normal hemodynamics, propofol is a good option for short-term sedation. **Propofol** does not provide analgesia; it is the most commonly used medication when sedation is required for ICU patients and CCAT transports due to its rapid onset and clearance. It is a GABAA agonist with rapid onset and clearance. Propofol can cause hypotension and should be used with caution in patients with intravascular depletion. Propofol is dissolved in a 10% lipid solution. It is an excellent drug for ICU patients scheduled to undergo aeromedical evacuation. Propofol should only be administered to patients who have a definitive airway (endotracheal tube, tracheostomy), are hemodynamically stable and are continuously monitored by trained personnel.^{4,25,26}

Dexmedetomidine is being used with increasing frequency in ICU patients and occasionally for transport. It minimally decreases respiration, so it can be used for patients on non-invasive mechanical ventilation or sedation for an awake intubation. It has some mild analgesic effects. It should be used with caution in patients with bradycardia or heart block. Dexmedetomidine is a relatively selective alpha-2 agonist; it is a good option for short-term sedation and anxiolysis. Dexmedetomidine has minimal impact on respiratory drive allows for ongoing assessment of the patient's mental status.⁴

Clonidine is an effective drug for treating patients with anxiety and agitation; it is particularly effective for patients with hypertension associated with agitation.^{5,27} Clonidine acts as an alpha-2 adrenergic agonist and also has sedative properties that do not result in respiratory suppression. It may also be used for mild sedation and analgesia.²⁷

TREATMENT OF DELIRIUM

The typical antipsychotic **haloperidol (Haldol®)** and the atypical antipsychotic **quetiapine (Seroquel®)** are commonly used for the treatment of delirium. Quetiapine can also be used as an anxiolytic; it is particularly effective when used QHS PRN to help regulate sleep in a patient at risk for anxiety and delirium. Both of these drugs may be associated with prolongation of the QT interval potentially resulting in fatal arrhythmias secondary to torsades des pointes. If these drugs are used, the QTc interval should be monitored with an EKG on a daily

basis. They should be discontinued if the QTc exceeds 500 msec or the interval increases 60 msec from baseline.⁴

PREVENTING COMPLICATIONS

Medications should be specifically directed and dosed to achieve a defined goal, for example:

- Achieve a pain score of 4 or less;
- Maintain sufficient patient consciousness to assess the evolution of injuries by physical exam;
- Decrease the need for mechanical ventilation;
- Amelioration of symptoms of anxiety, delirium or agitation.

BENEFITS OF SEDATION HOLIDAY AND INTERMITTENT MEDICATION DOSING

INTERMITTENT DOSING

Intermittent dosing of analgesics and anxiolytics, as opposed to continuous dosing, has been shown to reduce the duration of mechanical ventilation and intermittent dosing of analgesics and anxiolytics should be instituted prior to continuous dosing. Although many sedative agents are utilized for their short duration of action (e.g. midazolam), administration as a continuous infusion will often result in a prolonged duration of action and effect due to fat storage and accumulation of active metabolites. It is recommended that intermitted sedation be used whenever feasible. For patients who require dosing more frequently than every 1-2 hours, continuous dosing titrated to effect can be used; however, continuous infusions should be converted to intermittent dosing as early as possible.

SEDATION VACATIONS

Daily interruptions of sedation (“sedation vacations”) have repeatedly demonstrated reduction in the duration of mechanical ventilation as well as the incidence of ventilator-associated pneumonia.²¹ Intermittent dosing and daily sedation holidays prevent the accumulation of active metabolites, which may impede patient assessment for prolonged periods of time.^{25,28}

- Continuous infusions should be stopped daily to obtain a reliable physical examination, including neurologic assessment, and to perform a spontaneous breathing trial in ventilated patients.
- Sedation Goals should be assessed every day following sedation holidays and every effort should be made to reduce infusion doses.

CONTRAINDICATIONS TO THE DAILY SEDATION HOLIDAY:

- Intractable intracranial hypertension
- Hemodynamic instability
- Inability to adequately oxygenate or ventilate mechanically ventilated patients.

See [Appendix G](#) for a **sample order set** including medication options and dosing.

See Table 1 in [Appendix A](#) for **suggested management algorithms**.

LOCAL ANESTHETIC TOXICITY

Local anesthetic toxicity is extremely rare in a patient who has an established neuraxial or peripheral nerve catheter. If suspected, all local anesthetic infusions should be immediately stopped. Occasionally the presenting symptom is cardiac arrest. In cardiac arrest, the patient should immediately receive 1.5 ml/kg of 20% **Intralipid**[®] while receiving chest compressions and other ACLS interventions such as airway management. Repeat the bolus 1-2 times as needed for persistent asystole, pulseless electrical activity or reemergence of hemodynamic instability. Increase the infusion rate to 0.5 mL/kg/min if hemodynamic instability persists or recurs. Continue the infusion for at least 10 min after hemodynamic stability is restored; discontinue within 1 hour if possible. Another rare symptom of local anesthetic toxicity is seizure. Once again, the infusion should be stopped, seizure should be treated with an anti-seizure medication and the airway should be controlled if necessary. Much more common symptoms of local anesthetic toxicity are tinnitus, anxiety, restlessness, dizziness and blurred vision; in the case of these symptoms, the infusion should be stopped.

1000 ml of 20% **Intralipid**[®] should accompany patients receiving local anesthetic infusions during transport in the AE System.

NAUSEA

Nausea is a common side effect of both trauma and the medications used to treat pain, anxiety, and delirium. Consider prophylactic treatment whenever possible and treat immediately upon patient report of symptoms. If the patient has recently undergone an emergency general anesthetic or any type of abdominal surgery, then ensuring that they are not at aspiration risk is important prior to medication. If there is a concern for gastric distention or any type of obstruction (functional or mechanical), then the patient should receive gastric decompression with an NG tube in addition to pharmacologic management for nausea.

Ondansetron is a safe antiemetic in the adult population and is increasingly the therapy of choice for acute undifferentiated and trauma-related nausea.²⁹ It has no effect on consciousness or the respiratory drive; additionally, at the doses recommended for these patients (4-8 mg per dose) has no clinically significant effect on QT interval.^{29,30}

COMPARTMENT SYNDROME

Compartment syndrome is a well-described complication of traumatic injury; for the purposes of this CPG, only extremity compartment syndrome will be discussed. Definitive treatment is complete surgical release of the extremity compartments affected. The acute pain anesthesiologist and trauma surgeon should have a detailed discussion regarding patients who are at high risk for compartment syndrome. Pain control may mask the typical early sign of compartment syndrome: increased pain in the compartment. Any patient at risk for extremity compartment syndrome who is awake and has an increased pain medication requirement should be promptly and thoroughly assessed for increased compartment pressure. For patients with regional or neuraxial analgesia affecting an extremity that is felt to be at risk for compartment syndrome, more frequent clinical assessments and monitoring of the extremity are warranted. If the patient is unable to reliably detect and report pain and there are any clinical or examination findings concerning for a compartment syndrome, then bedside assessment of compartment pressures or performance of a fasciotomy should be done promptly. If there is any concern for compartment syndrome, then full compartment release with fasciotomies must be completed prior to aeromedical transportation. Newer monitoring technologies such as near infrared spectroscopy; have shown some promise in early noninvasive detection of compartment syndrome; however, they are not currently standard of care.

AIR EVACUATION CONSIDERATIONS

The United States Air Force (USAF) Patient Movement Request (PMR) must state the type of regional anesthesia being utilized. All individuals participating in the care of the patient should have up-to-date training and experience with regional anesthesia, techniques, medications and the equipment. All equipment associated with the use of regional anesthesia must be approved for flight. The current infusion pump system that has been approved by the USAF for air evacuation is the small portable Ambit pump. Ambit pumps should be used for epidural, peripheral nerve catheters, ketamine infusions, narcotic infusions, and patient controlled anesthesia. For all patients receiving regional anesthesia/analgesia, coordinate with the Trauma Chief, Theater Validating Flight Surgeon and Theater CCATT Director prior to any planned fixed-wing tactical (Inratheater) or strategic (Intertheater) transport to ensure patient safety during flight operations.

Patients undergoing prolonged air evacuation are exposed to a multitude of austere environments over a relatively short period of time. CCATT providers recognize that turbulence, weather, temperature, limited patient access and monitoring constraints make it inherently difficult to maintain sedation and analgesia. It may be necessary to empirically increase sedation and pain regimens to maintain a safety margin that protects endotracheal tubes and other invasive devices. This clouds a patient's neurologic exam. Therefore patients with potential intracranial injury (TBI or stroke) who cannot be serially, neurologically evaluated should have intracranial pressure monitors.

In terms of peripheral nerve blocks or epidural catheters, no narcotics will be added to the infusions; the addition of narcotics to these regional therapies changes the validation for air transport by the USAF.

GUIDANCE

- The Military Advanced Regional Anesthesia and Analgesia handbook is an excellent APS reference text for pain care standards (www.bordeninstitute.army.mil or www.DVPMI.org)
- Tri-service policies for pain management can be found at www.DVPMI.org.
- Strategic issues on evacuation pain management should be referred by the health care facility APS physician to the Defense and Veterans Pain Management Initiative organization (www.DVPMI.org).

PERFORMANCE IMPROVEMENT (PI) MONITORING:

POPULATION OF INTEREST

All injured patients

INTENT (EXPECTED OUTCOMES)

1. Patients in the population of interest have a documented pain assessment at every role of care.
2. Patients in the population of interest in the intensive care unit are screened for delirium daily.
3. Intubated patients will not experience an inadvertent or unplanned extubation.

PERFORMANCE ADHERENCE METRICS

1. Number and percentage of patients in the population of interest who have a documented pain assessment at each role of care.

2. Number and percentage of patients in the population of interest in the intensive care unit with documented delirium screen daily.
3. Number and percentage of intubated patients who experience an inadvertent or unplanned extubation.

DATA SOURCE

- Patient Record
- Department of Defense Trauma Registry (DoDTR)

SYSTEM REPORTING & FREQUENCY

The above constitutes the minimum criteria for PI monitoring of this CPG. System reporting will be performed annually; additional PI monitoring and system reporting may be performed as needed.

The system review and data analysis will be performed by the JTS Chief and the JTS PI Branch.

RESPONSIBILITIES

All healthcare providers will:

1. Become familiar with the guidelines for the management of pain, anxiety and delirium in critically injured patients.
2. Appropriately manage patients with pain, anxiety and delirium.
3. Provide feedback on these guidelines and suggestions for changes to the CPG to the JTS Director.

The Trauma Chief, Pain Director and Intensivist at each level III facility will:

1. Implement care that is consistent with the intent of this CPG.
2. Monitor adherence with the CPG.

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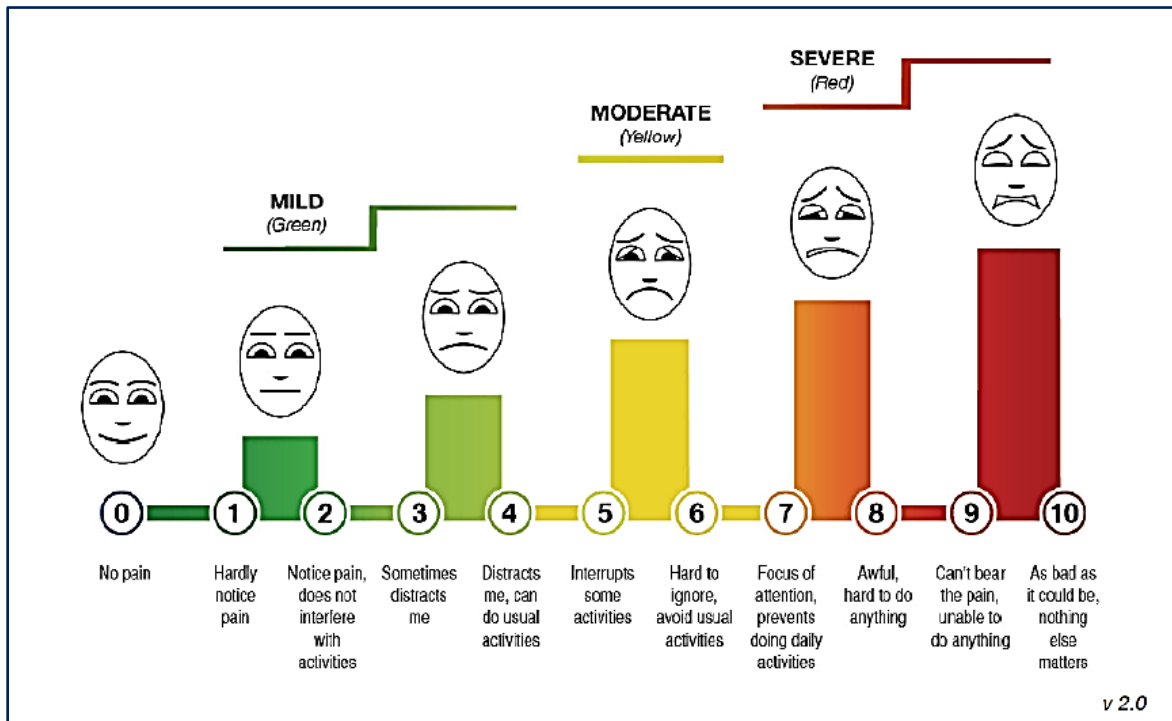
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APPENDIX A: PAIN, ANXIETY (SEDATION) AND DELIRIUM GUIDELINES

		Intubated Hemodynamically Unstable or severe ARDS	Intubated Hemodynamically Stable, adequate gas exchange	Not Intubated Stable
Background	Pain	Goals: Minimize pain, patient safety RASS -3 to -4, no sedation holiday, consider paralysis <i>Option 1:</i> Ketamine drip <i>Option 2:</i> Intermittent Narcotic (*Option 1 for TBI) <i>Option 3:</i> Fentanyl or drip or equivalent if tolerated	Goals: Minimize pain, patient safety RASS -1 to -2, daily sedation holiday or continuously interactive patient <i>Option 1:</i> fentanyl drip or equivalent <i>Option 2:</i> Ketamine Drip <i>Option 3:</i> Intermittent Narcotic (*Option 1 for TBI)	Goals: Minimize pain, patient safety RASS 0, continuously interactive patient <i>Option 1:</i> Scheduled Enteral or Parenteral Narcotic <i>Option 2:</i> Intermittent as needed enteral or parenteral narcotic
	Sedation	<i>Option 1:</i> Ketamine drip <i>Option 2:</i> Intermittent Benzodiazepine <i>Option 3:</i> Propofol drip if tolerated (*Option 1 for TBI)	<i>Option 1:</i> Propofol Drip <i>Option 2:</i> Demedetomidine Drip <i>Option 3:</i> Intermittent Benzodiazepines	NA
	Adjuncts	Consider first: Axial or regional anesthetic by catheter or injection Consider also: <ul style="list-style-type: none"> - scheduled acetaminophen or paracetamol - gabapentin and/or TCA for amputees 		
Breakthrough	Pain	<i>Option 1:</i> Intermittent/bolus ketamine <i>Option 2:</i> Intermittent/bolus narcotic	<i>Option 1:</i> Intermittent/bolus narcotic <i>Option 2:</i> Intermittent/bolus ketamine	<i>Option 1:</i> PCA <i>Option 2:</i> Intermittent as needed enteral or parenteral narcotic
	Sedation	<i>Option 1:</i> Intermittent/bolus ketamine <i>Option 2:</i> Intermittent/bolus benzodiazepine	<i>Option 1:</i> Intermittent/bolus benzodiazepine <i>Option 2:</i> Intermittent/bolus ketamine	<i>Option 1:</i> As needed enteral or parenteral benzodiazepine
	Adjuncts	Consider: <ul style="list-style-type: none"> - Dim, calm environment, reassurance, music, presence of friends/family - Give bolus and/or adjust dose of axial or regional anesthetic 		
Procedural	Pain	<i>Option 1:</i> Intermittent/bolus ketamine <i>Option 2:</i> Intermittent/bolus narcotic	<i>Option 1:</i> Intermittent/bolus ketamine <i>Option 2:</i> Intermittent/bolus narcotic	<i>Option 1:</i> Planned pre-procedural enteral or parenteral narcotic <i>Option 2:</i> Pre-procedural ketamine <i>Option 3:</i> Demedetomidine
	Sedation	<i>Option 1:</i> Intermittent/bolus ketamine <i>Option 2:</i> Intermittent/bolus benzodiazepine	<i>Option 1:</i> Increase dose of background propofol +/- propofol bolus <i>Option 2:</i> Intermittent/bolus benzodiazepine <i>Option 3:</i> Intermittent/bolus ketamine	<i>Option 1:</i> Pre-procedural ketamine +/- benzodiazepine <i>Option 2:</i> Planned pre-procedural enteral or parenteral benzodiazepine <i>Option 3:</i> Demedetomidine
Delirium	Prevention & Management	- Maintain day night cycles - Consider afternoon naps - Consider ear plugs at night - Consider less sedation and avoid benzodiazepines - Prioritize early mobility and patient interaction		
	Treatment	Consider dexmedetomidine for sedation and/or at night for sleep Consider quetiapine		

APPENDIX B: DOD AND VA PAIN RATING SCALE



APPENDIX C : DOD AND VETERANS PAIN SUPPLEMENTAL QUESTIONS

1. Circle the one number that describes how, during the past 24 hours, pain has interfered with your **ACTIVITY**:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10

Does not interfere Completely interferes

2. Circle the one number that describes how, during the past 24 hours, pain has interfered with your **SLEEP**:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10

Does not interfere Completely Interferes

3. Circle the one number that describes how, during the past 24 hours, pain has affected your **MOOD**:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10

Does not affect Completely affects

4. Circle the one number that describes how, during the past 24 hours, pain has contributed to your **STRESS**:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10

Does not contribute Contributes a great deal

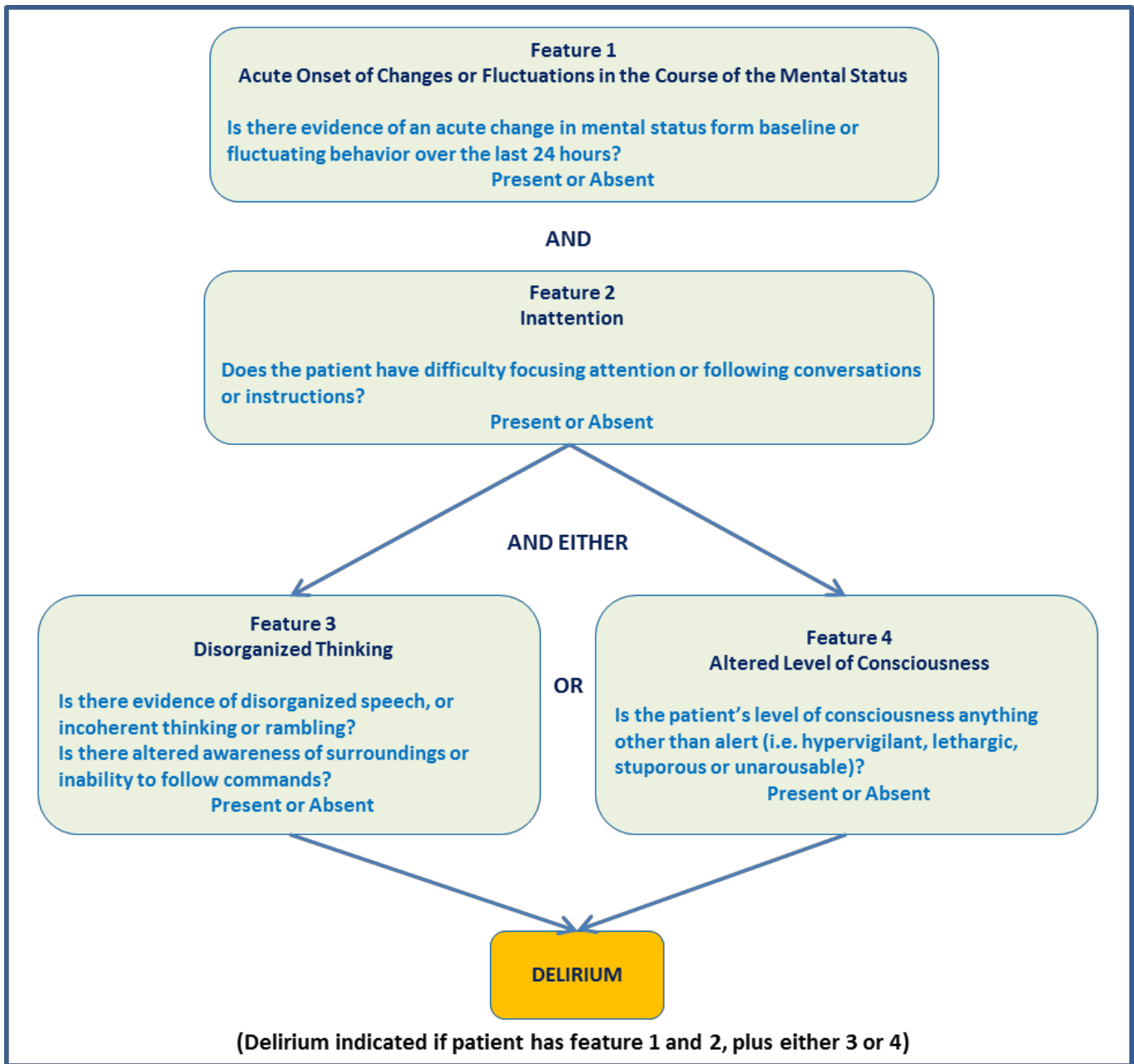
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APPENDIX D: RICHMOND AGITATION SEDATION SCALE (RASS)

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff.	
+3	Very Agitated	Pulls or removes tube(s) or catheter(s); aggressive.	
+2	Agitated	Frequent non-purposeful movement, fights ventilator.	
+1	Restless	Anxious but movements not aggressive vigorous.	
0	Alert, Calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (>10 seconds).	} Verbal Stimulation
-2	Light Sedation	Briefly awakens with eye contact to voice (<10 seconds).	
-3	Moderate Sedation	Movement or eye opening to voice (but no eye contact).	
-4	Deep Sedation	No response to voice, but movement or eye opening to physical stimulation.	} Physical Stimulation
-5	Unarousable	No response to voice or physical stimulation.	
Procedure for RASS Assessment			
1. Observe patient: Patient is alert, restless, or agitated.			Score 0 to+4
2. If not alert, state patient’s name and say to open eyes and look at speaker			
- Patient awakens with sustained eye opening and eye contact.			Score -1
- Patient awakens with eye opening and eye contact, but not sustained.			Score -2
- Patient has any movement in response to voice but no eye contact.			Score -3
3. When no response to verbal stimulation, physically stimulate patient by shaking shoulder and/or rubbing sternum.			
- Patient has any movement to physical stimulation.			Score -4
- Patient has no response to any stimulation.			Score -5
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APPENDIX E: THE CONFUSION ASSESSMENT METHOD



APPENDIX F: REGIONAL ANESTHETIC USE

Consensus Statement of American Society of Regional Anesthesia (ASRA) on LMWH as it relates to regional anesthetic use, adapted for use in combat casualties.

1. Antiplatelet or oral anticoagulant medications administered in combination with LMWH increase the risk of spinal hematoma. ASRA recommends against concomitant administration of antiplatelet drugs, standard heparin, dextran or coumadin, regardless of LMWH dosing regimen.
2. Needle placement should be delayed at least 10 to 12 hours after patient has received LMWH thromboprophylaxis.
3. Needle placement should be delayed at least 24 hours in patients receiving therapeutic LMWH.
4. In patients receiving twice daily dosing of LMWH:
 - Indwelling catheters should be removed before initiation of twice daily dosing regimen.
 - LMWH should be delayed for 2 hours after catheter removal.
5. In patients receiving single daily dosing of LMWH.
 - Catheters can be maintained in place.
 - Catheter can be removed no sooner than 10 to 12 hours after last dose of LMWH.
 - Subsequent LMWH should be withheld for two hours after catheter removal.
6. NSAIDs (including aspirin) alone do not add a significant risk for development of spinal hematoma.
7. Neuraxial anesthetic techniques should be avoided in patients who are receiving NSAIDs and LMWH.
8. These same recommendations apply for patients undergoing deep plexus or peripheral blocks.

APPENDIX G: SEDATION ORDERS

Allergies: _____ Weight: _____ kg

Diagnosis: _____

Service: _____ Attending: _____

SEDATION ANALGESIA DELIRIUM

See ICU Sedation Analgesia Delirium Algorithm

Nursing Orders

- Daily sedation Hold
 1. Hold sedation/analgesia daily.
 2. Assess pt for SBT if on ventilator.
 3. Restart sedation/analgesia at intermittent dosing;
 OR if patient's condition requires continuous infusion, restart infusion at ½ pre-interruption dose.
- Sedate to RASS goal of minus 2 to minus 1. See RASS scale. ([Appendix C](#))
- ICU Sedation Analgesia Delirium Protocol.
See CAM scale. ([Appendix D](#))
See Treatment Algorithm
- Notify MD
For delirium prior to initiating pharmacologic treatment
For patient on Clonidine - If SBP falls > 30 mmHg or DBP fall > 20 mmHg

ANALGESIA**Intermittent Dosing** Start with Intermittent Dosing. If required more than Q 2 Hours, go to Continuous Infusion.

- fentanyl IV _____ mcg (25-100 mcg). Intravenous, EVERY 1 HOUR AS NEEDED for mild to moderate pain.
Titrate pain medications to achieve a level 3 or _____ (pain scale 1-10).
Start with Intermittent Dosing. If required more than Q 2 hours, go to Continuous infusion.
Administer via slow IV.
- ketamine IV _____ mg (0.1-0.5 mg/kg). Intravenous, EVERY 1 HOUR AS NEEDED for mild to moderate pain.

Continuous Dosing Stop intermittent dosing if continuous infusion initiated and notify Pharmacy.

- fentanyl IV _____ mcg (25-250 mcg/hr), Intravenous, CONTINUOUS
Titrate pain medication to achieve a level 3 or _____ (pain scale 0-10).
Stop intermittent dosing if continuous infusion initiated and notify Pharmacy Services. ****High-Risk Medication****
- fentanyl IV bolus _____ mcg (25-100 mcg), Intravenous, EVERY 10 MINUTES AS NEEDED for breakthrough pain.
Titrate pain medication to achieve a level 3 or _____ (pain scale 0-10).
Administer via slow IV.
- ketamine IV _____ mg (10-40 mg/ hr for ≥70 kg and < 60 years old) CONTINUOUS
Titrate pain medication to achieve a level 3 or _____ (pain scale 0-10).
Stop intermittent dosing if continuous infusion initiated and notify Pharmacy Services.
- ketamine IV _____ mg (100 mcg/ kg/ hour) of ketamine CONTINUOUS
Titrate pain medication to achieve a level 3 or _____ (pain scale 0-10).
Stop intermittent dosing if continuous infusion initiated and notify Pharmacy Services.
- ketamine IV bolus 0.1-0.5 mg/kg , Intravenous, EVERY 10 MINUTES AS NEEDED for breakthrough pain.
Titrate pain medication to achieve a level 3 or _____ (pain scale 0-10).

SEDATION: See RASS scale.**Intermittent Dosing** Start with Intermittent Dosing. If required more than Q 2 hours, go to Continuous Infusion.

- lorazepam (aka ATIVAN) IV _____ mg (1-4 mg), Intravenous, EVERY 1 HOUR AS NEEDED for anxiety/agitation.
Start with Intermittent Dosing. If required more than Q 2 hours, go to Continuous Infusion.
Titrate sedation to RASS score of -1 to 0

Continuous Infusion Stop intermittent dosing if continuous infusion initiated and notify Pharmacy.

- lorazepam (aka ATIVAN) IV infusion _____ mg/hr (1-5 mg/hr), Intravenous, CONTINUOUS
Stop intermittent dosing if continuous infusion initiated and notify Pharmacy.

Titrate sedation to RASS score of -1 to 0

- lorazepam (aka ATIVAN) IV bolus _____ mg (1-2 mg), Intravenous, EVERY 20 MINUTES AS NEEDED for breakthrough agitation/anxiety.

Titrate sedation to RASS score of -1 to 0

- midazolam (aka VERSED) IV infusion (avoid in renal/liver dysfunction) _____ mg/hr (1-6 mg/hr), Intravenous, CONTINUOUS.

Stop intermittent dosing if continuous infusion initiated and notify Pharmacy.

Titrate sedation to RASS score of -1 to 0

DEXMEDETOMIDINE: Continuous Infusion

- dexmedetomidine IV _____ mcg/kg/hr (0.3-0.7 mcg/kg/hr), Intravenous, CONTINUOUS for 24 hours
 1. Is rapid extubation expected (24-48 hrs)? Yes No
 2. Ordered by IC fellow or ICU staff? _____
 3. Please select the indication (must meet one of the following):
 - Awake intubation
 - BIPAP use requiring sedation
 - Bridge to extubation
 - Desired light to moderate sedation
 - Titrate in increments of 0.1 mcg/kg/hr Q 10 minutes to achieve a sedation score of 2-3 and pain score < 4/10.
 - Do not exceed maximum dose of 0.7 mcg/kg/hr.
 - Keep heart rate greater than _____ beats per minute and systolic blood pressure greater than _____ mmHg and mean arterial pressure greater than _____ mmHg.
 - Discontinue for heart rate < 45 beats per minute or if patient develops 2nd or 3rd degree Atrioventricular block.
 - For persistent hypotension unresponsive to fluid challenge, decrease the rate by 50%.
 - Discontinue if systolic blood pressure and mean arterial pressure do not return to parameters specified above in 10 minutes. Call physician for further instructions.

DELIRIUM: See CAM scale

Initiating Therapy

- haloperidol (aka HALDOL) IV x 1 _____ mg (2-10 mg), Intravenous, ONCE For 1 Dose Administer over 1 minute. See CAM scale.
- haloperidol (aka HALDOL) IV PRN _____ mg (2-5 mg), Intravenous, EVERY 15 MINUTES AS NEEDED for agitation. Recommend not to exceed 20 mg over one hour. Slow administration over 5-10 minutes preferred to minimize hypotension. See CAM scale.

Maintenance Dosing QTc monitoring required for patients receiving more than 10 mg haloperidol per day

- haloperidol (aka HALDOL) IV _____ mg (2-5 mg), Intravenous, EVERY 1 HOUR AS NEEDED for delirium. Not to exceed dose 80 mg IV in 24 hours. Slow administration over 5-10 minutes preferred to minimize hypotension. See CAM scale.
- quetiapine (aka SEROQUEL) PO tablet (Day 1) 25 mg, Oral, TWICE DAILY. See CAM scale.
- quetiapine (aka SEROQUEL) PFT tablet (Day 1) 25 mg, Feeding tube, TWICE DAILY. See CAM scale.
- quetiapine (aka SEROQUEL) PO tablet (Day 2) 50 mg, Oral TWO TIMES DAILY. If patient responds to initial dose and PO/PFT available. See CAM Scale.
- quetiapine (aka SEROQUEL) PFT tablet (Day 2) 50 mg Feeding tube, TWO TIMES DAILY. If patient responds to initial dose and PO/PFT available. See CAM scale.
- clonidine (aka CATAPRES) tablet PRN 0.1-0.2 mg, Oral EVERY 1 HOUR AS NEEDED for hypertension due to agitation.
 - May repeat x 3 doses as needed, until SBP \leq 140 mmHg (160 mmHg if over 65 years of age).
 - If blood pressure goal is not achieved with clonidine 0.1 mg, give clonidine 0.2 mg every 1 hour as needed to achieve SBP \leq 140 mmHg (160 mmHg if over 65 years of age).
 - Once BP goal is met, move to maintenance and/or PRN dose.
 - Hold clonidine if systolic blood pressure falls more than 30 mmHg of diastolic blood pressure falls more than 20 mmHg and notify physician.
- clonidine (aka CATAPRES) tablet scheduled 0.1-0.2 mg, Oral, EVERY 8 HOURS Administer until SBP < 140 mmHg then change to maintenance/PRN dose. Hold clonidine if systolic blood pressure falls more than 30 mmHg or diastolic blood pressure falls more than 20 mmHg and notify physician.

APPENDIX H: ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

PURPOSE

The purpose of this Appendix is to ensure an understanding of DoD policy and practice regarding inclusion in CPGs of “off-label” uses of U.S. Food and Drug Administration (FDA)–approved products. This applies to off-label uses with patients who are armed forces members.

BACKGROUND

Unapproved (i.e., “off-label”) uses of FDA-approved products are extremely common in American medicine and are usually not subject to any special regulations. However, under Federal law, in some circumstances, unapproved uses of approved drugs are subject to FDA regulations governing “investigational new drugs.” These circumstances include such uses as part of clinical trials, and in the military context, command required, unapproved uses. Some command requested unapproved uses may also be subject to special regulations.

ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

The inclusion in CPGs of off-label uses is not a clinical trial, nor is it a command request or requirement. Further, it does not imply that the Military Health System requires that use by DoD health care practitioners or considers it to be the “standard of care.” Rather, the inclusion in CPGs of off-label uses is to inform the clinical judgment of the responsible health care practitioner by providing information regarding potential risks and benefits of treatment alternatives. The decision is for the clinical judgment of the responsible health care practitioner within the practitioner-patient relationship.

ADDITIONAL PROCEDURES**Balanced Discussion**

Consistent with this purpose, CPG discussions of off-label uses specifically state that they are uses not approved by the FDA. Further, such discussions are balanced in the presentation of appropriate clinical study data, including any such data that suggest caution in the use of the product and specifically including any FDA-issued warnings.

Quality Assurance Monitoring

With respect to such off-label uses, DoD procedure is to maintain a regular system of quality assurance monitoring of outcomes and known potential adverse events. For this reason, the importance of accurate clinical records is underscored.

Information to Patients

Good clinical practice includes the provision of appropriate information to patients. Each CPG discussing an unusual off-label use will address the issue of information to patients. When practicable, consideration will be given to including in an appendix an appropriate information sheet for distribution to patients, whether before or after use of the product. Information to patients should address in plain language: a) that the use is not approved by the FDA; b) the reasons why a DoD health care practitioner would decide to use the product for this purpose; and c) the potential risks associated with such use.