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1 **WILDERNESS MEDICAL SOCIETY CLINICAL PRACTICE GUIDELINES**

2
3 **Title:** Wilderness Medical Society Clinical Practice Guidelines for the Treatment of Acute Pain
4 in Austere Environments: 2024 Update

5
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21
22 Summary Tallies

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29 Abstract:

30 The Wilderness Medical Society (WMS) convened an expert panel to develop evidence-based
31 guidelines for the management of pain in austere environments. Recommendations are graded
32 based on the quality of supporting evidence as defined by criteria put forth by the American
33 College of Chest Physicians. This is an update of the 2014 version of the WMS Practice
34 Guidelines for the Treatment of Acute Pain in Remote Environments published in Wilderness &
35 Environmental Medicine 2014; 25:41–49.

36

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39

40

41

42 **Introduction**

43 The treatment of pain is important in the management of illness and injury in any context.
44 Beyond the ethical considerations of compassion and management of suffering, effective
45 management of acute pain in austere settings can facilitate the evaluation, packaging, and
46 transportation of patients whose management would otherwise be challenging or impossible
47 without pain control.

48 Management of acute pain is a multifaceted challenge which can involve physical
49 stabilization of an acute musculoskeletal injury or wound, medical management of peripherally
50 and centrally mediated pain responses, and management of psychological distress and anxiety.
51 Any treatment of pain carries with it risks and benefits which may be amplified when these
52 treatments are used in an austere environment. Limited patient access, difficulty of reevaluation
53 during transport, need to protect the patient from environmental insults, lack of monitoring
54 equipment, and limited means to respond to adverse effects of treatments can amplify risks.
55 Consequently, treatment of pain in an austere environment requires a thoughtful and progressive
56 approach that minimizes harms while managing the needs of the patient and treating team.

57 For the purposes of this guideline, austere environments are defined as wilderness,
58 remote, or highly resource-limited settings where access to typical hospital or EMS resources is
59 unavailable and evacuation may be challenging or prolonged. We include the setting of
60 wilderness, and include expedition settings and other travel to regions where parties must be self-
61 sufficient in their medical care. We exclude from this guideline pain management in the military
62 setting, where resources and availability of evacuation are generally greater and for which
63 guidelines already exist. We also exclude management of acute pain in space travel, where
64 physiology and resource limitations are truly unique. The term ‘austere’ has been chosen to

65 replace ‘remote’ in this guideline as it better describes a setting of limited resources and
66 environmental challenges. When terrain, weather, or altitude are challenges to care, resources do
67 not need to be geographically remote to be functionally unavailable.

68 The legal specifics of the acquisition, storage, and administration of controlled substances
69 is beyond the scope of this guideline. Variation between and even within nations and
70 jurisdictions is too great to facilitate recommendations specific to all settings. Further, we do not
71 limit the recommendations in this guideline to a particular class, certification, or training level of
72 responder. Whether an amateur recreational backcountry user or trained medical responder, users
73 of these guidelines must employ judgment as to which treatment modalities are within the scope
74 of their training and appropriate to their treatment setting and available resources. In each of the
75 sections to follow, we present the best available evidence identified by the panel as to the safety,
76 efficacy, and austere-specific considerations for available pain treatment modalities.

77

78 **Methods**

79 An expert panel was convened during the 2013 annual winter meeting of the Wilderness Medical
80 Society (WMS) in Park City, UT, and an original guideline was published in Wilderness and
81 Environmental Medicine in 2014. A subsequent expert panel was convened in 2019 and a partial
82 unpublished revision to the guideline was completed with integration of updated literature
83 sources. To complete this updated literature review, a panel was convened in July of 2022,
84 participation in which was based on the individual’s relevant clinical, research, and/or field
85 experience. The panel included representatives from emergency medicine, anesthesiology,
86 surgery, and the field of prehospital emergency medical services (EMS).

87 A review of relevant research articles was completed by a keyword search of the
88 MEDLINE and PubMed Central databases via the PubMed search interface in addition to queries
89 of SCOPUS and Google Scholar using keywords targeted to each subject area, with filters
90 applied to remove non-English language sources. Searches were completed during June-August
91 2022. Keywords searched were generated by section authors. Abstracts were screened by section
92 authors for relevance to austere settings, fundamental relevance to the understanding and
93 treatment of pain, or the pharmacology and pharmacodynamics of medications discussed.
94 Additional sources were identified by reviewing citations from identified sources and review
95 articles. Where evidence directly pertinent to austere settings was not available, the best
96 available evidence was included from EMS, tactical medicine, disaster medicine, emergency
97 medicine, and global health literature sources. Pain control modalities were included based on
98 expert consensus, and any modalities suggested by any member of the panel were subjected to a
99 literature search for relevant evidence and applications.

100 Articles were excluded for lack of relevance as determined by expert review. Additional
101 relevant review articles obtained for background as well as relevant guidelines on the
102 management of acute pain and traumatic injuries were also selected for inclusion.

103 Recommendations were developed by section authors and revised by consensus
104 approach. Where evidence relevant to austere environments was limited or of low quality,
105 recommendations were made by the consensus of the group based on the clinical experience of
106 panel members and relevant literature from hospital and pre-hospital medicine.

107 Recommendations were graded according to the criteria developed by the American College of
108 Chest Physicians (Supplemental Table) (1). Final recommendations included were approved
109 unanimously by all members of the panel.

110 Terms used in the guideline to discuss pain such as ‘pain’, ‘nociception’, and
111 ‘sensitization’ are used in a manner consistent with the International Association for the Study of
112 Pain terms and definitions (2).

113

114 **General Approach to Pain Management in an Austere Environment**

115 Musculoskeletal injuries, including strains, sprains, dislocations, and fractures, are the most
116 common cause of pain treated in austere environments. Other circumstances that may require
117 pain management include acute medical ailments and environmental injuries such as cold injury,
118 bites, stings, and burns (3-5).

119 In all cases, the management of pain is a secondary consideration to the management of
120 immediate threats to life, including compromise of airway, breathing, or circulation, and
121 secondary to scene safety for both the patient and the treating party. After scene safety and a
122 primary survey have been addressed, a secondary survey should be undertaken to evaluate the
123 cause and severity of pain (6).

124 Traumatic tissue injury, heat, cold, and ischemia can cause pain by different mechanisms,
125 and understanding the mechanism of injury or illness informs appropriate treatment. In an alert
126 patient, a description of mechanism, location, quality, and severity of pain can guide treatment.
127 In an uncooperative or unresponsive patient, evaluation of patient setting and the completion of a
128 thorough secondary survey can identify traumatic as well as environmental injuries on the basis
129 of deformity and tissue appearance (7). Pain control should not be withheld out of concern for
130 masking injury or limiting examination quality, and myths to the contrary have been addressed
131 by quality evidence and expert recommendation (8-11).

132 If possible, prior to treatment of pain, providers should evaluate pain severity, so as to be
133 able to evaluate response to treatment. A numerical rating scale (e.g. Numerical Rating Scale
134 [NRS-11] or Visual Analog Scale [VAS]) or the patient’s subjective description of their pain
135 severity should be used to evaluate response to treatments (12). However, protocols should not
136 compel obligatory use of medications or other interventions in response to specific scores, as a
137 rigid approach requiring treatment in response to a specific threshold has been shown to increase
138 medication-related adverse events (13, 14).

139 Except for some psychosocial interventions, all pain treatment modalities discussed
140 henceforth are accompanied by both benefits and risks to the patient. In general, centrally acting
141 pharmacologic agents (e.g. opioid medications, benzodiazepines) carry greater risk than
142 peripherally acting agents (non-steroidal medications, local anesthetics) due to their potential to
143 affect hemodynamics and respiration. Parenteral routes of administration (intranasal
144 [IN]/intramuscular [IM]/intravenous [IV]/intraosseous [IO]) carry more risk of adverse effects
145 than enteral or topical routes on account of accelerated absorption and shorter time to peak serum
146 concentration. Importantly, risk and benefit are not directly correlated in all cases, and some low-
147 risk interventions like psychological support or injury immobilization can be substantially
148 effective in the treatment of pain.

149 While previous WMS guidelines have recommended a stepwise and escalating approach
150 to pain control, we update this approach to consider situations in which the treating clinician
151 recognizes an inherently severe cause of pain and immediately initiates more aggressive
152 treatment measures (15). Accordingly, we recommend an approach to pain treatment that selects
153 and simultaneously applies pain treatment modalities based on the clinician’s experience, the
154 cause of pain, and appraisal of reported and anticipated pain severity. When possible, we still

155 recommend the use of lower-risk interventions before or in concert with higher-risk
156 interventions. Figure 1 provides a conceptual schematic of how different modalities might be
157 selected based on pain severity and available resources.

158 *Figure 1*

159 After application of a given treatment, the patient’s pain level should be reevaluated, and
160 the treating provider should determine if pain control is adequate to meet the needs of the patient
161 and the treating provider or team. Given that different modalities of pain control are appropriate
162 for different mechanisms of injury and illness, there can be no clear prescriptive approach or
163 linear road map for the treatment of pain. In some patients, anxiety and psychological distress
164 may significantly amplify a response to a minor injury, while in others, an isolated orthopedic
165 injury may be amenable to a specific intervention (e.g. hematoma block) which is inappropriate
166 in other cases. Experience and judgment, paired with frequent reevaluation of the patient and
167 environment, are critical.

168 Medical responses in an austere environment are inherently limited, so one must evaluate
169 and select pain treatments to minimize packed weight and bulk. An ideal medication for austere
170 settings is compact, lightweight, durable against crush, abrasion, heat, and cold, nonsedating, has
171 a large therapeutic index, works across multiple routes of administration, and has no potential for
172 abuse or dependence (16-18). Since no such medication exists, providers must weigh the
173 advantages and disadvantages of each medication carried considering the above constraints.

174 A survey of providers at the WMS summer conference in 2016 demonstrated that among
175 practicing medical provider respondents, 90% carried oral (PO) nonsteroidal anti-inflammatory
176 drugs (NSAIDs), 81% carried acetaminophen (APAP), and 47% carried PO opioids when
177 selecting medications for organized treks (19). These medications, in addition to training in

178 nonpharmacologic pain management, are likely to suffice in many settings, as minor orthopedic
179 injuries and soft tissue wounds comprise the majority of cases (5). In the management of severe
180 acute pain, however, these medications may be inadequate.

181 In the following sections we provide further discussion of pain control modalities. In each
182 section we discuss the risks and benefits of these interventions as well as the applications to
183 which they are best suited. Additionally, we discuss treatment considerations such as the need for
184 monitoring for adverse effects. Some of these treatments are advanced and require experience
185 that can only be developed in high-volume clinical environments such as hospitals and EMS
186 services. These treatments provide opportunities for organized rescue teams and advanced
187 medical providers to further refine their treatment of pain, but they are not necessary *per se*, and
188 in some settings may be inappropriate or excessive.

189
190 *Recommendation: We recommend that providers should manage pain to a level that provides*
191 *adequate relief, that meets the needs of the treating team, and that recognizes the limitations*
192 *imposed on the team by the austere environment (Strong recommendation, moderate-quality*
193 *evidence).*

194
195 *Recommendation: We recommend that, when appropriate to the clinical setting, providers*
196 *should evaluate patient response to low-risk pain treatments before progressing to higher-risk*
197 *treatment modalities or routes of administration so as to minimize harm in the austere*
198 *environment (Strong recommendation, low-quality evidence).*

199

200 *Recommendation: We recommend that, when appropriate to the clinical setting, providers may*
201 *initiate multiple simultaneous treatments to control pain of greater reported or anticipated*
202 *severity (Strong recommendation, low-quality evidence).*

203

204 **Nonpharmacologic Pain Management**

205 *Psychosocial Interventions*

206 The experience of pain is a product of nociceptive nerve signals from the peripheral nervous
207 system that are interpreted and given emotional valence in the central nervous system.

208 Practically, this means that the psychological state of the patient can affect their experience of
209 pain (20, 21). Laboratory studies have demonstrated that empathetic statements, caring touch,
210 and the presence of a partner perceived as caring can modulate the experience of pain, reduce
211 pain scores, and affect the autonomic response to pain (22-24).

212 Anxiety, a threat-detection function mediated by the amygdala, is also a potent mediator
213 of pain. High-anxiety situations induced in the laboratory setting are associated with higher pain
214 scores for a given pain stimulus (25). Additionally, greater acute pain intensity in the emergency
215 department has been associated with elevated anxiety states, and postoperative pain has been
216 correlated with preoperative anxiety levels (26, 27). Indeed, perioperative behavioral
217 interventions have been demonstrated to reduce postoperative pain and pain-related disability
218 (28). Attention can also be manipulated to treat pain; distraction from a noxious stimulus is
219 associated with lower acute pain scores, while attention focused on the source is associated with
220 higher pain scores (20, 25, 29, 30).

221 As empathy, caring, and distraction can mitigate pain, and conversely, coincident anxiety
222 can increase pain, psychosocial interventions are potentially useful in the treatment of pain.
223 Further, they are well-suited to an austere context, as they are weightless, durable, portable, and
224 cost nothing. The most robust literature targeting the acute reaction to stress and its mitigation
225 comes from work around post-traumatic stress disorder (PTSD) stemming from combat.
226 Treatment modalities targeting reactions to stress in survivors of trauma have been codified into
227 a toolset referred to collectively as Psychological First Aid (PFA) (31). PFA, while developed to
228 treat survivors of combat, has more recently been directed towards wilderness responders and
229 expedition members and has been integrated into wilderness medical texts and curricula (32-34).

230 The full extent of PFA is beyond the scope of this guideline. However, its principal
231 components provide a framework and shared vocabulary for psychosocial interventions that are
232 likely to aid in the treatment of pain through mitigation of negative emotional states, limitation of
233 stress response, and facilitation of adaptive behaviors (21). These components have been adapted
234 by the authors into a useful mnemonic for the application of PFA in austere environments (Table
235 1) (35).

236

237 *Table 1: The ABCDE mnemonic for the psychosocial treatment of pain.*

238

239 *Recommendation: We recommend that providers should train in and apply relevant*
240 *psychological first aid techniques for treatment of pain in austere environments (Strong*
241 *recommendation, low-quality evidence).*

242

243 *Splinting, Bandaging, Immobilization, Cryotherapy*

244 Treatment of acute musculoskeletal injuries has traditionally involved variations of the
245 ‘protection, relative rest, ice, compression, and elevation’ (PRICE) treatment protocol. Limited
246 evidence supports this practice. However, PRICE remains in widespread use based on moderate
247 quality evidence and expert opinion (36, 37).

248 The physiological basis underlying this approach is to reduce edema formation. Extensive
249 edema can be both painful and detrimental to mobilization and tissue healing (38, 39). Currently,
250 the PRICE protocol is considered the best initial treatment regimen for suspected soft-tissue
251 injury and fractures. An alternative strategy called the ‘movement, exercise, analgesics, and
252 treatment/therapy’ (MEAT) protocol has been proposed for managing isolated ligament and
253 tendon injury when fractures have been excluded. The MEAT protocol embraces inflammation,
254 as the inflammatory process promotes healing and quicker return to normal function. One
255 randomized trial showed that early therapeutic exercise resulted in quicker return to normal
256 function vs PRICE therapy (40). If an isolated ligament or tendon injury is highly suspected and
257 fracture is unlikely, MEAT therapy can be substituted. In an austere environment, however,
258 providers may be unable to differentiate between an acute fracture or isolated soft tissue injury,
259 and thus PRICE remains the recommended therapy for most acute musculoskeletal injuries.

260 The following treatment strategies are recommended for optimal outcomes when utilizing
261 the PRICE protocol:

- 262 1. Protection from further injury and providing additional stability with taping, bracing,
263 and/or splinting (41).
- 264 2. Relative rest will reduce inflammation and pain. If necessary for evacuation, patients can
265 ambulate.

- 266 3. Ice or snow application, when available, will decrease skin temperature below 15°C
267 which is the temperature at which nerve conduction is inhibited and pain decreases (42).
268 Lower tissue temperature also reduces edema formation (39). Cooling should be
269 performed with cycles of 10 minutes of cooling followed by 10 minutes of passive
270 rewarming, whenever practical, for the first 24 to 48 hours post-injury (43). This schedule
271 may not be logistically feasible during an evacuation. The tissues should not be cooled to
272 the degree that might result in frostbite or hypothermia (7, 44). When ice or snow is not
273 available, cold water may be substituted for cooling therapy. Evidence for cryotherapy is
274 limited, so the risks of exposing the extremity and patient to potential frostbite and
275 hypothermia must be weighed against the modest benefits of cryotherapy (37).
- 276 4. Compression with an elastic bandage or compression stocking can be used with the intent
277 to reduce swelling. Some evidence exists to support this practice, though only a small
278 number of trials have been published and results are mixed (45). The compression should
279 be form fitting while still allowing adequate muscle expansion and sufficient blood flow.
280 Capillary refill, sensation, and movement of the distal extremities should be checked
281 regularly to monitor for excessive compression.
- 282 5. Elevation of the injured area above the level of the heart will reduce potential swelling.

283
284 *Recommendation: We recommend that applicable elements of the PRICE treatment protocol*
285 *should be used for acute musculoskeletal injury as first-line pain therapy in austere*
286 *environments. Injuries in which fracture is thought unlikely should use the MEAT treatment*
287 *protocol (Strong recommendation, low-quality evidence).*

288

289 **Acetaminophen, Anti-Inflammatories, and NSAIDs.**

290

291 *Acetaminophen (paracetamol)*

292

293 Acetaminophen (APAP), also known as paracetamol, is a widely used analgesic and antipyretic
294 agent. It acts by inhibiting cyclooxygenase (COX) pathways in the CNS, enzyme pathways
295 required for the production of prostaglandins and prostacyclins (46). Both the analgesic and
296 antipyretic effects of APAP are attributed to reduction in prostaglandin production (47). More
297 recently, research suggests that APAP may also act as a cannabinoid system modulator (48). The
298 analgesic and antipyretic actions of APAP appear to be limited to the CNS, as the medication has
299 not been shown to act on peripheral COX pathways. For this reason, APAP is ineffective as an
300 anti-inflammatory (48).

301 The most common reported side effect of APAP administration, though rare, is GI
302 discomfort (49-51). The most common severe effects of APAP ingestion are seen with
303 hepatotoxicity from significant overdose. APAP has been associated with hepatocellular damage
304 and death. This is usually seen in high doses, typically a single administration >4 g/day in
305 healthy adults or in chronic use of high doses (though toxicity from a single administration <150
306 mg/kg for adults or 200 mg/kg for children is rare). Care should be taken in chronic alcoholics
307 and other patients with hepatic dysfunction, where the maximum safe daily dose of APAP may
308 not be known (50, 52, 53).

309 APAP has the advantage of being lightweight and low bulk. APAP is available in PO
310 formulations (tablets, capsules, syrup, and suspension or solution), as a rectal suppository (PR),
311 and as an IV infusion. Multiple studies have evaluated the efficacy of IV APAP against PO and

312 rectal (PR) administrations and have found clinical equipoise amongst all formulations (54, 55).
313 The analgesic activity of all formulations of APAP diminishes over 6 hours (56).

314 PO administration of APAP is generally the preferred route in most environments if the
315 patient can swallow. The IV route may be utilized with good effect, but no benefit has been
316 shown with this route over others. If the patient cannot take medications PO, PR administration
317 is likely faster, easier, and equally effective. No evidence has suggested teratogenic effects from
318 APAP use in pregnancy (57).

319
320 *Recommendation: We recommend that APAP, in any formulation or route, should be limited to a*
321 *maximum daily dose of 60 mg/kg or 4 g in four divided doses (Strong recommendation,*
322 *moderate-quality evidence).*

323
324 *Recommendation: We recommend that in the austere setting, APAP should be administered PO if*
325 *possible. If a patient cannot tolerate PO medications, we recommend rectal administration of*
326 *APAP as second line with suppository (preferred) or PO tablet given rectally (second line)*
327 *(Strong recommendation, moderate-quality evidence).*

328
329 *Non-Steroidal Anti-Inflammatories*

330 Non-steroidal anti-inflammatory drugs (NSAIDs) are a class of medications which act by
331 inhibiting COX to produce anti-inflammatory as well as antipyretic and analgesic effects (58,
332 59). They are further classified into salicylates (e.g. aspirin), propionic acids (e.g. naproxen,
333 ibuprofen), acetic acids (e.g. diclofenac, indomethacin), enolic acids (e.g. meloxicam), and
334 selective COX-2 inhibitors (e.g. celecoxib). Except for the selective COX-2 inhibitors, NSAIDS

335 are non-selective inhibitors of both COX enzymes: COX-1 and COX-2. COX-1 expression is
336 involved in renal function, platelet aggregation, and maintenance of the gastrointestinal (GI)
337 lining. COX-2 expression is generally quiescent until induced during an inflammatory response
338 (60). NSAIDs have been demonstrated to be effective analgesic agents that avoid or reduce the
339 requirement for opiate medications (61, 62).

340 NSAIDs have numerous potential adverse effects, mainly related to their non-selective
341 inhibition of COX-1 activity. While appropriately dosed short-term use of over-the-counter
342 NSAIDs has been shown to be safe and well tolerated, prolonged use and/or high doses of
343 NSAIDs may lead to gastritis and peptic ulcer disease (63-65). COX inhibition may lead to
344 diminished platelet aggregation that may be compounded by concurrent NSAID-induced gastritis
345 and/or underlying coagulopathies (66). However, multiple studies have shown that no increase
346 in postoperative bleeding occurs with short-term use of NSAIDs (67, 68). Patients with reduced
347 renal function or altered hemodynamics due to acute volume depletion or underlying disease
348 may be at risk for renal injury from renal papillary necrosis leading to further renal dysfunction,
349 electrolyte disturbances, and nephrotic or nephritic syndromes (69). While generally well-
350 tolerated in those with normal renal function, recent data suggest that ibuprofen may have a
351 nephrotoxic effect even in those with no prior renal disease (70).

352 Studies of multiple NSAIDs have suggested an analgesic ceiling at submaximal doses,
353 e.g. 400 mg PO for ibuprofen (71, 72). The question of whether an additional anti-inflammatory
354 effect is seen at higher doses is unclear. A 2015 Cochrane review could not find evidence of
355 “clinically important differences in analgesic efficacy between NSAIDs and other PO
356 analgesics”, suggesting that any additional anti-inflammatory effect for doses above the

357 analgesic ceiling has no significant effect on pain, though this is based on low- or very-low
358 quality evidence (73).

359 Ibuprofen and naproxen are the two most common PO NSAIDs used for analgesia.
360 Aspirin, though a common medication, is usually eschewed for analgesic use, particularly in
361 traumatic injury, due to its anticoagulant properties. Recommended analgesic dosing of
362 ibuprofen is 200-400 mg as needed every 6 hours PO for adults, or 5-10 mg/kg for children. In
363 short term applications, an ibuprofen dose of 1200 mg/day or less has been shown to lead to no
364 further adverse GI effects than placebo in otherwise healthy patients (74). Naproxen is also
365 administered PO and is available in either immediate and extended-release tablets or suspension
366 forms. Recommended analgesic dosing is generally a 550 mg loading dose, followed by 250 mg
367 every 12 hours PO for adults, 5 mg/kg every 12 hours for children (maximum 10 mg/kg/d).
368 Meloxicam is another PO NSAID notable for austere use in that its recommended analgesic
369 dosing for adults is 7.5-15 mg PO as needed only once daily.

370 Ketorolac is an NSAID that is available PO and in a parenteral form, given IV or IM.
371 Studies show no difference in reduction of pain scores when IM ketorolac is compared with PO
372 ibuprofen, though the IM form may be useful when PO medications cannot be administered (75,
373 76). Doses for adults are 15 mg IV or 30 mg IM every 6 hours (77).

374 Topical NSAIDs, though proven to be effective analgesics, have a limited role for
375 treatment of significant injury in the austere environments given the increased weight, bulk, and
376 limited stability of these preparations (78).

377

378 *Recommendation: We recommend NSAIDs as an effective class of analgesic agents that should*
379 *be employed as a first-line treatment for mild to severe pain in the austere environment in the*
380 *absence of contraindications (Strong recommendation, moderate-quality evidence).*

381

382 *Recommendation: We recommend that treatment strategies with NSAIDs should employ the*
383 *lowest effective dose for the shortest possible duration to minimize adverse effects (Strong*
384 *recommendation, high-quality evidence).*

385

386 *Recommendation: We recommend that NSAIDs should not be used with known renal*
387 *dysfunction, pregnancy, history of bariatric surgery, and/or history of GI bleeding (Strong*
388 *recommendation, high-quality evidence).*

389

390 *Synergistic Effects of Non-Opioid Analgesics*

391 Combinations of NSAIDs with APAP have been demonstrated to provide superior pain control to
392 either drug alone or in combination with a PO opioid. The side effects are fewer and patient
393 satisfaction is higher. These benefits have been seen in a variety of injury patterns and in
394 postoperative patients (79-81). A systematic review of 21 studies over 10 years found a
395 combination of APAP and an NSAID was superior to either drug alone (82).

396 Military applications of NSAIDs/APAP combinations have been successful (82, 83). US
397 military units give combat-deployed soldiers a ‘pill pack’ to be taken immediately after a
398 penetrating extremity wound of any type. These packs contain APAP, meloxicam, and an
399 antibiotic (84).

400 Acute traumatic pain can be treated with a combination of APAP and an NSAID
401 effectively, and in many cases, without opioids. For severe pain, the initial doses of APAP and an
402 NSAID should be simultaneous, after which the medications should be administered according
403 to their appropriate dosing intervals. As the foundation of medical therapy for pain due to acute
404 injury, these medications should be regularly administered throughout the acute injury period.

405

406 *Recommendation: We recommend that a combination of APAP/NSAID should be considered in*
407 *the treatment of moderate to severe acute pain in the austere environment (Strong*
408 *recommendation, moderate-quality evidence).*

409

410 **Opioid Analgesia**

411 If psychological first aid, PRICE therapy, and non-opioid therapy are inadequate, or pain is
412 sufficiently severe, an escalation of analgesic agents may be considered. Providing opioid
413 analgesia must be undertaken with care in the austere environment as opioid use can be
414 associated with a wide range of side effects, most concerning respiratory depression and loss of
415 airway protective reflexes. Other opioid side effects include dysphoria, euphoria, pruritus,
416 nausea, vomiting, and constipation. (85-87). Nonetheless, opioids have an established role in the
417 treatment of severe acute pain in the wilderness or austere environment (85, 88, 89). Choice of
418 opioid, route of administration, and dosage are dependent upon many factors, including scope of
419 practice, mechanism and extent of injuries, logistical issues of extraction and transport of the
420 patient, comorbidities, and presence of hypovolemic shock.

421 Respiratory depression and loss of protective airway reflexes caused by opioids should
422 always be considered when administering opioid analgesia, especially when using fast acting or

423 potent formulations. With careful titration and administration by experienced physicians and
424 other providers, these problems can usually be avoided (85, 88). Whether opioids are part of the
425 analgesic plan for an expedition, personal use, or wilderness EMS, consideration should be given
426 to management of complications, and a risk/benefit analysis must be performed in advance of
427 carrying and administering opioids. At a minimum, providers administering opioid analgesia
428 should have basic training in airway management as this is the primary means of managing
429 respiratory depression due to opioid use. Naloxone is a competitive opioid receptor antagonist
430 that is useful in temporarily reversing respiratory depression and sedation due to opioids but also
431 carries the risk of precipitating acute opioid withdrawal in chronic users. Carrying naloxone as a
432 rescue medication should be considered when more potent forms of opioid medications are in
433 use.

434

435 *Recommendation: We suggest that opioid analgesia can be an effective component of acute pain*
436 *management in austere environments; however, consideration of risk should be weighed against*
437 *the benefit of these medications (Weak recommendation, moderate-quality evidence).*

438

439 *Recommendation: We recommend that providers who administer opioid analgesics be prepared*
440 *to recognize and manage respiratory depression. Naloxone availability should be considered*
441 *when non-oral opioids are in use (Strong recommendation, low-quality evidence).*

442

443 *Oral Opioids*

444 Compared with parenteral preparations, PO formulations of opioids have the benefit of being
445 easier to carry, store, and administer. These medications carry the least concern among opioid

446 formulations for acute respiratory depression and are generally considered safe for unmonitored
447 use. However, caution should be used in opioid naïve patients, and short-acting opioids should
448 be chosen over long-acting formulations (90). Durability and ease of administration make PO
449 opioids an attractive form of analgesia for the austere environment.

450 PO opioids are often combined by manufacturers with other analgesics such as APAP to
451 provide synergistic pain relief (91). When using these combined medications, care should be
452 taken to monitor the total dose of both medications. It is preferable to separate the medications
453 when possible and carry opioid and non-opioid medications independently to allow for titration
454 of each medication. Non-opioid PO analgesics have been shown to be equally effective as or
455 non-inferior to PO opioid analgesics and opioid combination medications and they generally
456 have a better side effect profile (92-94). This knowledge should prompt a serious consideration
457 of whether PO opioid analgesia provides any additional benefit over non-opioids in an austere
458 environment. Psychological first aid, PRICE, and non-opioid medications should also be
459 employed where appropriate to reduce the requirement for opioids.

460

461 *Recommendation: We recommend that PO opioids or opioid/APAP combination drugs are*
462 *effective for the treatment of acute severe pain in austere settings. However, non-opioid PO*
463 *analgesic regimens may be preferred for their equivalent efficacy and superior safety profile*
464 *(Strong recommendation, moderate-quality evidence).*

465

466 *Intranasal, Transmucosal, Sublingual, and Transdermal Opioids*

467 Noninvasive methods of parenteral opioid administration include IN, transmucosal (TM), SL,
468 and transdermal (TD) routes. Fentanyl is the most frequently utilized opioid medication for non-

469 IV parenteral use given its relatively predictable pharmacokinetics (95, 96). PO fentanyl is
470 generally ineffective due to extensive first pass metabolism. However, IN, TM, and SL opioids
471 are not subject to this metabolism and have the advantage of providing acute pain relief without
472 the requirement for IV access. TM and SL formulations have traditionally been utilized for
473 treatment of breakthrough cancer pain with great success (97, 98).

474 Intranasal opioid administration also provides a method for acute pain relief without the
475 need for IV access. The IN route provides for rapid absorption of opioids. IN Fentanyl is most
476 widely utilized in EDs, by EMS systems, as well as in wilderness setting such as on-hill ski
477 patrol care (99-103). It has also been found to be safe for pediatric use in multiple settings (104-
478 108). IN opioids are best delivered in a volume of 0.2-0.3 ml into each nostril (109). Volumes
479 greater than 1 ml per nostril are not absorbed nasally but rather swallowed, undergoing first pass
480 metabolism. The drug dose administered should be split between the two nostrils to maximize
481 the absorptive area available and to keep volumes as low as possible. IN medications are most
482 effectively administered through use of an atomizer device (110, 111). The standard 50 ug/ml
483 concentration IV fentanyl is used for IN administration.

484 When larger doses of opioids are desired IN, the volume of fentanyl required must be
485 given as multiple doses over time to limit volumes per nostril. To overcome this volume
486 limitation and provide greater analgesia in small volume doses, the more potent fentanyl analog
487 sufentanil has been utilized. Sufentanil is nearly 100% bioavailable when given IN and at 20
488 minutes achieves equivalency with similar IV doses (112). It has been successfully and safely
489 utilized in clinic and ED settings (113, 114).

490 Oral transmucosal fentanyl citrate (OTFC) in lozenge form delivers fentanyl by TM
491 absorption. OTFC was originally developed for treatment of cancer-related pain. OTFC has been

492 used extensively by the US military and is safe when utilized in appropriate doses in a healthy
493 military population (115,116). Safe use in the military has also led to safe and effective OTFC
494 use in prehospital environments and recommendations for use in mountain rescue (18, 117).

495 Sublingual fentanyl administration has been shown to have pharmacokinetics similar to
496 IV fentanyl (118). Recently, sufentanil SL has been approved for treatment of acute pain in
497 opiate naive patients in a monitored setting, developed with support from the United States
498 Department of Defense to provide a non-IV method of battlefield pain control. The SL
499 formulation is safe, effective, and has a decreased side-effect and euphoric profile in comparison
500 to fentanyl (119). Studies of sufentanil SL use have been limited to ED- and hospital-based
501 settings, but pooled studies of 436 and 806 patients suggest that it is safe and efficacious in
502 monitored healthcare settings (120-122). There have not yet been any published studies on
503 prehospital use.

504 Transdermal opioids are designed for long term maintenance of pain control in opioid
505 tolerant individuals and have limited utility in the wilderness setting due to their slow onset of
506 action. Due to a paucity of evidence for the treatment of acute pain, transdermal opioids are not
507 recommended for use in austere environments.

508

509 *Recommendation: We recommend OTFC for safe and effective treatment of pain in austere*
510 *settings (Strong recommendation, moderate-quality evidence).*

511

512 *Recommendation: We recommend intranasal fentanyl for safe and effective pain control in*
513 *austere environments (Strong recommendation, moderate-quality evidence).*

514

515 *Recommendation: We suggest that despite limited documented prehospital use, sublingual*
516 *fentanyl and sufentanil are likely safe and effective for austere use provided that patient*
517 *monitoring is available (Weak recommendation, moderate quality evidence).*

518

519 *Intravenous, Intramuscular, and Intraosseous Opioids*

520 IV opioid administration can provide fast and effective analgesia (85, 89, 123-125).

521 However, obtaining and maintaining IV access may be difficult in austere environments as it
522 requires appropriate skills, suitable equipment, and ongoing maintenance. Environmental factors
523 such as cold or freezing temperatures may also weigh on the decision to pursue IV access.

524 IV opioids carry an increased licensing and regulatory burden and fall outside the scope
525 of practice for many austere medical providers. The availability of IV medications may be more
526 reasonable within organized wilderness EMS systems or in expedition base camps where
527 prolonged stays and delayed evacuations may occur. Consideration should be given to the
528 potential complications of parenteral opioid use and all providers administering these
529 medications should be proficient at basic airway management (87, 88, 124). Naloxone can be
530 considered as rescue medication.

531 Intraosseous access (IO) is an alternative route that is more easily established in certain
532 situations and should be considered when IV access is needed and cannot be readily obtained
533 (126). IV and IO routes have several advantages over the PO route: they provide rapid pain
534 relief and reliable drug delivery, are titratable, and may be a familiar mode of administration for
535 healthcare professionals.

536 Fentanyl has been recommended as the drug of choice for prehospital IV pain control in
537 the EMS setting (88, 125, 127). In austere or prolonged settings, a longer acting opioid might be

538 preferred. Although the invasive nature of the IV route makes it impractical for many austere
539 environments, once IV/IO access is established, these medications are still considered the gold
540 standard for control of acute, severe pain (88). The IM route avoids the need to establish IV or
541 IO access, but due to variable absorption, onset and efficacy may be inferior. IM fentanyl and
542 morphine have been compared prospectively and proven equivalent in terms of analgesia and
543 side effects when given in equipotent doses (128).

544

545 *Recommendation: We recommend that parenteral opioids be used to provide analgesia for acute*
546 *severe pain in austere environments when benefits outweigh risks and when more conservative*
547 *modalities do not provide sufficient analgesia (Strong recommendation, moderate-quality*
548 *evidence).*

549

550 **Ketamine**

551 Ketamine is a dissociative anesthetic agent which is an N-methyl-D-aspartate (NMDA)
552 antagonist suspected to block afferent effects of pain perception in the medullary reticular
553 formation, alter certain CNS transmitter systems, and suppress spinal cord activity (129). In
554 common formulation, ketamine is a 50:50 racemic mixture of *s*- and *r*-ketamine. The *s*-ketamine
555 enantiomer is a more potent analgesic agent and in sub-dissociative doses has fewer psychiatric
556 side effects than the racemic mixture, which has led to its growing use as an analgesic in some
557 countries (130). The more widely available racemic form is discussed here.

558 In lower doses, ketamine has a long history of pre-hospital use for acute pain. Ketamine
559 can be administered via several routes including IM, IV/IO, IN, PO, SL, and PR (131). Most
560 wilderness applications involve IM, IN, and IV/IO routes.

561 Ketamine is unique among pain control medications in that it has variable effects at
562 different doses, and care must be taken to remain within the range of ‘pain dose’ or ‘low dose’
563 ketamine (0.1-0.5 mg/kg IV or 1-2 mg/kg IM) (131,132). At higher doses (1-2 mg/kg IV or 3-5
564 mg/kg IM), ketamine causes dissociation, a type of moderate sedation often employed in hospital
565 use (133). Between these dosing ranges, ketamine can cause hallucinations, euphoria/dysphoria,
566 delirium, and other undesirable effects.

567 For pain control, ketamine is administered within the low dose range as above by slow IV
568 push, IV infusion, or IM injection. If repeat dosing is undertaken, care must be taken to avoid
569 rapid redosing and induction of hallucinations or sedation. Ketamine can be safely used in
570 combination with opioids to enhance pain control if multiple modalities are needed (134).

571 Ketamine is well tolerated and has been shown to be safe when administered in dissociative
572 doses by non-physician practitioners to facilitate procedures, which reinforces its safety when
573 used in pain control doses (135).

574 Ketamine has been reported to be safe, useful, and to have few associated adverse events
575 when used by physicians working in an air medical mountain rescue service (136). It has also
576 been safely used at dissociative doses for procedures at high altitude (>3900m) by primary care
577 physicians without anesthesia training. This application in 11 cases found no significant
578 complications or hypoxia associated with ketamine use (137).

579 In appropriately titrated pain doses, patients can maintain their own airway as pharyngeal
580 reflexes and spontaneous ventilation are usually preserved. However, salivation is often
581 increased, and airway obstruction has been reported with dissociative doses (138). Unlike many
582 anesthetic and analgesic agents, cardiovascular function is often well preserved in the setting of

583 ketamine administration. This makes ketamine a suitable choice for trauma patients if
584 hemorrhagic shock is suspected (139).

585
586 *Recommendation: We recommend ketamine for the control of acute severe pain in the austere*
587 *setting using pain-control doses (0.1-0.5mg/kg IV, 1-2mg/kg IM). Providers should be*
588 *experienced in using the medication and equipped to manage airway complications should they*
589 *arise (Strong recommendation, moderate-quality evidence).*

590

591 **Local Anesthetics**

592 Local anesthetic (LA) agents act by prolonging deactivation of voltage-gated sodium channels.
593 When acting on peripheral neurons, they reduce or reversibly block neuronal transmission,
594 leading to local analgesia or anesthesia. However, when absorbed systemically, these
595 medications can cause severe adverse effects by acting on sodium channels in the myocardium or
596 CNS, such as cardiac arrest and seizure. Attention must thus be given to weight-based maximum
597 doses to avoid toxicity (e.g. lidocaine 4-5 mg/kg, maximum 300 mg/dose and 2400 mg/day), and
598 care must be taken to avoid intravascular or intraneural injection.

599 Worldwide, the most used LAs are lidocaine (lignocaine) and bupivacaine, although there
600 are many variations and preparations within the category. The onset, duration of action, and
601 density of the local analgesia or anesthesia produced by LAs depend upon multiple medication
602 factors including the lipid solubility, dissociation constant, concentration, and total dose.

603 Typically, agents with more-rapid onset tend to have shorter duration of action, whereas longer-
604 acting drugs carry higher risks of toxicity (140).

605 LAs can be applied topically to the skin or mucous membranes, injected directly into
606 peripheral tissues, or adjacent to regional nerves or even the spinal cord to produce regional or
607 neuraxial analgesia or anesthesia.

608

609 *Topical Local Anesthesia*

610 Topical anesthetic agents are directly applied on or around peripheral sites of nociception in gel,
611 liquid, ointment, or cream form, blocking noxious stimuli at their source (141-144).
612 Administration is simple, and the low systemic absorption reduces the risk of side effects (145).

613 There are many available formulations of anesthetics for topical use including
614 combination products and viscous formulations to facilitate easy application (e.g.
615 lidocaine/epinephrine/tetracaine (LET) and the eutectic mixture of lidocaine/prilocaine (EMLA).
616 The efficacy and safety of these formulations has been demonstrated for treatment of wounds
617 and stings and for the facilitation of laceration repairs (146, 147). The efficacy of these
618 formulations outside of recommended storage temperatures of 0-30° C has not been studied and
619 may limit their use in some austere environments.

620

621 *Recommendation: We recommend locally instilled and topically applied local anesthetic agents*
622 *for safe and effective treatment of pain related to burns, stings, and soft tissue injuries in austere*
623 *environments (Strong recommendation, moderate-quality evidence).*

624

625 *Ophthalmic/Otic Solutions*

626 Ophthalmic and otic solutions of topical anesthetics are useful in the treatment of conditions
627 including corneal abrasions or ulcerations, ultraviolet keratitis, otitis media, and otitis externa

628 (148, 149). These preparations differ from plain aqueous solutions of LAs in that they often
629 contain preservatives, buffers, viscosity agents, and other additives to make them more effective
630 and tolerable at the target site (150). Lacking alternatives, an aqueous solution of lidocaine, as
631 used for local infiltration, can be used in topical ocular application. However, the lack of pH
632 buffering reduces penetration into the tear film and causes significant discomfort on instillation,
633 reducing efficacy and tolerability (151). Ophthalmic and otic solutions are generally similar in
634 composition, though ophthalmic solutions are sterile and free of particulate matter, so ophthalmic
635 solutions may be instilled in the ear, but otic solutions should not be used in the eye. Otic
636 solutions are generally less expensive (152).

637 Ophthalmic solutions can be of great use in the care of a patient who has become
638 debilitated by a corneal abrasion or keratitis, as analgesia can facilitate eye opening and allow the
639 patient to participate in their evacuation. Concerns over delayed corneal healing have led many
640 providers to withhold repeated use in the setting of corneal injury (153). However, a meta-
641 analysis pooling two randomized, prospective studies in the emergency department showed no
642 clinically significant adverse effects in the repeated use of ophthalmic proparacaine for less than
643 72 hours (154). Accordingly, it is reasonable to use a short course of ophthalmic anesthetics to
644 aid in the evacuation of otherwise debilitated patients. Due to reduced capacity for self-
645 monitoring, care should be taken to protect an anesthetized eye from insults, including dryness,
646 exposure to foreign bodies, or to UV radiation (155).

647

648 *Recommendation: We suggest that ophthalmic anesthetic solutions are, when used*
649 *appropriately, safe, and useful for the treatment of acute ocular and auricular pain in austere*
650 *environments (Strong recommendation, low-quality evidence).*

651

652 *Regional Analgesia*

653 Regional analgesia employs LA injection near and about nerves or nerve plexi to achieve broad
654 areas of analgesia and anesthesia. The use of regional analgesia/anesthesia in the austere
655 environment has the potential to meet many goals of austere pain management, such as avoiding
656 sedation, respiratory depression, cardiovascular instability and other unwanted side-effects
657 (156,157). Regional anesthesia also uses a limited amount of compact equipment to provide
658 rapid and predictable onset of excellent pain control. However, such approaches require
659 additional equipment, pharmacological agents, training, and experience. Selection of patient,
660 setting, and technique must thus be carefully considered (157). Neuraxial (intrathecal/spinal and
661 epidural) injections are unlikely to be suited to austere conditions outside of specific
662 circumstances, and thus fall beyond the scope of these guidelines.

663

664 *Field-expedient regional blocks*

665 In contrast to neuraxial techniques, regional anesthesia and analgesia can be achieved in many
666 settings with minimal equipment and limited training while still retaining an acceptable margin
667 of safety. Well-executed nerve blocks can provide excellent and long-lasting analgesia, or full
668 anesthesia of a limb or region to allow interventions and even mobilization and self-rescue.
669 However, these advantages must be balanced with safety; nerve blocks may also hamper self-
670 rescue or render a limb unusable for hours.

671 The concept of field-expedient regional blocks (FERBs) refers to nerve block techniques
672 which:

- 673 • Have consistent approaches using reliable anatomical landmarks;

- 674 • Can be performed reliably with a predictable distribution of effect;
- 675 • Avoid structures which carry high risk or consequences of injury (e.g. pleura or major
- 676 vessels);
- 677 • Have a low risk of unwanted effects (e.g. phrenic nerve block and diaphragmatic paralysis
- 678 which frequently accompanies interscalene brachial plexus block);
- 679 • Require drug volumes which are well within the maximum safe dose of the selected LA;
- 680 • Tend towards slower drug absorption, reducing the risk of systemic toxicity;
- 681 • Are easily learned and can be practiced by austere medicine practitioners working in a
- 682 variety of settings to become proficient before using them in the field;
- 683 • Do not require highly specialized equipment (158).

684 While a full discussion of suitable FERBs is beyond the scope of these guidelines,
685 examples of the concept include certain orbital, dental and occipital blocks in the head and neck,
686 coracoid, wrist, and interdigital blocks in the upper limb, the fascia iliaca plane block, popliteal,
687 peroneal, ankle, and intermetatarsal blocks in the lower limb, and ring blockade of any digit
688 (159-164).

689 Ultrasound has become the standard of care in-hospital for many regional blocks and is
690 mandatory for some techniques. It allows visualization of tissue planes, nerves, blood vessels and
691 other structures with minimal discomfort, and has many other uses in austere medicine (156).
692 However, ultrasound requires additional training and practice to be used effectively for regional
693 blocks, which should be obtained in a controlled setting.

694 Practitioners should know the potential risks and complications of regional nerve blocks
695 and seek patient consent wherever possible before performing a block. Knowledge of the signs,
696 symptoms, and management of local anesthetic systemic toxicity (LAST) is essential. IV access

697 should be obtained before all but the most simple blocks to facilitate treatment of complications
698 as needed, and equipment and drugs for resuscitation should always be available before
699 commencing a regional block (165). These techniques are therefore limited to well-equipped and
700 trained rescue teams and responders.

701

702 *Recommendation: We suggest that when performed by experienced practitioners with necessary*
703 *administration and monitoring equipment, field-expedient regional nerve blocks may be an*
704 *effective tool to manage pain and facilitate procedures in an austere environment. (Weak*
705 *recommendation, low-quality evidence).*

706

707 *Recommendation: We recommend that portable ultrasound be used for FERBs in austere*
708 *environments when appropriate equipment and skills are available (Strong recommendation,*
709 *moderate quality evidence).*

710

711 *Care of patients with nerve blocks in the field*

712 Local and regional analgesia may facilitate (but should not delay) life- and limb-saving
713 interventions. Well-executed regional analgesia may improve a patient's ability to communicate
714 or partake in self-care and self-rescue activities, but it does not negate the responsibility to
715 perform ongoing monitoring and assessment. Care should be given to assessing for symptoms
716 and signs of LAST and to the care of the region under analgesia/anesthesia to prevent further
717 injury. Patients with well-executed blocks may not be able to feel pressure points, control an
718 anesthetized limb, or perceive inadequate perfusion from compartment syndrome, dressings, or
719 immobilization measures which are too restrictive.

720

721 *Recommendations: We recommend immobilization with adequate padding, pressure care, and*
722 *frequent assessments for perfusion and absence of clinical signs of compartment syndrome as*
723 *necessary for patients who have received regional blocks in austere environments (Strong*
724 *recommendation, low-quality evidence).*

725

726 *Hematoma blocks*

727 In contrast to all other modern regional analgesia techniques, a hematoma block aims to
728 deliberately aspirate blood by advancing a 20G needle directly into the hematoma surrounding a
729 fracture using sterile technique. It is nearly exclusively used for reduction of distal radius/ulna
730 fractures, although its use has also been described for fractures of the tibia (166, 167). As
731 fracture hematomas can be considered contiguous with the bone marrow space, absorption of
732 LAs via hematoma could theoretically be as rapid as IO drug administration (168). For this
733 reason, only lidocaine is used for this block, at a maximum dose of 1.5-2 mg/kg. For most adult
734 patients, a volume of 5-10 ml of 1% lidocaine solution is safe and effective (169, 170).

735

736 *Recommendations: We suggest that hematoma blocks with plain lidocaine can be performed by*
737 *suitably experienced practitioners in austere environments (Weak recommendation, moderate*
738 *quality evidence).*

739

740 *Field infiltration of local anesthetics*

741 Although not a true regional block, infiltration of LAs around the margins of a wound or in an
742 injured region is an effective means of providing analgesia and can extend to procedural

743 locoregional anesthesia. In this setting, there is little advantage to using concentrated LA, and
744 dilutions of 0.5 to 1% lidocaine and as little as 0.1% of long-acting agents can be effective. Use
745 of a narrow-gauge needle and injection with smooth continuous withdrawal reduces the risk of
746 intravascular injection. Caution should still be employed in calculating the maximum safe dose;
747 particularly when providing repeated injections within a limited timeframe.

748

749 *Recommendations: We recommend field infiltration of dilute LA for safe management of acute*
750 *pain due to soft tissue wounds in austere environments (Strong recommendation, moderate-*
751 *quality evidence).*

752

753 *Infiltration of diphenhydramine*

754 Diphenhydramine (DPH) is an antihistamine that is an inverse agonist at the H1 receptor. It is
755 usually employed in the treatment of allergy or anaphylaxis and may be carried as a component
756 of austere medical kits for this reason. While PO formulations of DPH are limited to these
757 traditional indications, a 1% aqueous DPH formulation diluted from the 5% typical for IV use is
758 also useful as a LA, particularly in those patients with allergies to typical LAs such as lidocaine.
759 Local injection of 1% DPH achieves adequate analgesia for wound care within 5 minutes in 80%
760 of patients (171-173). In comparison to lidocaine, the injection of DPH is more painful, the
761 analgesic effect slightly less than that of lidocaine but adequate for suturing and wound care, and
762 DPH analgesia has shorter duration than that of lidocaine (174, 175). DHP infiltration can cause
763 dose-dependent mild sedation, and this should be taken into account if the patient is expected to
764 ambulate or participate in self-rescue (171). The potential adverse effects of intraarterial
765 injection DPH are minimal, particularly in comparison to lidocaine. Local DPH infiltration can,

766 rarely, cause skin irritation (171, 175). To date, DPH has not been studied for use in nerve,
767 regional, and hematoma blocks.

768
769 *Recommendation: We recommend aqueous DPH solution as safe and effective for local*
770 *infiltration and wound care as an alternative to lidocaine in the austere environment when*
771 *lidocaine is not available, or allergy limits its use. Consideration should be given to its sedating*
772 *effects (Strong recommendation, moderate-quality evidence).*

773
774 *Intravenous Lidocaine*

775 IV lidocaine use as an infusion for the treatment of pain has been widely reported in hospital-
776 based applications and has shown equivalent effect relative to opioids in some applications, as
777 well as opioid sparing effects (176, 177). However, anesthesia guidelines describe the use of IV
778 lidocaine as “high risk” even in the hospital setting due to its narrow therapeutic window (178).
779 In hospital application, access to lipid emulsion therapy is considered necessary to treat possible
780 overdose. In a systematic review of its use in hospital application, of 289 patients treated with IV
781 lidocaine, 44 adverse events were reported of which 36 (12.4%) were ‘serious’, including altered
782 mental status and cardiac dysrhythmias (177). Meta-analysis of its use in the emergency
783 department yielded similar adverse event rates but showed equivocal performance in comparison
784 to opioids (176)

785 A case report is available describing two patients treated with IV lidocaine in an austere
786 setting. Both patients experienced improved pain, however, both patients were treated without
787 the availability of lipid emulsion and both experienced prodromal symptoms of LAST (179).
788 This highlights the hazard of employing this method without hospital-level resources. Because of

789 the degree of monitoring and resuscitation equipment required, and given the very poor
790 therapeutic index of this method, IV use of LAs is not recommended.

791

792 *Recommendation: We recommend that IV lidocaine should not be used in the austere*
793 *environment (Strong recommendation, low-quality evidence).*

794

795 **Inhalational Analgesics**

796 Inhalational analgesia is provided by breathing specific gases or volatile agents which induce
797 analgesic effects after absorption in the lung. This should be distinguished from topical/TM
798 administration of agents using atomization or nebulization.

799 Inhalational analgesia is characterized by rapid on- and offset, ease of administration,
800 lack of immediate requirement of IV access, and comparable efficacy to other systemic
801 agents. Currently, there are only two inhalational analgesics in clinical use: nitrous oxide (a
802 gas), and methoxyflurane (a vapor). Both require specific equipment and methods to administer
803 and are discussed further below.

804

805 *Nitrous Oxide*

806 Nitrous oxide (N₂O) is a non-flammable, colorless gas with a slightly sweet scent which has
807 euphoric and dissociative anesthetic properties at high partial pressures, and significant analgesia
808 at lower doses. N₂O is typically self-administered by breathing through a demand-valve and
809 mouthpiece that is held between the teeth, or directly through an anesthetic face mask. Onset of
810 action is rapid, within several breaths; clinically significant analgesia occurs within 5 minutes
811 (180). While the precise mechanism of action is not fully understood, anesthetic effects are likely

812 through non-competitive central NMDA-receptor antagonism, while analgesic effects are
813 mediated by endogenous opioid release in the midbrain (181). It is commonly used as a
814 synergistic agent during induction and maintenance of general anesthesia but has also been
815 extensively administered in combination with oxygen (O₂) as an analgesic for painful conditions
816 and procedures such as labor and delivery or dental work. Outside of the operating theater, it is
817 most commonly available in an equal, preblended (50%) mixture with oxygen, known as
818 Entonox. N₂O can also be mixed with a separate supply of pure O₂ using a blender, though this is
819 more cumbersome for prehospital use. N₂O has been used with considerable success as an
820 analgesic in pre-hospital care for many years (180, 182).

821 Patient-administered N₂O analgesia has been shown to have a low rate of adverse events
822 and sedation, in both children and adults (183, 184). The most-common side effects, such as
823 nausea, dizziness, and mild sedation, are normally short lived. At analgesic doses, it exhibits
824 cardiovascular stability and no respiratory depression and can provide analgesia on par with
825 systemic opiate administration (181, 185-187). The rapid diffusion of N₂O can lead to
826 accumulation in gas-filled spaces within the body, and it should be used cautiously in head and
827 chest trauma victims so as not to worsen pneumothorax or pneumocephalus, and its use is
828 contraindicated in recently-ascended divers (188).

829 Three important limitations for the use of N₂O in the austere setting exist. First, it is
830 stored in bulky, heavy, pressurized cylinders (e.g. Entonox), which require the use of regulators
831 and a demand valve, making transport and storage challenging.

832 Second, the nature of the pressurized gas mixture reduces the range of ambient
833 temperatures in which it can be used. Direct sunlight and hot temperatures can risk cylinder
834 rupture due to overpressure, and subzero (below -5.5°C) temperatures will cause the N₂O to

835 liquify. Initially, this can result in the inhalation of oxygen with limited N₂O in unpredictable
836 concentrations. However, as the cylinder empties, an increasing concentration of N₂O is
837 delivered, and the mixture becomes dangerously hypoxic (213). Accordingly, N₂O/O₂ mixtures
838 must be administered with care at below-freezing temperatures.

839 Third, N₂O is delivered as a gas, and increasing altitude will cause a corresponding
840 decrease in the inhaled partial pressure of gases. This in turn decreases the analgesic effect of
841 N₂O at altitude (189). Thus, while it is a useful agent at sea level, the value of N₂O is greatly
842 decreased at high altitude (190-192). Additionally, N₂O can accumulate in small and poorly
843 ventilated spaces, so adequate ventilation should be assured to prevent unintentional inhalation
844 among bystanders.

845 These restrictions on the portability of the agent and use under adverse conditions has
846 discouraged austere use. Although N₂O has been employed among ski patrols in Canada,
847 Australia, and the United States, its use on the ski hill, including efficacy and safety, has not
848 been reported (193).

849
850 *Recommendation: We suggest N₂O as a safe and effective analgesic in austere environments for*
851 *short painful procedures or for limited periods of time. Although evidence pertinent to austere*
852 *use is limited, it can be safely used at low altitude, with appropriate monitoring, and where*
853 *appropriate storage of cylinders can be assured (Weak recommendation, low-quality evidence).*

854
855 *Methoxyflurane*

856 Methoxyflurane is a halogenated volatile anesthetic with analgesic properties (194). Its
857 mechanism of action is not well understood, but it is a known GABA receptor agonist and

858 reduces gap junction function in the brain. Although it is no longer used for anesthesia, it has
859 been widely used as an analgesic in Australia and New Zealand by paramedic, military and
860 civilian first aid providers for over 30 years (195).

861 Methoxyflurane is self-administered by inhalation through a hand-held whistle-like
862 device which functions as a simple, disposable draw-over vaporizer. Onset of analgesia is rapid
863 (within 5 minutes) and continues while the patient breathes through the device (196). When used
864 continuously, a single dose (3 ml) lasts for approximately 25-30 minutes (197). Its effects are
865 rapidly reversed once inhalation stops.

866 Changes in cardiovascular, respiratory and neurological function during methoxyflurane
867 administration are not clinically significant and therefore IV access is not essential (196, 198).
868 The most common side effects are dizziness, headache and feeling somnolent (197, 199). Serious
869 adverse effects are rare, but methoxyflurane is contraindicated in patients with renal or hepatic
870 impairment as well as those who have a personal or family history of malignant hyperthermia
871 (101, 199).

872 Concerns have been raised as to whether methoxyflurane will suffer the same decrease in
873 efficacy at altitude which is experienced with N_2O (200). However, as saturated vapor pressure is
874 not influenced by ambient pressure, altitude should not affect the partial pressure delivered by
875 the device, a theory which has been borne out in initial laboratory work (189, 201). Questions
876 which remain to be studied are the effect of low ambient temperatures on device performance
877 and whether environmental factors influence clinical efficacy of methoxyflurane in the
878 field. Efficacy for analgo-sedation at high altitude (4470 m) appears to be preserved in one case
879 study (202).

880 Methoxyflurane has been shown to have more rapid onset and comparable or better initial
881 analgesia compared to IV opiates or APAP (203-206). In addition, its portability, stability, and
882 ease of administration make it highly suitable for use in austere settings (101, 207, 208). The
883 rapid onset of action and limited side effect profile make methoxyflurane useful as a temporizing
884 measure until other modalities can be established or as a definitive short-term analgesic (195,
885 209).

886

887 *Recommendation: We recommend methoxyflurane as safe and effective to treat pain in sub-*
888 *anesthetic doses in austere environments (Strong recommendation, moderate-quality evidence).*

889

890 **Adjuncts**

891 *Benzodiazepines*

892 Benzodiazepines (BZDs), which have long been used in the treatment of anxiety, have
893 previously been recommended as a possible analgesic adjunct (15). This was rational because, as
894 previously discussed, there is a correlation between anxiety states and increased perception of
895 acute pain. However, no quality evidence has emerged to support the administration of BZDs for
896 analgesia.

897 BZDs act centrally on GABA-A receptors, resulting in CNS depression (210).

898 Additionally, the combination of BZDs with other CNS depressants can potentiate their
899 concerning adverse effects. The combination of BZDs with opioids has been well-studied and
900 has the potential to induce significant respiratory depression (211-213).

901

902 *Recommendation: We recommend that BZDs should not be used for the treatment of pain in*
903 *austere settings (Strong recommendation, high-quality evidence).*

904

905

906 *Further Modalities and Adjuncts*

907 A variety of additional medication classes and techniques have been studied as adjuncts for pain
908 in both the hospital an outpatient environment. These include antihistamines, battlefield
909 acupuncture, antipsychotics, non-BZD muscle relaxants, capsaicin, and antidepressant
910 medications. While there is heterogenous but generally supportive evidence for the use of these
911 medications in the long-term treatment of chronic pain, there is inadequate evidence to support
912 their use for the treatment of acute pain in the austere environment, and austere use cannot be
913 recommended.

914

915 **Conclusion**

916 In all cases, the comfort of the patient must be balanced with the risk of any tools used to address
917 pain. In comparison to hospital-based or EMS medicine, evidence for pain control modalities
918 specific to the austere environment is generally limited. Accordingly, the experience of the
919 responder, consideration for available resources, and clinical judgment are of paramount
920 importance in the selection of pain control modalities appropriate to the patient and the setting.
921 Some interventions may enable the patient to participate in their own rescue while others may
922 generate unacceptable risk to the patient or team. Backcountry recreationalists, expedition
923 leaders, and professional rescuers alike should consider the resources, hazards, and limitations
924 specific to their unique settings and should both plan for appropriate modalities to manage acute

925 pain, and for the training, monitors, equipment, and antidotes needed to manage the risks of
926 those interventions. The paucity of austere-specific research also opens numerous opportunities
927 for further study.

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932

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936 Drafting of the manuscript: (PF, AW, WS, GBZ, JL, SM, CVT, IW, JW, RH, DW)

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945

946

947 *Table 1: The ABCDE mnemonic for the psychosocial treatment of pain.*

A	Anchoring, Attention & Acknowledgement	Provide the patient with an attentive provider who identifies themselves as responsible for their comfort and who acknowledges their distress.
B	Breathing	Encourage controlled breathing depth and rate, limiting rapid, shallow breathing or hyperventilation.
C	Control and Cognitive Shift	Provide the patient with a role that allows an element of control over their situation, and which shifts their mindset away from catastrophizing.
D	Decrease nociception, Distract, Diffuse.	Use other pharmacological/nonpharmacological interventions to treat nociceptive signals. Distract the patient from the source of pain. Diffuse tension using empathy and humor.

E	Explanations and Expectations	Provide the patient with an understanding of what to expect in novel situations, such as technical rescue or vehicle/helicopter transport. Explain procedures to be performed, personnel involved, timelines to be expected, etc.
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948

949 **Figure Legends**

950 Figure 1: Conceptual schematic of escalating pain treatment stratified by risk posed to the patient
951 and the need for monitoring when used. With greater anticipated or reported pain severity, a
952 clinician may elect to use one or more modalities appropriate to that degree of severity. IV,
953 intravenous; IM, intramuscular; IN, intranasal; NSAID, non-steroidal anti-inflammatory drug.

954

955 Table 1: The ABCDE mnemonic for the psychosocial treatment of pain: Suggested mnemonic
956 for the field application of psychological first aid to reduce acute pain.

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