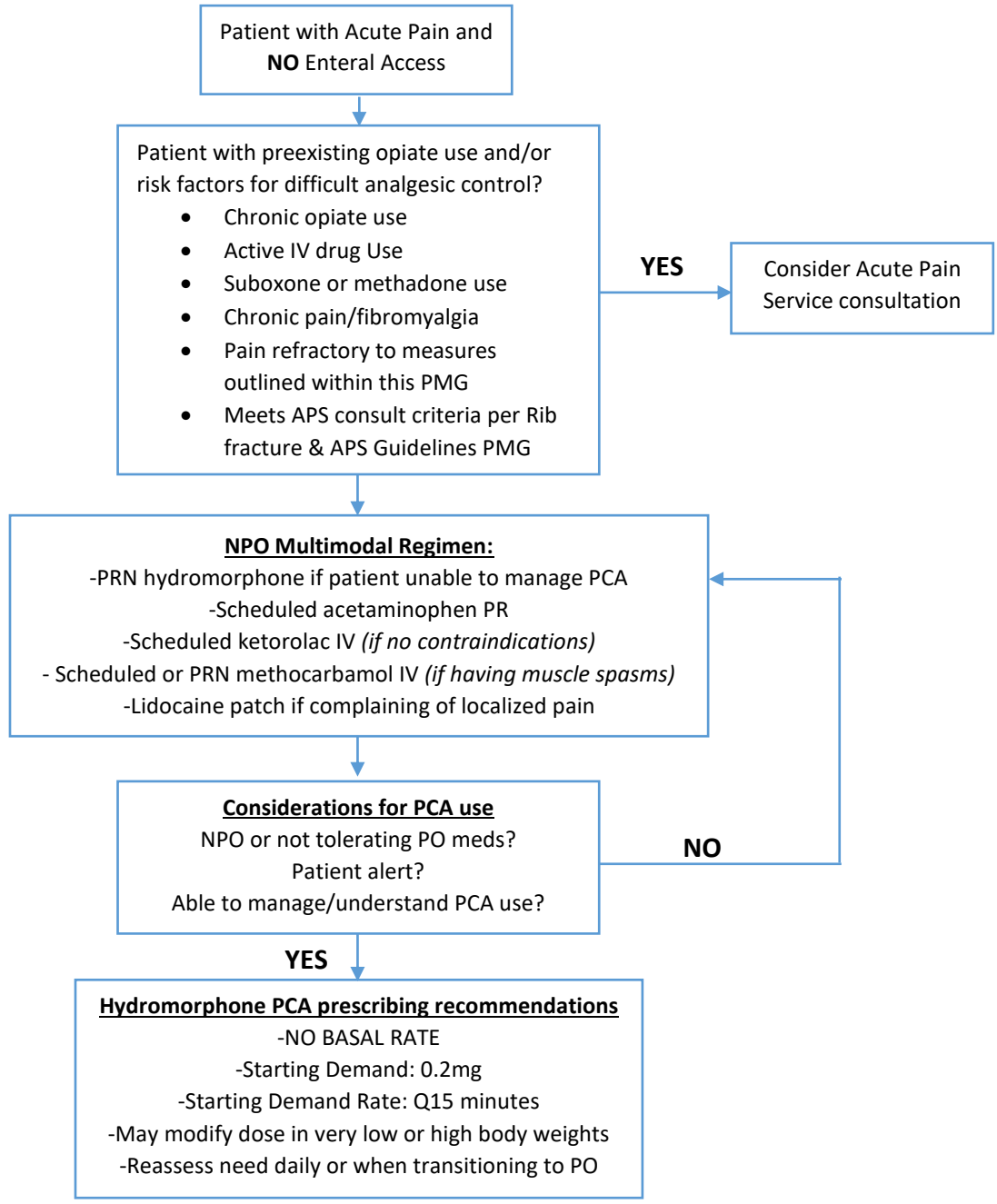
Practice Management Guidelines for Analgesia in the Non-Intubated Patient

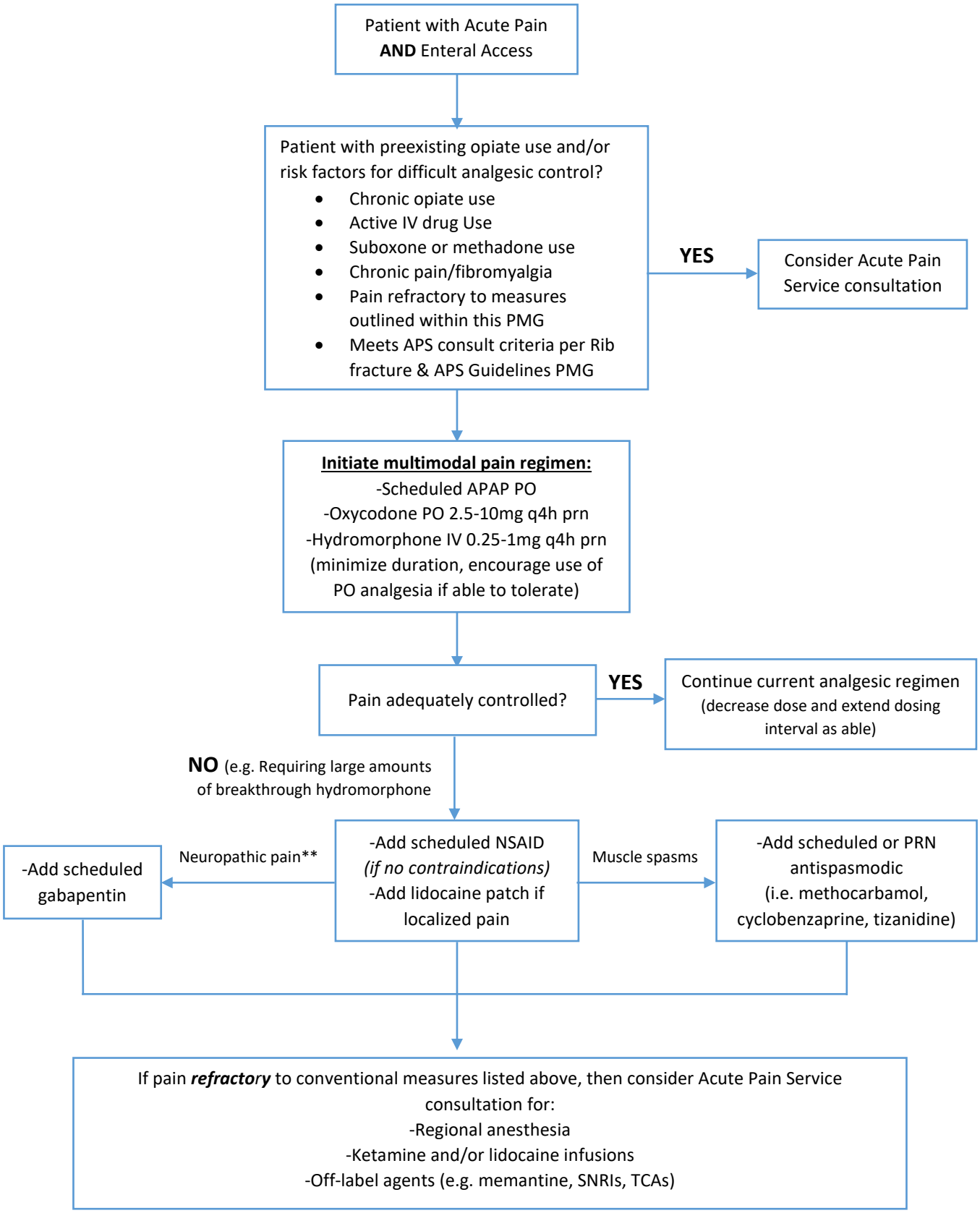
Division of Trauma and Surgical Critical Care

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**



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



**Neuropathic pain: pain described as lancinating, shooting, electrical-like, stabbing, numbness, tingling, prickling

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. Gabapentnoids

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 effectives 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

NON-OPIOID PAIN MEDICATIONS			
Drug Class	**Drug Name**	**Dosing**	**Clinical Pearl**
Acetaminophen	Acetaminophen	PO: 1000mg q8h	• Do not exceed 3g/d • Reduce to 2g/day in liver dysfunction • Consider all sources of APAP
NSAIDS	Celecoxib	PO: 100-200mg BID	• Prolonged use predisposes to GI, cardiovascular, and renal dysfunction • Ketorolac: minimal benefit >10-15mg/dose • Celecoxib: reduced GI side effects; best choice for patients at high risk for GI bleed; avoid in patients with significant cardiac comorbidities
	Ibuprofen	PO: 400-800mg q8-6h	
	Ketorolac	PO: 10mg q6h IV: 15mg q6h *Limit to 5 days*	
	Naproxen	PO: 500mg BID	
Anesthetic	Lidocaine 5% patch	1 patch daily	• Leave on for 12h and then remove • Can cut patch
Muscle Relaxants (Antispasmodics)	Cyclobenzaprine	PO: 5-10mg TID	• Caution in age ≥65 (reduce dose or avoid) • Causes dizziness, somnolence • Tizanidine: causes hypotension • Consider limiting to 14 day duration
	Methocarbamol	PO: 500-1000mg TID	
	Tizanidine	PO: 2mg TID to maximum dose of 36mg/day	
Gabapentinoids	Gabapentin	PO: 300-3600mg/day	• For neuropathic pain ONLY • May cause dizziness and drowsiness • Reduce dose or avoid in renal dysfunction or age ≥65
	Pregabalin	PO: 75-300mg/day	• 90% bioavailability vs gabapentin • Restricted use: ONLY if resuming home pregabalin or failed gabapentin (requiring >2700mg/d)
NMDA Antagonist	Memantine	PO: 5-10mg BID	• May cause dizziness, agitation, headaches • Doses >20mg/d associated with more side effects
Tricyclic Antidepressants	Amitriptyline	PO: 10-25mg daily up to 150mg/day daily or in 2 divided doses	• Anticholinergic side effects • Use caution when combining with other serotonergic and noradrenergic medications
	Desipramine	PO: 12.5mg once daily up to maximum dose of 250mg/day	
Serotonin-norepinephrine Reuptake Inhibitors	Duloxetine	PO: 30mg daily x 1 week then 60mg daily	• Better tolerated than TCAs • Use caution when combining with other serotonergic and noradrenergic medications
	Venlafaxine Extended Release	PO: 37.5-75mg daily, increase by 75mg/wk (max 225mg/d)	

V. References

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