Practice Management Guidelines for Analgesia in the Non-Intubated Patient

I. **Rationale:** Multimodal analgesia (MMA) regimens are defined as the use of a variety of medications to target different physiologic mechanisms of action in either the central and/or peripheral nervous system to effect pain relief. [1] MMA has been shown through randomized trials to result in overall better pain relief with less opioid consumption compared to single modality pain regimens. [2,3] MMA includes, but is not limited to, usage of acetaminophen, non-steroidal anti-inflammatory drugs, muscle relaxants, narcotics, and gabapentinoids. Locoregional and neuraxial blockade can also serve as important adjuncts in MMA regimens.

II. **Algorithm**

- **Patient with Acute Pain and NO Enteral Access**

- **Patient with preexisting opiate use and/or risk factors for difficult analgesic control?**
  - Chronic opiate use
  - Active opioid use disorder
  - Suboxone or methadone use
  - Chronic pain/fibromyalgia
  - Pain refractory to measures outlined within this PMG
  - Meets APS consult criteria per Rib fracture & APS Guidelines PMG

  - **YES** Consider Acute Pain Service consultation

- **NPO Multimodal Regimen:**
  - PRN hydromorphone if patient unable to manage PCA
  - Scheduled acetaminophen PR
  - Scheduled ketorolac IV (if no contraindications)
  - Scheduled or PRN methocarbamol IV (if having muscle spasms)
  - Lidocaine patch if complaining of localized pain

- **Considerations for PCA use**
  - NPO or not tolerating PO meds?
  - Patient alert?
  - Able to manage/understand PCA use?

  - **YES**

- **Hydromorphone PCA prescribing recommendations**
  - NO BASAL RATE
  - Starting Demand: 0.2mg
  - Starting Demand Rate: Q15 minutes
  - May modify dose in very low or high body weights
  - Reassess need daily or when transitioning to PO

  - **NO**

If pain refractory to conventional measures listed above, then consider Acute Pain Service consultation for:
  - Regional anesthesia
  - Ketamine and/or lidocaine infusions
Patient with Acute Pain AND Enteral Access

Patient with preexisting opiate use and/or risk factors for difficult analgesic control?
- Chronic opiate use
- Active opioid use disorder
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- Chronic pain/fibromyalgia
- Pain refractory to measures outlined within this PMG
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**Initiate multimodal pain regimen:**
- Scheduled APAP
- Scheduled NSAID *(if no contraindications)*
- Oxycodone PO 2.5-10mg q4h prn
- Hydromorphone IV 0.25-1mg q4h prn *(minimize duration)*

Pain adequately controlled?

**YES**
- Continue current analgesic regimen *(decrease dose and extend dosing interval as able)*

**NO** *(e.g. Requiring large amounts of breakthrough hydromorphone)*
- Add scheduled muscle relaxer
- Add scheduled gabapentin *(if complaining of neuropathic pain)*
- Add lidocaine patch *(if localized pain)*

If pain refractory to conventional measures listed above, then consider Acute Pain Service consultation for:
- Regional anesthesia
- Ketamine and/or lidocaine infusions
- Off-label agents *(e.g. memantine, SNRIs, TCAs)*
III. Literature Review

a. Nonsteroidal anti-inflammatory drugs (NSAIDs)
High level evidence supports the use of NSAIDs in MMA as it reduces opioid requirements, improves overall analgesia, and may reduce length of stay. [1] NSAIDs may work synergistically with acetaminophen and opioids by working through differing mechanisms of action. Multiple studies suggest that route of administration (i.e. intravenous versus oral) likely produces no analgesic difference, though I.V. administration likely leads to faster onset of effect. [1]. Risks for prolonged NSAID use include increase risk of gastrointestinal bleeding, cardiovascular events, and renal dysfunction, all of which needs to be taken into consideration when using routinely. [4] Animal models suggest possible effects on bone healing via inhibition of prostaglandins, but no high-level evidence exists to support this in humans and a meta-analysis found no link between NSAID use and bone nonunion. [5]

b. Gabapentinoids
The use of preoperative gabapentinoids has been shown to decrease narcotic requirement, pain scores, and narcotic-related side effects. [6] However, data supporting their effectiveness as part of a postoperative MMA regimen are limited. One RCT comparing gabapentin and placebo for 72 hours postoperatively in a mixed surgical population found no difference in postoperative pain resolution but a 24% increase opioid cessation rates in the gabapentin arm. [7] No benefit, though, was seen with scheduled postoperative gabapentin in patients undergoing total knee arthroplasty, total hip arthroplasty, thoracotomy, and shoulder arthroscopy [8-11] Studies of gabapentin use specifically in trauma patients have been limited to rib fractures, blunt thoracic trauma, spinal cord injury, and amputations. Gabapentin did not decrease pain scores or opioid requirements in patients with multiple rib fractures. [12] In thoracic surgery and chest wall trauma patients with persistent chest wall pain (≥4 weeks post initial operation or trauma), 73% reported a reduction in pain after a mean gabapentin duration of 22 weeks. [13] In patients with spinal cord injury, gabapentinoids significantly decreased neuropathic pain.[14] RCTs have shown conflicting data regarding gabapentin for phantom limb pain in patients who underwent an amputation. [15-16] Until further studies can verify the role of gabapentinoids in MMA regimens, these agents should be reserved for patients experiencing neuropathic pain given their ability to cause dizziness and somnolence. Avoid or use reduced doses in the elderly and in patients with renal dysfunction.

c. Muscle Relaxers
High quality studies describing the effectiveness of antispasmodics (i.e. cyclobenzaprine, methocarbamol, tizanidine, metaxalone) are lacking. A systematic review by Chou et al. described the benefit seen with cyclobenzaprine compared to placebo in patients with back pain and muscle spasms secondary to trauma, musculoskeletal strain, radiculopathy, and osteoarthritis. [17] In head-to-head trials of antispasmodics, no differences in outcomes were seen. Since that systematic review a RCT comparing the addition of baclofen, tizanidine, methocarbamol, or metaxalone to ibuprofen or naproxen for acute lower back pain showed no improvement in function or pain compared to the NSAID alone. [18-19] In patients undergoing inguinal hernia repair, the addition of tizanidine to acetaminophen and an NSAID significantly lowered pain scores and analgesic consumption compared to placebo. [20] In a heterogeneous trauma population, methocarbamol did not improve pain control. [21] However, its use was associated with decreased hospital length of stay in patients with rib fractures. [22] Thus, muscle relaxants may be beneficial in specific injury patterns, surgeries, or in patients complaining of debilitating muscle spasms but should not be a part of the initial MMA regimen for all trauma patients. Short-term courses (~14 days) were used in the majority of studies. Therefore, the risk versus benefit of muscle relaxants for extended courses is unknown. Side effects of these agents are well documented with dizziness and drowsiness being the most common. Tizanidine is an alpha-2 agonist and can cause significant hypotension. These medications should be used with caution in the geriatric population as they have shown to increase the risk of injury in these patients. [23]

IV. Dosing and Clinical Pearls
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug Name</th>
<th>Dosing</th>
<th>Clinical Pearl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Acetaminophen</td>
<td>PO: 1000mg q8h</td>
<td>• Do not exceed 3g/d</td>
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<td></td>
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<td>• Reduce to 2g/day in liver dysfunction</td>
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<td></td>
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<td></td>
<td>• Consider all sources of APAP</td>
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<tr>
<td>NSAIDS</td>
<td>Celecoxib</td>
<td>PO: 100-200mg BID</td>
<td>• Prolonged use predisposes to GI, cardiovascular, and renal dysfunction</td>
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<tr>
<td></td>
<td>Ibuprofen</td>
<td>PO: 400-800mg q8-6h</td>
<td>• Ketorolac: minimal benefit &gt;10-15mg/dose</td>
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<tr>
<td></td>
<td>Ketoroloc</td>
<td>IV: 10mg q6h</td>
<td>• Celecoxib: reduced GI side effects; best choice for patients at high risk for</td>
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<tr>
<td></td>
<td></td>
<td>q6h Limit to 5 days</td>
<td>GI bleed; avoid in patients with significant cardiac comorbidities</td>
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<tr>
<td></td>
<td>Naproxen</td>
<td>PO: 500mg BID</td>
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<tr>
<td>Anesthetic</td>
<td>Lidocaine 5% patch</td>
<td>1 patch daily</td>
<td>• Leave on for 12h and then remove</td>
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<td></td>
<td></td>
<td></td>
<td>• Can cut patch</td>
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<tr>
<td>Muscle Relaxants</td>
<td>Cyclobenzaprine</td>
<td>PO: 5-10mg TID</td>
<td>• Caution in age ≥65 (reduce dose or avoid)</td>
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<tr>
<td>(Antispasmodics)</td>
<td>Methocarbamol</td>
<td>PO: 500-1000mg TID</td>
<td>• Causes dizziness, somnolence</td>
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<td></td>
<td>Tizanidine</td>
<td>PO: 2mg TID to maximum dose of 36mg/day</td>
<td>• Tizanidine: preferred muscle relaxer in elderly; causes hypotension</td>
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<td></td>
<td></td>
<td></td>
<td>• Consider limiting to 14 day duration</td>
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<tr>
<td>Gabapentinoids</td>
<td>Gabapentin</td>
<td>PO: 300-3600mg/day</td>
<td>• For neuropathic pain ONLY</td>
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<td></td>
<td></td>
<td></td>
<td>• May cause dizziness and drowsiness</td>
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<td>Pregabalin</td>
<td>PO: 75-300mg/day</td>
<td>• Reduce dose or avoid in renal dysfunction or age ≥65</td>
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<tr>
<td>NMDA Antagonist</td>
<td>Memantine</td>
<td>PO: 5-10mg BID</td>
<td>• 90% bioavailability vs gabapentin</td>
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<td>• Restricted use: ONLY if resuming home pregabalin or failed gabapentin</td>
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<td></td>
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<td>(requiring &gt;2700mg/d)</td>
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<td>Tricyclic Antidepressants</td>
<td>Amitriptyline</td>
<td>PO: 10-25mg daily up to 150mg/day daily or in</td>
<td>• Anticholinergic side effects</td>
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<td></td>
<td></td>
<td>2 divided doses</td>
<td>• Use caution when combining with other serotoninergic and noradrenergic</td>
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<td></td>
<td>Desipramine</td>
<td>PO: 12.5mg once daily up to maximum dose of</td>
<td>medications</td>
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<td></td>
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<td>250mg/day</td>
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<td>Serotonin-norepinephrine</td>
<td>Duloxetine</td>
<td>PO: 30mg daily x 1 week then 60mg daily</td>
<td>• Better tolerated than TCAs</td>
</tr>
<tr>
<td>Reuptake Inhibitors</td>
<td>Extended Release</td>
<td></td>
<td>• Use caution when combining with other serotoninergic and noradrenergic</td>
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<td></td>
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<td>PO: 37.5-75mg daily, increase by 75mg/wk</td>
<td>medications</td>
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<td>(max 225mg/d)</td>
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V. References

6. Kok-Yuen Ho, Tong J Gan, Ashraf S. Habib; Gabapentin and postoperative pain – a systematic review of randomized controlled trials; *Pain* 2006, 126: 91-101

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