Focus on...
Emergency Care

Managing pain in trauma patients on maintenance treatment for opioid addiction
After a car accident, Robert arrives at the emergency department with multiple traumatic orthopedic injuries, including painful rib fractures. He tells you he was recently released from an inpatient treatment center for heroin addiction and is being treated with buprenorphine/naloxone. Robert’s rib fracture pain, which is difficult to control, interferes with his breathing. In the context of Robert’s maintenance therapy for opioid addiction, what do you do for his acute pain?

Opiate abuse and addiction is a growing epidemic in the United States. Medications like methadone or buprenorphine combined with naloxone are used as maintenance therapy to address this epidemic. Researchers have investigated how these medications affect pain control in the perioperative period for planned procedures, but there’s little data for the treatment of acute unplanned pain like that experienced by Robert.
This article addresses the inpatient treatment of acute traumatic pain in patients receiving the most common opioid maintenance treatments—methadone or buprenorphine combined with naloxone.

**Patients’ rights in pain management**

A joint statement from the American College of Emergency Physicians, American Pain Society, American Society for Pain Management Nursing, and the Emergency Nurses Association asserts that all patients need to be treated appropriately for pain, including those with addictive disease. Without treatment, pain may result in tachycardia, hypertension, and increased myocardial demand, along with decreases in lung volumes, cough, gastric emptying, and bowel motility. Untreated pain also can lead to muscle spasm, impaired muscle mobility and function, as well as anxiety and fear. In trauma patients with multiple injuries, like Robert, any of these added insults can delay recovery.

While treating Robert, keep in mind that he’ll continue to struggle with his underlying chronic pain throughout the acute pain event. In fact, most patients receiving maintenance therapy for opioid addiction are opioid tolerant after just 1 week, so address baseline opiate requirements to prevent complete withdrawal and provide adequate analgesia. Work closely with Robert’s outpatient prescriber to identify his dosing and current treatment plan. This not only will help to manage his acute pain, but also will help with the transition back to maintenance therapy.

For more on treatment programs, see the infographic on page 55.

**Special considerations for chronic opioid therapy**

While methadone is indicated for pain management, it’s more widely prescribed to prevent opioid withdrawal symptoms and can be safer.

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**Initiating pain control**

Start acute pain control treatment for patients on opioid therapy by determining if they’re being treated with methadone or buprenorphine/naloxone. For patients taking methadone, contact the outpatient prescriber to get the baseline regimen or, if your state allows, check your state’s Prescription Drug Monitoring Program. For patients taking buprenorphine/naloxone whose pain is well controlled, the dose may be continued but reduced while treating acute pain. Fentanyl and tramadol may be effective as add-on opioids, while hydrocodone and hydromorphone may require high doses to overcome buprenorphine’s strong mu receptor blockade. If pain is severe or expected to be of a long duration, buprenorphine/naloxone may be discontinued and substituted with methadone to facilitate opioid use. Keep in mind that higher doses than usual of the prescribed acute pain opioids may necessary.

The following options may be considered to supplement opioid therapy.

- **Scheduled acetaminophen** may be added for any patient who doesn’t have a contraindication, such as liver dysfunction or failure. Acetaminophen treats pain differently than opioids and, although it has no anti-inflammatory effects, it’s effective for headaches associated with intracranial bleeds for patient who can’t take nonsteroidal anti-inflammatory drugs (NSAIDs).

- **NSAIDs** (aspirin, ibuprofen, ketorolac, naproxen) provide peripheral and central anti-inflammatory effects and analgesia, and they’re particularly effective in controlling pain from the systemic inflammatory response early in the traumatic process. However, they may not be appropriate for patients taking oral steroids with a history of upper GI bleeds, peptic ulcer disease, or renal dysfunction.

- **Anti-epileptics** (gabapentin, pregabalin) suppress neuronal hyperexcitability and reduce the neuronal influx of calcium, diminishing the release of excitatory neurotransmitters. As an adjunct in multimodal pain therapy, anti-epileptics also can be opioid sparing and anxiolytic, and they can act as an adjunct for alcohol withdrawal. Watch for somnolence or dizziness as adverse reactions. A nerve lies under each rib, so these drugs would be useful in a patient who has rib fractures, like Robert.

- **Local anesthetics** (lidocaine patches, bupivacaine, capsaicin cream) inhibit the generation of nerve impulses by blocking sodium channels. Used in epidurals, local anesthetics provide better pain control than opioids and are effective in controlling pain from rib fractures.

- **An NMDA receptor agonist** (ketamine) provides analgesia at 1 to 10 mcg/kg/minute and is particularly appropriate for patients with opioid tolerance or hypersensitivity. These drugs can be given by continuous infusion while monitoring the patient for negative psychological effects, such as hallucinations, memory deficits, or panic attacks.

- **I.V. patient-controlled analgesia** offers relief to patients who can’t take medications orally. Because patients control when doses are given, they must remain functional. Use basal rates only if the patient is opioid tolerant and in a bed closely monitored for adverse reactions such as respiratory depression.

- **Oral, short-acting opiates** (morphine, hydromorphone, oxycodone, codeine, hydrocodone, methadone, tramadol) should be introduced as soon as the patient can tolerate oral intake. After determining the chronic pain patient’s baseline opioid needs, start low and go slow. Don’t introduce other extended-release opioids until after trying immediate-release and multimodal therapies.
ly continued during acute pain treatment with other therapies and appropriate monitoring.

Methadone’s long half-life and slow elimination from the liver creates a risk of interacting with other drugs long after the analgesic effects of 4 to 6 hours have worn off. Any drugs that inhibit CYP450 metabolism will decrease the clearance of methadone and increase risk of respiratory depression. Monitor your patient’s corrected QT interval (QTc) for prolongation, which can be exacerbated when methadone is given with haloperidol, diazepam, ciprofloxacin, droperidol, levofloxacin, or moxifloxacin. Maintain normal magnesium and potassium levels with supplements to help avoid cardiac arrhythmias while using methadone.

The combination of buprenorphine and naloxone is not indicated for use as a pain medication. Naloxone, which is added to buprenorphine to deter abuse of the drug, has poor oral bioavailability, but it’s highly available when administered intravenously. So if someone attempted to crush and inject this combination of buprenorphine and naloxone, the naloxone would negate the effects of the buprenorphine at the opiate receptor.

Initially, baseline doses of buprenorphine and naloxone may need to be reduced for full opiate agonists to take effect and treat acute pain. Buprenorphine and naloxone may displace full agonists, reducing activation of the receptors and precipitating opiate withdrawal. Mild opiate withdrawal may appear as lacrimation, rhinorrhea, yawning, sneezing, coughing, piloerrection, restlessness, or tremor.

If your patient experiences withdrawal, continue with acute pain treatment. Both the baseline opiate dosing for addiction treatment and any new opiates prescribed will treat the withdrawal and pain. Determine when the patient took the last dose of buprenorphine and naloxone and closely monitor for oversedation for 72 hours after the last dose, particularly when adding opiates such as hydrocodone or hydromorphone to the pain-control regimen regimen, which can cause respiratory depression. The antagonist included in the buprenorphine and naloxone combination may require higher doses of opioids for adequate pain control but will also wear off sooner, increasing the risk of respiratory depression.

Pain can be treated along different pathways, making multimodal therapy key to addressing acute pain. (See Initiating pain control.)

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Tips for multimodal therapy
Treatment using multimodal therapy requires patient education, treatment flexibility, and multidisciplinary collaboration. Keep the following tips in mind to ensure a good outcome for your patient.

• Start education and interdisciplinary coordination immediately and include weaning from opiates for acute pain, instructions for administration, drugs to avoid, and necessary follow-up.
• Use consulting resources such as acute pain services and substance abuse experts early to take full advantage of their knowledge.
• Encourage deep breathing, incentive spirometry, and ambulation to reduce risks of pneumonia and infection.
• Treat the pain appropriately with the right drug. For instance, neuropathic pain is more responsive to a drug like an antiepileptic rather than an opiate.
• When increased pain control is needed, try adding a drug from another class rather than relying on increased dosing from one class. This is particularly relevant when opiate receptors are unavailable to agonists, which might be the case for someone on maintenance therapy.
• Don’t underestimate the value of adjunct therapies such as acupuncture, guided imagery, and massage therapy.

Getting the upper hand on pain control
For patients like Robert with acute injuries, using multimodal therapy, while considering individual opiate requirements, history, and response, will gain better pain control that leads to improved outcomes.

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Selected references
Maintenance treatment programs for opioid addiction

The most common maintenance treatments for opioid addiction are methadone and buprenorphine combined with naloxone. This table provides information on their pharmacology as well as pros and cons for use.

<table>
<thead>
<tr>
<th></th>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Naloxone</th>
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</thead>
<tbody>
<tr>
<td>Receptor pharmacology</td>
<td>Full mu opioid agonist</td>
<td>Partial mu opioid agonist</td>
<td>Mu opioid antagonist</td>
</tr>
<tr>
<td>Metabolism</td>
<td>CYP450 3A4 and other hepatic enzymes Requires individualized dosing to account for differences in drug clearance</td>
<td>CYP450 3A4 the liver, extensive first pass metabolism</td>
<td>Primarily by conjugation in</td>
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<tr>
<td>Half-life (hours)</td>
<td>36</td>
<td>24-60</td>
<td>6</td>
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<tr>
<td>Onset of action (minutes)</td>
<td>30</td>
<td>90-100</td>
<td>2-5</td>
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**Buprenorphine/naloxone**

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Once daily</th>
<th>Tablets available in:</th>
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<tbody>
<tr>
<td></td>
<td>Stable dosing at 80-120 mg/day</td>
<td>2 mg buprenorphine/0.5 mg naloxone OR 8 mg buprenorphine/2 mg naloxone Stable dosing at 2 to 32 mg/day</td>
</tr>
</tbody>
</table>

**Pros**

- Affordable
- For pregnant patients, maintains stable level of opiate in blood to avoid stressful cycle of intoxication and withdrawal in fetus
- Less risk of respiratory depression
- May require less frequent dosing than methadone
- Fewer drug interactions than methadone
- Easier to discontinue than methadone

**Cons**

- More risk of respiratory depression, sedation, and QTc prolongation
- Serious drug interactions
- Potential for abuse
- Potential for abuse
- Possible interaction with CYP3A4 inhibitors and inducers

The opioid epidemic—by the numbers

- Increase in the death rate from synthetic opioids other than methadone (including drugs such as tramadol and fentanyl) from 2014 to 2015: 72.2%
- Number of Americans who die every day from an opioid overdose: 91
- Number of heroin deaths in the United States in 2015: 12,989
- Increase in the number of prescription opioids dispensed in the United States from 1999 to 2013: 4X
- Approximate number of Americans who abused or were dependent on prescription opioids in 2014: 2 million
- Drug-overdose deaths involving an opioid: 6 of 10