Analgesics for Acute Pain in Adults

Acute pain can result from acute illness (e.g., renal colic, sickle cell crisis), injury, or surgery.[7,86] As opposed to chronic pain, its etiology and location is usually clear.[4] Acute pain is self-limited, improving over hours to weeks as the injury heals.[4] Treatment minimizes detrimental physiologic responses (e.g., tachycardia, shallow breathing, immobility, muscle spasms, ileus, impaired immune response), adverse psychological effects (e.g., anxiety, fear), and progression to chronic pain.[87,] However, use of opioids for acute pain should be with the lowest necessary dose for the shortest duration possible to prevent help transition of acute use to chronic use.[88] Set realistic goals for pain relief and function (e.g., 33% to 50% decrease in pain).[59] Some hospitals are developing **AL**ternatives **T**o **O**pioid (ALTO)[74] or **E**nhanced **R**ecovery **A**fter **S**urgery (ERAS) protocols. Perioperatively, different medications and routes are combined (i.e., a multimodal or balanced approach) to increase efficacy and decrease side effects.[56,59] The charts below review various analgesics to treat different types and severities of acute pain in adults. The first chart reviews preferred or first-line analgesics for acute pain. The second chart reviews other analgesic options that can be considered for use in patients with acute pain.

Preferred Analgesics for Acute Pain in Adults

Drug or Drug Class	Consider for…	Comments
NSAID (e.g., ibuprofen 400 mg every four to six hours)	• osteoarthritis[58] • dental pain (including surgery)[6,86] • renal colic[89] • low back pain[83] • fractures[82] • musculoskeletal pain[75] • tension headache[81] • migraine headache[10,78] • biliary colic[14] • abdominal surgery[86] • orthopedic surgery[86] • episiotomy[85] • opioid-sparing effect.[56] • Use WITH acetaminophen for better efficacy (e.g., [adults] acetaminophen 500 to 1,000 mg WITH ibuprofen 200 to 400 mg every six hours as needed).[17]	• One in two to three patients with moderate to severe pain has a 50% reduction in pain over four to six hours.[1] • Oral ibuprofen at doses of 400, 600, and 800 mg provide similar pain relief.[76] • Ibuprofen 400 mg plus acetaminophen 1,000 mg reduces moderate-to-severe musculoskeletal pain as well as many opioid and acetaminophen combinations.[75] • Oral ketorolac has similar efficacy to other NSAIDs, but the risks associated with its use outweigh the possible benefits.[57,58] • **Topical NSAIDs** may work as well as oral NSAIDs for acute musculoskeletal pain (e.g., sprain).[16] ○ For more on topical NSAIDs and other topical pain relievers, see our chart, *Topicals for Pain Relief*. • **Available injectable NSAIDs and cost per dose**[a]: ibuprofen (*Caldolor* [US: ~$23]), ketorolac (*Toradol* [Canada], generics [US: ~$10, Canada: ~$1.50]), meloxicam (*Anjeso* [US: ~$93]). • Injectable ketorolac and ibuprofen have not been proven more effective than oral ibuprofen.[8,12,40] Consider an injection for renal colic, and for patients unable to take oral NSAIDs.[5,12]

Continued…

Drug or Drug Class	Consider for…	Comments
NSAIDs, continued		• Injectable meloxicam may not be appropriate for acute pain due to slow onset (~2 to 3 hours vs ~1 hour with other IV NSAIDs).[42] There is no good evidence that it is safer than other injectable NSAIDs, despite being more COX-2 selective. • Limit use to <15 days/months to reduce the risk of medication overuse headache.[72] • In the US, NSAIDs are contraindicated for perioperative pain due to CABG. • For information on the use of NSAIDs in patients with kidney or cardiovascular disease, and mitigation of gastrointestinal risk, see our FAQ, *Managing NSAID Risks*.
Acetaminophen	• osteoarthritis[58,*] • dental pain (including surgery)[86,*] • renal colic[5,*] • fractures[9] • musculoskeletal pain[86] • tension headache[11] • migraine headache[10] • abdominal surgery[86] • orthopedic surgery[86] • episiotomy[85,*] • opioid-sparing effect[56] ***NSAID may be more effective** • Use WITH an NSAID for better efficacy (e.g., acetaminophen 500 to 1,000 mg WITH ibuprofen 200 to 400 mg every six hours as needed in adults).[17]	• One in three to four patients with moderate to severe pain has a 50% reduction in pain over four to six hours with acetaminophen 1,000 mg.[1] • Acetaminophen 1,000 mg may not relieve pain much better than 500 mg.[1,84] • Ibuprofen 400 mg plus acetaminophen 1,000 mg reduces moderate-to-severe acute extremity pain as well as many opioid and acetaminophen combinations.[75] • In chronic liver impairment, limit the total daily dose to 2 to 3 grams (instead of the usual 4 gram max adult daily dose).[13] • May post a higher risk of medication overuse headache than NSAIDs.[73] Limit use to <15 days/month to reduce the risk.[72]
Strong oral opioids (e.g., hydrocodone, oxycodone) *Continued…*	• Pain not relieved by nonopioids, assuming patient can take oral medications.[7,56] • Pain not expected to be relieved by non-opioids (e.g., invasive surgery [open abdominal surgery], major trauma [crush	• Not proven more effective than ibuprofen 400 mg at achieving 50% reduction in moderate to severe pain.[1] • Do not use extended-release opioids for acute pain.[7] • May be as effective as IV opioids, even after significant surgeries (e.g., cardiac surgery).[43] • Consider combining with nonopioids to provide better analgesia and minimize side effects (e.g., opioid-sparing effect).[56,59]

Drug or Drug Class	Consider for…	Comments
Strong oral opioids, continued	injuries, burns], assuming patient can take oral medications.[4,7,56]	• Advise patients to taper off the opioid as their pain resolves, being mindful of the total daily dose of acetaminophen if weaning from an opioid/acetaminophen combo to acetaminophen.[7] • For more safety considerations, see our toolbox, *Appropriate Opioid Use*.
Parenteral opioids (IV, epidural, or spinal [intrathecal])	• Pain not expected to be relieved by non-opioids (e.g., invasive surgery [open abdominal surgery], major trauma [e.g., crush injuries, burns]) in patients who cannot take oral medications.[4,7,56] • Moderate to severe pain in patients with suspected malabsorption.[56] • Moderate to severe pain requiring immediate relief or rapid dose titration.[56] • Painful procedures.[59] • Pain due to MI despite nitroglycerin and beta-blocker (IV morphine).[35]	• IV opioids have a quicker onset of action than oral opioids, allowing for faster titrations, but have more risks (e.g., adverse effects,), and shorter duration of action.[56] • Consider combining with nonopioids to provide better analgesia and minimize side effects (e.g., opioid-sparing effect).[56,59] • PCAs may be preferred over intermittent dosing or continuous infusion due to improved pain control (despite lower doses), improved tolerability, and patient satisfaction (e.g., post-op patients).[4] • Use our chart, *Equianalgesic Dosing of Opioids for Pain Management*, for help with initial IV dosing, converting between opioids, or converting from IV to oral opioids once pain is controlled and oral intake is tolerated. • Follow policies to get pain service approval before adding a systemic opioid to a regional (e.g., epidural, spinal) opioid. **Fentanyl**: • Consider fentanyl for patients with true allergy to morphine or hydromorphone.[18] • Consider when a fast onset but short duration of action is needed (e.g., procedures). IV: peaks in four to six minutes, and a single dose lasts 30 to 60 minutes.[4,42] Epidural: a single dose lasts two to three hours.[42] • Accumulates in fat with repeat dosing; may not be a good choice in obesity.[4] • A preferred opioid in kidney disease.[15] Dose cautiously.[42] **Hydromorphone** • A preferred opioid in kidney impairment.[15] However, use lower starting doses for CrCl <60 mL/min.[15] **Morphine**: • Use IV **morphine** with caution in acute MI patients with bradycardia, right ventricular infarct, or hypotension.[4] • Not recommended in kidney impairment.[4] • Intrathecal or epidural morphine can last up to 24 hours.[4,19]

Drug or Drug Class	Consider for…	Comments

Local Anesthetics (e.g., bupivacaine, ropivacaine, lidocaine, mepivacaine)
 	
(For more on lidocaine patches and other topical pain relievers, see our chart, *Topicals for Pain Relief*.)
 	
Continued…
	• Opioid-sparing effect for patients at high risk from opioids (e.g., patients with lung disease, obstructive sleep apnea, morbid obesity, opioid tolerance, opioid misuse).[20,21]
	• Intrathoracic, abdominal, or spinal surgery (e.g., epidural anesthesia)[22]
	• Upper extremity/hand surgery (e.g., peripheral nerve block).[24]
	• Lower extremity surgery (e.g., total hip/knee arthroplasty (e.g., spinal or epidural anesthesia, peripheral nerve block)[24]
	• Carotid endarterectomy (e.g., peripheral nerve block)[33]
	• Deep laceration repair (e.g., local infiltration, peripheral nerve block)[37]
	• Post-op pain (e.g., surgical site pain [e.g., local anesthetics], intravenous lidocaine)[32,38]
		• For epidural administration, local anesthetics are often combined with an opioid to reduce the amount of local anesthetic needed.[4]
		• Ensure safe antithrombotic management in patients receiving regional anesthesia.
		• Elastomeric pumps (e.g., *On-Q*) can provide continuous infusion of local anesthetics to the surgical site for up to five days.[31]
		• Liposomal bupivacaine (***Exparel*** [US]) is indicated for single-dose infiltration at the surgical site and as an interscalene brachial plexus nerve block to produce postsurgical local (infiltration) or regional (peripheral nerve block) analgesia.[36] The bupivacaine implant (***Xaracoll*** [US]) is indicated for placement into the surgical site to produce postsurgical analgesia for up to 24 hours after open inguinal hernia repair.[39] Bupivacaine/meloxicam extended-release (***Zynrelef*** [US]) is applied to the surgical site prior to suturing after foot and ankle, small-to-medium open abdominal, and lower extremity joint arthroplasty surgical procedures.[41] ***Posimir*** (US) is a bupivacaine solution approved for administration into the subacromial space at the end of arthroscopic shoulder surgery.[90]
		  ○ Data do not demonstrate consistent or substantial clinical advantages with use of liposomal bupivacaine over other local anesthetics.[30]
		  ○ Compared to standard bupivacaine, bupivacaine/meloxicam extended-release reduces opioid use by ~5 to 10 mg of morphine in the first 24 hours, and pain score differences don't seem clinically significant after about 24 hours.[41]
		  ○ Avoid repeat bupivacaine doses, or other local anesthetics, for at least 96 hours after administration of *Exparel*, *Xaracoll*, or *Zynrelef*, and at least 168 hours after *Posimir*, due to persistence of bupivacaine in the systemic circulation and potential for overdose.[36,39,41,90]
		  ○ Expensive; ~$365 for *Exparel* (266 mg), ~$250 for *Xaracoll* (300 mg), or ~$280 for *Zynrelef* (400 mg/12 mg), *Posimir* ($319) vs a few dollars for regular bupivacaine.[a]
		• Continuous IV lidocaine infusion may be an option when local or regional anesthesia is not possible.[61] IV lidocaine may be most beneficial for patients undergoing abdominal surgeries in reducing early post-op pain and opioid use.[53]
		  ○ Lidocaine may not be appropriate for patients with heart disease, electrolyte disturbances, seizure disorders, or kidney or liver impairment.[38] Dose based on ideal body weight (unless actual body weight is less) and stop within 24 hours.[38] Monitor for signs of toxicity (e.g., ringing in the ears, lightheadedness, tingling

Drug or Drug Class	Consider for…	Comments
Local anesthetics, continued		around the mouth), and treat serious toxicity with 20% lipid infusion.[38] For details, see https://anaesthetists.org/Home/Resources-publications/Guidelines/Management-of-severe-local-anaesthetic-toxicity. • Use our clinical resource, *Safe Use of Local Anesthetics*, for tips to minimize risks associated with local anesthetics.

Ketamine	• Surgery in which severe post-op pain is expected (e.g., abdominal, thoracic, orthopedic)(best evidence).[27]
	• Surgical patients who are opioid-tolerant.[27]
	• Surgical patients at high risk of respiratory depression caused by opioids (e.g., patients with sleep apnea).[27]
	• As an opioid adjunct for sickle cell crisis.[27]
	• Acute pain in patients presenting to the ED in whom an opioid is undesirable (e.g., opioid-tolerant, history of opioid misuse, opioid-naïve, elderly, taking medication-assisted treatment for opioid use disorder).[60]
		• Low-dose IV ketamine (<0.5 mg/kg) may provide similar pain relief compared to opioids in the ED for pain from a variety of causes.[60]
		• Ketamine at doses ≥0.3 mg/kg may be associated with more neuropsychiatric side effects compared to standard care (e.g., dizziness, drowsiness, emergence phenomena, dissociation, dysphoria, hallucinations, nightmares).[60,47]
		• Consider doses of ≤0.35 mg/kg (bolus), or an infusion of 0.1 to 0.5 mg/kg/hour (max 1 mg/kg/hour).[27]
		  ○ Many studies and protocols use bolus doses of 0.1 to 0.3 mg/kg given over 15 minutes.[62] Dose can be repeated once after 30 minutes if needed.[55]
		  ▪ Infusion over 15 minutes instead of 5 minutes helps minimize neuropsychiatric side effects.[64]
		  ○ There is less evidence for nasal administration. Consider a dose of 0.7 to 1 mg/kg, with a maximum of 1 mL per nostril.[62]
		  ○ Some ED protocols set a maximum cumulative dose of 0.3 mg/kg, up to 50 mg.[54]
		  ○ Examples of monitoring in the ED include continuous pulse oximetry, telemetry (or vitals every 10 minutes), and immediate availability of the ED physician for at least 30 min post-dose.[54,55]
		• Perioperative ketamine does not seem to benefit patients undergoing surgery not associated with moderate to severe pain.[27]
		• A meta-analysis of ketamine administered preoperatively, intraoperatively, or postoperatively, mostly at doses of 0.25 to 1 mg/kg as boluses or an infusion at 0.12 to 0.3 mcg/kg/hour seems to reduce postoperative opioid use and pain scores.[20,46] However, other studies have not shown benefit of pre-op boluses.[20,47]
		• Avoid ketamine in patients with psychosis, uncontrolled cardiovascular disease or hypertension, pregnancy, moderate to severe liver impairment, or increased intraocular or intracranial pressure.[27]

Drug or Drug Class	Consider for…	Comments
		• For information on use of ketamine in the ICU, see our chart *Meds for ICU Analgesia and Sedation*.

a. Wholesale acquisition cost (WAC). US pricing by Elsevier, accessed October 2023.

Not Preferred for Acute Pain

Drug or Drug Class	Comments
Buprenorphine (partial agonist [mu]/ antagonist [kappa])	• Buprenorphine is a mixed opiate with partial agonist and antagonist activity.[42] • See our chart, *FAQs About Buprenorphine for Chronic Pain*, for more on buprenorphine, including why sublingual, buccal, and transdermal buprenorphine products should NOT be used for **acute** pain, and drawbacks of parenteral buprenorphine.
Codeine	• Codeine is metabolized to morphine via CYP2D6.[2] o Genetic polymorphisms may result in poor response to codeine (poor metabolizers) or toxicity (ultrarapid metabolizers).[2,23] o Efficacy of codeine is reduced by strong CYP2D6 inhibitors (e.g., bupropion, fluoxetine).[23] • Avoid codeine in children and breastfeeding women.[23,28] • See our chart, *Keeping Pediatric Patients Safe* for information on codeine in children.
Fentanyl (non-injectable formulations [e.g., patches, transmucosal lozenge, buccal tablet])	• Reserve the **non-injectable fentanyl products** for patients with chronic pain who are **opioid-tolerant** (e.g., have been taking the equivalent of at least 60 mg of morphine equivalent daily for at least one week) due to risk of toxicity, including respiratory depression.[34,50]
Gabapentinoids (gabapentin or pregabalin)	• Mounting evidence suggests any benefit of pre-op gabapentin or pregabalin are marginal and likely don't outweigh risks, such as delirium, dizziness, respiratory depression, or visual disturbances.[3,44] • Avoid gabapentinoids in the elderly, patients with kidney impairment, and patients with sleep apnea.[3,45] • See our chart, *Enhanced Recovery After Surgery: Developing an ERAS Protocol* for dosing.
Meperidine	• Meperidine has a neurotoxic metabolite, normeperidine, that can cause anxiety, tremors, myoclonus, hallucinations, and seizures.[29] Normeperidine can accumulate with repeated meperidine dosing, especially in patients with kidney or liver impairment and in the elderly.[29,42,48] • Meperidine poses a higher risk of postoperative delirium than other opioids.[42]

Drug or Drug Class	Comments
	• Other side effects include confusion and dysphoria.[42] • Meperidine is poorly effective orally.[48] • Naloxone is not effective for treating normeperidine toxicity, and in fact may worsen it.[77] • Meperidine's vagolytic activity can cause increased ventricular response in patients with supraventricular tachyarrhythmias.[42] • Poses risk of serotonin syndrome with other serotonergic medications.[42]
Oliceridine (*Olinvyk*)	• There is a ceiling dose of 27 mg/day due to risk of QT prolongation. Once a cumulative daily dose of 27 mg is met, a different analgesic will be needed until the next day.[80] • There is limited safety data beyond 48 hours.[80] • Patients taking a moderate to strong CYP2D6 or CYP3A4 inhibitor may need less frequent dosing; monitor response CYP3A4 inducers may reduce efficacy.[80] • Poses risk of serotonin syndrome with other serotonergic medications.[80]

Other mixed agonist/antagonists (e.g., butorphanol, nalbuphine)	• Analgesic effects of partial agonists (kappa)/antagonists (mu) are limited by a dose ceiling.[51]
	• Avoid in opioid-tolerant patients, as use may lead to withdrawal symptoms.[42]
	• **Butorphanol** use is often reserved for pain when other options are not effective, tolerated, or inadequate.[63]
	  o Use may also be limited by adverse effects (e.g., psychotomimetic effects) and prolonged respiratory depression at higher doses.[63]
	• **Nalbuphine** efficacy and safety data compared with morphine are inconsistent.[52]
	  o Avoid doses greater than 20 mg/dose, especially in opiate-naive patients.[42]
	  o Nalbuphine may be associated with less itching and less respiratory depression compared to morphine.[52]
	• See our chart, *Equianalgesic Dosing of Opioids for Pain Management*, for equivalent doses, other considerations, and potential side effects.

Muscle Relaxants	• Adverse effects (e.g., sedation, dizziness, etc) are common with all muscle relaxants.[79] The CNS depression commonly seen with muscle relaxants is additive with other CNS depressants (e.g., opioids, alcohol, benzodiazepines) and has led to respiratory depression and death.[79] Muscle relaxants should be used cautiously in the elderly as most are listed on the Beers Criteria as potentially inappropriate for use in older adults due to their sedative effects, increased risk of falls, etc.[79] • Muscle relaxants may be used for acute pain that is not relieved with NSAIDs and acetaminophen.[79] They should not be used longer than two to three weeks, and many recommend limiting their duration to no more than seven days.[79]

Drug or Drug Class	Comments
	• The old product *Orphengesic Forte* (orphenadrine 50 mg, aspirin 770 mg, caffeine 60 mg) was reintroduced in 2020 for mild to moderately painful musculoskeletal conditions.[65] It is important to note the aspirin content of this product; the maximum dose provides a total daily aspirin dose of 3,080 mg. • For more information on orphenadrine and other muscle relaxants for pain, see our chart, *Muscle Relaxants*.

Tramadol	• One in eight patients with moderate to severe pain has a 50% pain reduction over four to six hours with tramadol (i.e., less effective than NSAIDs or acetaminophen).[1]
	• Tramadol's abuse potential may be similar to that of strong opioids.[67]
	• In addition to the usual opioid toxicities such as respiratory depression, tramadol can cause serotonergic effects such as nausea, vomiting, and perhaps seizures, hyponatremia, and hypoglycemia even at therapeutic doses.[48,66-70]
	• Hallucinations are reported in <1% of patients taking tramadol; however there may be an increasing number of cases. A Health Canada review established a link between normal doses and visual and auditory hallucinations in patients ≥65 years of age.[71]
	• Efficacy of tramadol is reduced in poor CYP2D6 metabolizers and by strong CYP2D6 inhibitors.[23] Conversely, effects are increased in ultrarapid CYP2D6 metabolizers due to increased levels of tramadol's active metabolite.[23]
	• Tramadol also interacts with CYP3A4 inhibitors and inducers, and serotonergic drugs.[67]
	• Withdrawal from tramadol usually presents as a typical opioid withdrawal syndrome, but 10% of cases are characterized by confusion, hallucinations, paranoia, extreme anxiety and panic, and numbness and tingling in the extremities.[70]
	• Maximum adult daily dose 300 mg or 400 mg, depending on product.[25,26] See product labeling for dosing in elderly patients, or in patients with renal or hepatic dysfunction.
	  ○ In elderly patients with CrCl <30 mL/min., avoid extended-release tramadol products due to central nervous system adverse effects.[48]
	• Although tramadol overdose can be treated with naloxone, seizures have been reported in some instances.[42]
	• Avoid tramadol in children and breastfeeding women.[23,28,49]
	  • See our chart, *Keeping Pediatric Patients Safe* for information on tramadol in children.

Abbreviations: CABG = coronary artery bypass graft; ED = emergency department; IV = intravenous; MI = myocardial infarction; NSAID = nonsteroidal anti-inflammatory drug; PCA = patient-controlled analgesia

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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