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Approach to the management of acute pain in adults

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INTRODUCTION

The goals of acute pain management are to relieve suffering, facilitate function, enhance recovery, and satisfy patients. After surgery, additional goals are to achieve early postoperative mobilization and reduce length of hospital stay. Pain control regimens must take into account medical, psychological, and physical condition; age; level of fear or anxiety; surgical procedure, if applicable; personal preference; and response to agents given. The optimal strategy for acute pain control consists of multimodal therapy to increase efficacy, reduce side effects of therapy, and minimize the need for opioids.

This topic will discuss the rationale for and concepts of multimodal analgesia and creation of an individualized strategy for analgesia, primarily in the hospital. Much of the focus is on perioperative pain, though the principles are applicable to all types of acute pain. Use of regional anesthesia techniques, nonopioid analgesics, and postoperative opioids, are discussed in more detail separately.

- (See "Nonopioid pharmacotherapy for acute pain in adults".)
- (See "Use of opioids for postoperative pain control".)
- (See "Continuous epidural analgesia for postoperative pain: Technique and management".)
- (See "Overview of peripheral nerve blocks".)

Use of opioids for acute pain in the ambulatory setting is also discussed separately. (See "Management of acute pain in opioid naïve adults in the ambulatory setting".)

MECHANISM OF PERIOPERATIVE PAIN AND ANALGESIA

Pain pathways — Acute pain results from the combination of tissue trauma (eg, surgical incision, dissection, burns), local and systemic inflammation, and direct nerve injury (ie, nerve transection, stretching, or compression) (figure 1) [1]. The patient senses pain through the afferent pain pathway (figure 2), which is the target of various pharmacologic agents.

Tissue trauma releases local inflammatory mediators that can produce augmented sensitivity to stimuli in the area surrounding an injury (hyperalgesia) or misperception of pain due to non-noxious stimuli (allodynia) (figure 3). Other mechanisms contributing to hyperalgesia and allodynia include sensitization of the peripheral pain receptors (primary hyperalgesia) and increased excitability of central nervous system neurons (secondary hyperalgesia) [1-3].

Nociception is a physiologic response to a painful stimulus and involves the processes of transduction, transmission, modulation, and perception [4]. Various analgesic agents and techniques can be used to target each of these four processes, as shown in a figure (figure 4).

Acute pain can consist of both somatic and visceral components, which travel via different paths to reach the spinal cord.

- Somatic pain originates in the periphery from free nerve endings, by a process called **transduction**. These signals are **transmitted** to the central nervous system by way of primary afferent neurons (A-delta and C fibers) which have cell bodies located in the dorsal root ganglion. These fibers synapse with secondary afferent neurons in the dorsal horn of the spinal cord [4].

- Visceral pain originates from deeper internal structures (eg, organs), and differs from somatic pain mainly in the mode of transmission [4]. Visceral afferent signals from abdominal organs arrive first at the parasympathetic ganglia (eg, celiac for the pancreas) then are carried by the greater or lesser splanchnic nerves to prevertebral and paravertebral ganglia and eventually to the dorsal root ganglion and spinal cord [4].

Modulation of both somatic and visceral pain occurs in the spinal cord, via complex mechanisms involving inhibitory and excitatory neurons, and descending neural input from the central nervous system. **Perception** of both types of pain can be enhanced by central sensitization, and can be blocked with centrally acting analgesics.

The relative contribution of somatic versus visceral pain may vary by surgical procedure. Both somatic and visceral pain may be blocked using regional anesthesia, depending on the technique. As an example, epidural analgesia typically blocks both somatic and visceral pain, whereas thoracic and abdominal fascial plane blocks act primarily on somatic pain.

Traditionally, acute perioperative pain management has relied solely on systemic opioid medications to target central mechanisms involved in the perception of pain (figure 5). A better approach is based on a biopsychosocial model of pain [5] and uses several agents or techniques, each acting at different sites along the pain pathway, known as multimodal analgesia. This approach reduces the dependence on a single medication and mechanism, and importantly, may reduce or eliminate the need for opioids. Synergy between opioid and nonopioid medications reduces both the overall opioid dose and unwanted opioid-related side effects. (See 'Use multimodal analgesia' below.)

Pain receptor activity can be directly blocked (eg, local anesthetics), or anti-inflammatory agents (eg, aspirin, nonsteroidal anti-inflammatory drugs) can be used to diminish the local hormonal response to injury, thus indirectly decreasing pain receptor activation.

Some analgesic agents target the activity of neurotransmitters by inhibiting or augmenting their activity (eg, ketamine, clonidine, acetaminophen, gabapentin, pregabalin) (figure 6). Neurotransmitters are responsible for carrying electrical signals across the gap junctions between neurons. To produce analgesia, the activity of several neurotransmitters can be targeted, including substance P, calcitonin gene-related peptide, aspartate, glutamate, and gamma-aminobutyric acid (GABA).

Preventive analgesia for postoperative pain — Management of postoperative pain employs a variety of medications and other techniques to prevent acute and chronic pain. The concept of "preemptive" analgesia (ie, analgesic strategies administered prior to surgical incision or stimulus) is controversial. The rationale for preemptive analgesia has been the idea that administration before the stimulus could modify peripheral and central nervous system processing of noxious stimuli, thereby reducing central sensitization, hyperalgesia, and allodynia [1-3]. A number of studies have concluded that it is not necessary to administer analgesic agents preoperatively to achieve a reduction in postoperative pain and opioid use [6].

A broader approach to the reduction of acute and chronic postoperative pain involves "preventive" analgesia. The aim is to prevent sensitization induced by noxious stimuli arising at any time in the perioperative period, using treatments administered in the pre-, intra-, or postoperative period. A preventive analgesic is considered effective when postoperative pain and/or analgesic consumption is reduced beyond the duration of action of the treatment drugs or techniques [7,8]. Some components of multimodal analgesia may be started before surgery, but preempting the surgical stimulus is not mandatory; rather, the drug or regional

block should be in effect by the time the anesthetic has ended and last beyond the emergence from anesthesia. In the case of local or regional anesthesia, preoperative administration may also reduce (or eliminate) the need for intraoperative anesthetics and systemic analgesics.

There are many effective preventive analgesic techniques using various pharmacological agents and interventions. They reduce nociception by blocking or decreasing receptor activation and inhibiting the production or activity of pain neurotransmitters, interfering with transmission and/or influencing modulation or perception. The ultimate result is a reduction in postoperative opioid use and opioid-related side effects.

GENERAL APPROACH

Goals and principles for acute pain management — The primary goals of acute pain management are to improve outcomes and patient experience. Often this entails balancing analgesia with achieving functional goals, while avoiding preventable complications.

While guidelines for perioperative pain management have been published [9], widespread adoption has not occurred [10]. In response to a call from the US Health and Human Services (HHS) to develop evidence based guidelines, in 2022 a consortium of representatives from 14 medical societies published a set of seven guiding principles for acute perioperative pain management [11], as shown in a table (table 1). Our approach to the management of acute perioperative pain is consistent with these principles.

Use multimodal analgesia — We suggest a multimodal approach to analgesia for acute pain, rather than the use of opioids alone, with nonpharmacologic techniques, regional anesthesia techniques as appropriate, nonopioid analgesics, and opioids as necessary. The use of multimodal analgesia is a key concept and a guiding principle for perioperative pain management, and is applicable to other types of acute pain. The simplest definition of multimodal analgesia is the use of two or more agents that employ different mechanisms for pain management [12]. Multimodal analgesia represents a comprehensive approach to pain management that follows a biopsychosocial model of pain, and decreases the overreliance on any single class of agents, most importantly opioids. Multimodal analgesia is frequently incorporated into protocols for enhanced recovery after surgery (ERAS) [13], and is currently a national quality metric defined as the use of two or more non-opioid classes of analgesic modalities for eligible surgical cases [14].

The specifics of multimodal analgesia must be individualized for etiology of the pain and patient factors. A number of studies of various patient populations have found that the use of multimodal analgesia may improve pain management, reduce opioid consumption, and reduce opioid related side effects. As an example, in a database study of over 1,500,000

patients who underwent knee or hip arthroplasty, the addition of 1, 2 or more than 2 analgesic modalities in addition to opioids was associated with incremental reduction in opioid use and some opioid related side effects, compared with opioids alone [15].

The efficacy of various nonopioid analgesic options is discussed separately. (See "Nonopioid pharmacotherapy for acute pain in adults".)

Minimize opioids — An overarching principle of pain management is to avoid the excessive use of perioperative opioids. Opioids are associated with short-term side effects (ie, respiratory depression, excessive sedation, nausea and vomiting, pruritus, urinary retention, constipation) and long-term adverse effects (ie, tolerance, dependence, opioid induced hyperalgesia or withdrawal upon conclusion of therapy) and possible opioid misuse. (See 'Opioids' below.)

CREATING A PLAN FOR ANALGESIA

The initial plan for analgesia should be based on patient factors and the predicted or existing degree of pain. The degree of pain cannot be precisely predicted. Thus, patients must be monitored for pain and for treatment side effects, and management should be adjusted accordingly. (See 'Postoperative monitoring for pain control and side effects' below.)

Patient evaluation — Patient evaluation should include assessment of baseline medical and psychological conditions, substance use disorder, pain treatment history, and long-term medications, all of which may affect the plan for analgesia. This evaluation is the first principle of acute perioperative pain management (table 1) [11]. Examples of the implications of issues that may be identified include the following:

- Some conditions make regional anesthesia techniques difficult to perform (eg, obesity, ankylosing spondylitis, prior spine surgery).
- Neuraxial block and deep peripheral nerve blocks may be contraindicated in the patients with abnormal coagulation or platelet dysfunction. (See "Neuraxial anesthesia/analgesia techniques in the patient receiving anticoagulant or antiplatelet medication".)
- Patients who chronically use opioids may require complex multimodal plans for perioperative pain control. (See "Management of acute pain in the patient chronically using opioids for non-cancer pain".)
- Older patients and patients with obstructive sleep apnea (OSA) may be more prone to the side effects of sedatives and opioids, requiring either dose modification or

avoidance of these medications. (See "Postoperative management of adults with obstructive sleep apnea", section on 'Pain control'.)

Risk factors for greater intensity and duration of acute pain — Both patient factors and the type of planned surgery may predict the need for enhanced or specialized acute or postoperative pain management.

- Patient factors that have been associated with poor postoperative pain control include younger age, female sex, active smoking, depression and anxiety, pain catastrophizing, history of substance use disorder, obesity, and existence of preoperative pain at baseline [16-19]. In a single institution prospective observational study of 360 patients who underwent elective surgery (major orthopedic, urologic, colorectal, pancreatic/biliary, thoracic, or spine surgery), patient factors associated with a high level pain trajectory in the week after surgery included younger age (eg, 54 ± 12 versus 66 ± 13), female sex, anxiety, and presence of pain behaviors [20]. Five pain trajectories were identified over the range of surgical procedures, with pain assessed with the Patient-Reported Outcomes Measurement Information System (PROMIS).

- Certain surgical procedures (eg, knee arthroplasty) may also have a longer duration of moderate to severe postoperative pain than others [21,22]. (See 'Pain trajectories' below.)

Early preoperative evaluation for some patients — For most patients without complex needs for postoperative analgesia, routinely scheduled, routine preanesthetic evaluation with education and counseling about multimodal analgesia and postoperative pain expectation-setting may be appropriate. However, complex surgical patients such as those with chronic pain or substance use disorder, especially those taking buprenorphine preoperatively [23], will likely benefit from advanced preoperative preparation and coordination between surgery, anesthesiology, pain medicine, and addiction medicine, when applicable. One model of care for managing this subset of complex surgical patients has been described as a transitional pain service [24,25]. In addition to complex preoperative preparation and coordination, the transitional pain service can provide access to pain medicine specialists for patients with inadequately controlled postoperative pain. Such patients may be at higher risk of persistent postsurgical pain. Access to pain medicine specialists as necessary is a basic principle of acute perioperative pain management (table 1) [11].

Patients who take medications long term for chronic pain or substance use disorder are encouraged to continue them perioperatively, including the day of surgery, unless specifically instructed to hold them for surgery (eg, NSAIDs). Buprenorphine, a medication commonly used for opioid use disorder, should not be routinely discontinued in the

perioperative period [23]. (See "Management of acute pain in adults with opioid use disorder", section on 'Whether to continue buprenorphine during pain management'.)

Patients with untreated depression may benefit from starting antidepressant medication in the perioperative period, and continuing as appropriate in coordination with the patient's primary care clinician or with a behavioral medicine specialist.

Shared decision-making, patient expectations and education — Patients should understand that the goal for acute pain management is often not the total absence of pain, but rather an acceptable level of pain that allows the patient to achieve functional goals.

For postoperative analgesia, clinicians should provide individually tailored, patient- and family-centered education that presents treatment options for managing postoperative pain. This is one of the basic principles of acute perioperative pain management and is consistent with shared decision-making (table 1) [11]. Setting realistic expectations for patients about postoperative pain is critical; written educational materials regarding multimodal perioperative analgesia should be provided at the sixth grade reading level [26]. Proper education of patients and engaging them in their own care has been shown to reduce postoperative in-hospital opioid consumption without negatively affecting analgesia [27].

Patient education should include individualized opioid tapering, proper storage of opioids, and options for disposal of unused opioids (table 1) [11].

Patient involvement in decision-making regarding perioperative care has been explored only to a limited extent, and there is currently no standardized way of presenting anesthetic and analgesic options to patients [28]. In addition to education and shared decisions regarding pain management, preoperative consultation on the day of surgery can alleviate anxiety by establishing rapport and trust. As an example, clinicians may set expectations for postoperative recovery and pain treatment by providing clear expectations: "You will have some soreness around the surgical site and discomfort when you swallow or move your neck. We typically treat that with ice packs, acetaminophen, and ibuprofen. Most patients need very little, if any, opioid. We will see how you do and make sure that your pain is adequately controlled with this regimen" [29].

Strategy based on expected degree and duration of pain — Following evaluation and assessment of risk factors that may predispose a patient to greater-than-expected acute pain, a tailored multimodal analgesic plan should be instituted. For all patients, the analgesic strategy starts with nonpharmacologic techniques, non-opioid analgesics, and local or regional analgesia techniques as appropriate. Opioids should be added only as necessary. These options are discussed below. (See 'Options for managing postoperative analgesia' below.)

Multiple recommendations regarding multimodal perioperative pain management (eg, Procedure-specific Postoperative Pain Management (PROSPECT) recommendations) and other society guidelines have been published [9,12]. In general, these recommended regimens serve as checklists (not recipes) and should be modified as needed to be procedure- and patient-specific. When possible, local and regional anesthesia techniques (eg, neuraxial analgesia, peripheral nerve blocks, inter-fascial plane blocks, local infiltration analgesia, wound infiltration) should be used in addition to systemic analgesics. (See 'Regional anesthesia techniques' below.)

Pain trajectories — The expected degree of pain and time course of resolution varies with both patient factors and the type of surgery or injury. For many patients, acute pain peaks at one to three days after injury or surgery, and should be much less by seven days.

In general, peripheral superficial injuries or procedures (eg, carpal tunnel release) should result in mild pain of relatively short duration, moderate pain should be expected after most laparoscopic and other minimally invasive surgeries, most soft tissue surgeries, and non-compound and non-comminuted fractures, and severe pain occurs after major open surgery, spine surgery, and arthroplasty, and may occur after major trauma. However, the degree of pain varies widely within these categories. Knowing that we cannot reliably predict the trajectories of pain resolution and opioid cessation for every patient, we recommended routinely using multimodal analgesia while allowing for individual adjustment (algorithm 1) [13,21].

The literature on expected pain trajectories after most types of surgery is limited. One example of a procedure specific pain trajectory comes from a systematic review of 71 studies (approximately 600 patients) that evaluated pain after total hip arthroplasty [30]. In patients who had general anesthesia (GA), pain peaked in the first two hours after surgery and declined gradually during the first eight hours. In patients who had spinal anesthesia, once the spinal anesthetic wore off the trajectories were similar to the patients who had GA. Notably, there was wide interpatient variability in pain intensity, even in patients who received the same analgesic regimen.

Basic strategy for all patients — For all patients, regardless of the expected degree of pain, perioperative pain management should include nonpharmacologic approaches, acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) unless there are contraindications, and local or regional anesthesia/analgesia techniques when appropriate (algorithm 1 and table 2).

It is reasonable to create a management strategy based on the expected or existing degree of pain and the likely trajectory. However, the expected degree of pain and time course of resolution vary with both patient factors and the type of surgery and may be difficult to predict, and the degree of pain may not fit into discrete categories of mild, moderate or

severe pain. Thus, patients should be monitored for pain, function, and side effects of therapies, and management adjusted accordingly. (See 'Adjusting the plan' below.)

Expected mild pain — For patients who have mild pain or are expected to have mild postoperative pain, the basic strategy described above may be sufficient. A discharge prescription for oral opioids is usually not necessary, and should involve a shared decision between the prescribing clinician, patient, and caregiver, if applicable.

Expected moderate pain — For these patients, in addition to the basic strategy described above, we add the following:

- If regional block techniques are used, a continuous perineural infusion of local anesthetic may be beneficial if moderate pain is expected to last ≥2 days.
- Opioids may be prescribed in oral and/or intravenous formulations on an as-needed basis in the hospital. (table 3) A discharge prescription for oral opioids should be a shared decision between the prescribing clinician, patient, and caregiver, if applicable, and tailored to the individual patient with clear instructions for tapering and cessation. (See "Use of opioids for postoperative pain control".)

Expected severe pain — For patients with existing or expected severe pain, we use the basic strategy described above for all patients, and in addition:

- If regional block techniques are used, a continuous perineural infusion of local anesthetic may be beneficial if severe pain is expected to last ≥2 days.
- For some patients, single injection neuraxial opioid or continuous neuraxial analgesia may be indicated. (See "Continuous epidural analgesia for postoperative pain: Technique and management".)
- Gabapentinoids, ketamine infusion, and lidocaine infusion may be indicated for selected patients, and are often used concurrently. (See 'Nonopioid analgesics and adjuncts' below and "Nonopioid pharmacotherapy for acute pain in adults", section on 'Options for nonopioid pharmacotherapy'.)
- Opioids may be prescribed in oral and/or intravenous formulations. For patients with severe pain who receive oral opioids, we usually prescribe them on a scheduled basis for the first two to three days, or longer if necessary, and then change to as needed administration. Patient-controlled analgesia (PCA) with intravenous opioids may be indicated, especially in patients who are not able to take oral medications.
- A discharge prescription for oral opioids should be a shared decision between the prescribing clinician, patient, and caregiver, if applicable, and tailored to the

individual patient with clear instructions for tapering and cessation. (See "Use of opioids for postoperative pain control".)

Options for managing postoperative analgesia

Nonpharmacologic therapy — Nonpharmacologic interventions are an essential part of multimodal analgesia and should be routinely included in the acute perioperative pain management plan [31].

Psychological therapy — We do not routinely suggest preoperative psychological therapy, though it may be helpful for some patients. As examples, anxiety and depression have been associated with prolonged time to resolution of postoperative pain [32], and there may be an association between pain catastrophizing and greater pain interference and intensity [18,19]. These psychological conditions are amenable to behavioral therapy in other settings, but consistent benefits of behavioral therapy for acute pain management have not been established. Cognitive-behavioral therapy (CBT) has been suggested as an intervention to manage emotional intensity and its role in pain [33]. However, in a randomized trial of 80 patients with high catastrophizing scores who underwent total knee arthroplasty, preoperative CBT reduced catastrophizing scores but did not improve three month pain outcomes [34]. Psychological interventions delivered after surgery or traumatic injury may also be effective in reducing acute and subacute pain [35].

Patient education can be considered a form of psychological therapy, as it can reduce anxiety about postoperative pain. (See 'Shared decision-making, patient expectations and education' above.)

Other nonpharmacologic options — Other potential nonpharmacologic options for pain management include compression and elevation, cryotherapy (eg, icing), acupuncture, transcutaneous electrical stimulation, and music [31,36]. These techniques are low risk, and may be beneficial, though robust supporting evidence is lacking and some are not available in some institutions.

Nonopioid analgesics and adjuncts — For preventive analgesia, non-opioid systemic analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, antiseizure medications, and alpha$_2$agonists can in some cases replace opioids, or can be effectively combined with opioids as part of a perioperative multimodal analgesic regimen, especially for opioid-tolerant patients (table 2) [37,38]. While most commonly used for perioperative pain, these agents can be considered for inpatients with moderate to severe acute pain unrelated to surgery. The nonopioid analgesics we use most frequently are discussed briefly here. Nonopioid analgesics used for acute pain are discussed in more detail separately. (See "Nonopioid pharmacotherapy for acute pain in adults".)

- **Acetaminophen and NSAIDs –** NSAIDs and acetaminophen are typically included in multimodal analgesic protocols. In our practice, we administer acetaminophen with nonselective NSAIDs or celecoxib before surgery for postoperative pain in most patients without contraindications to the drugs.

  Acetaminophen and NSAIDs have different mechanisms of action, and most studies have found that the combination is more effective than either drug alone [39], though the benefits may be procedure specific, and may not apply to all surgeries [40]. A systematic review of randomized trials found that the combination of acetaminophen (paracetamol) with NSAID was more effective for postoperative pain after a variety of surgical procedures than acetaminophen or NSAID alone in 85 percent and 64 percent of studies, respectively [39]. (See "Nonopioid pharmacotherapy for acute pain in adults", section on 'Acetaminophen' and "Nonopioid pharmacotherapy for acute pain in adults", section on 'Nonsteroidal anti-inflammatory drugs'.)

- **Gabapentinoids –** Use of gabapentinoids (gabapentin and pregabalin) as part of multimodal postoperative analgesia has become controversial, and practice varies, including among UpToDate contributors. Some studies have found reduced postoperative opioid requirements after some surgical procedures, whereas others have not found benefit. The decision to use gabapentinoids must balance the potential improved postoperative analgesia against side effects of sedation, dizziness, and respiratory depression when combined with opioids. The author of this topic does not advise routine prescribing of gabapentinoids but considers administering gabapentinoids for specific patients expected to have moderate to severe postoperative pain who already use gabapentinoids preoperatively, use opioids chronically, or have chronic neuropathic pain conditions. (See "Nonopioid pharmacotherapy for acute pain in adults", section on 'Gabapentinoids'.)

- **Ketamine –** Perioperative administration of low-dose intravenous ketamine has been shown to provide opioid-sparing analgesia and to prevent hyperalgesia [41]. We usually administer ketamine for patients with chronic pain (especially those on long term opioid therapy) who are expected to have severe postoperative pain, and who have general anesthesia without regional anesthesia techniques. Ketamine is associated with potential side effects [42] and therefore should be used selectively and in the appropriate setting. (See "Nonopioid pharmacotherapy for acute pain in adults", section on 'Ketamine'.)

- **Intravenous lidocaine –** IV lidocaine can be administered by infusion intraoperatively and/or postoperatively for the management of pain. We use IV lidocaine for some patients as part of a multimodal pain strategy when regional anesthesia techniques are not possible. Whenever IV lidocaine is administered, the possibility of local anesthetic

systemic toxicity should be considered. (See "Nonopioid pharmacotherapy for acute pain in adults", section on 'Intravenous lidocaine'.)

- **Glucocorticoids** – Glucocorticoids (most commonly dexamethasone) are usually administered intraoperatively for prevention of PONV or at the request of the surgeon to reduce postoperative edema (eg, during spine or airway surgery), but these medications may also improve pain control since edema, inflammation, and pain are interrelated. (See "Nonopioid pharmacotherapy for acute pain in adults", section on 'Glucocorticoids'.)

- **Alpha-2-receptor agonists** – The author does not routinely use either clonidine or dexmedetomidine for postoperative analgesia. Some others use clonidine to mitigate side effects of ketamine, and dexmedetomidine to reduce emergence delirium. The literature on the analgesic efficacy of clonidine and dexmedetomidine is scant. (See "Nonopioid pharmacotherapy for acute pain in adults", section on 'Alpha-2 receptor agonists'.)

- **Skeletal muscle relaxants** – Non-benzodiazepine skeletal muscle relaxants (eg, cyclobenzaprine, baclofen, tizanidine) may be beneficial for patients with acute pain from postoperative muscle spasm. Muscle relaxants may be of benefit for other types of acute pain, though evidence is limited [43,44]. (See "Treatment of acute low back pain", section on 'Combination with muscle relaxants'.)

  Skeletal muscle relaxants are sedating and should be used cautiously in patients who receive opioids and other medications that may also cause sedation and/or respiratory depression.

Regional anesthesia techniques — Whenever possible, local anesthesia, neuraxial analgesia, or peripheral nerve blocks should be used as part of the multimodal regimen for postoperative pain control. In some cases, a regional analgesic or anesthetic technique will provide adequate pain control without additional systemic medication (eg, brachial plexus block for upper extremity surgery). In other cases, opioids or nonopioid analgesics will be required in addition to one of these modalities. As an example, transversus abdominis plane blocks or local anesthetic wound infiltration may alleviate incisional pain for intraabdominal and abdominal wall surgery (eg, hernia repair) but will not help with visceral pain that results from these procedures.

The location of the surgery and anticipated sites of pain determine which nerve blocks should be performed, at which level(s) they should be performed, and whether they are even indicated. As an example, in a patient having upper abdominal surgery for whom epidural analgesia cannot be used, other regional block techniques (eg, paravertebral or fascial plane

blocks) may contribute to pain relief, although additional systemic analgesia using opioids and nonopioid medications in a multimodal regimen will be required.

For some common major surgical procedures (eg, lower extremity arthroplasty), there are international consensus recommendations for the use of regional anesthesia techniques both intra and postoperatively [45,46].

General considerations for regional anesthesia, including indications and contraindications, are discussed separately. (See "Overview of peripheral nerve blocks", section on 'Indications' and "Overview of neuraxial anesthesia".)

Techniques for performing neuraxial anesthesia/analgesia and various peripheral nerve blocks are discussed in topics on individual techniques.

Wound infiltration — For most operations, even those with very small incisions, the surgeon typically injects local anesthetic at the incision site(s). This practice is low risk, and may provide short term analgesia for some patients. However, the literature regarding wound infiltration is conflicting, with some studies finding decreases in pain scores or postoperative analgesic consumption, and others finding no benefit [47-51]. Studies comparing pre-incision wound infiltration with injection at the end of surgery have also been conflicting. In a meta-analysis of randomized trials that compared preincision versus postincision use of various analgesic techniques, preincision injection of local anesthetic decreased postoperative analgesic consumption and increased time to first rescue analgesic request, but pain scores were similar with pre- or postincision injection [47]. If effective, wound infiltration reduces somatic pain, but does not affect visceral pain.

Periarticular infiltration — Local anesthetic infiltration around the joint is part of many analgesic protocols for hip and knee arthroplasty. This is referred to as periarticular injection (PAI) or local infiltration analgesia (LIA). The efficacy and technique are discussed separately. (See "Anesthesia for total knee arthroplasty", section on 'Periarticular injection (PAI)/local infiltration analgesia (LIA)'.)

Opioids

- **Opioid avoidance** – The epidemic of opioid overdose deaths has received a great deal of attention within health care settings due to the contribution of prescription opioids [52], and the role of surgery as the initial patient exposure to opioids [53]. (See "Risk of long term opioid use and misuse after prescription of opioids for pain", section on 'Surgery'.)

  One response to the opioid epidemic in the perioperative period has been the promotion of opioid avoidance or "opioid-free" anesthesia and analgesia [54]. While there are situations in which regional anesthesia may be used as the primary

anesthetic, making intraoperative opioids unnecessary [55], there is no convincing evidence that arbitrarily avoiding opioids when they are indicated has any beneficial effect on outcomes [56,57]. Instead, a pragmatic approach to opioid prescribing considers their use only when they are indicated and puts safeguards in place to prevent opioid-related adverse events [58]. (See "Use of opioids for postoperative pain control" and "Perioperative uses of intravenous opioids in adults: General considerations", section on 'Opioid-free and opioid-sparing anesthetic techniques'.)

- **Opioid formulations** – Oral opioids should be used whenever possible for patients who require opioids after surgery. When IV opioids are prescribed for patients who are unable to take oral medications, patient controlled analgesia (PCA) may be indicated if the patient is awake, aware, and capable of pressing the bolus delivery button. Commonly used opioids and PCA regimens for opioid naïve adults are shown in tables (table 3 and table 4). (See "Use of opioids for postoperative pain control", section on 'Inpatient postoperative pain control'.)

  For patients who are prescribed oral opioids, we agree with an international multidisciplinary consensus that short acting (rather than extended release/long acting) formulations should be used as a first line in most situations [58]. Combined formulations that include an opioid with acetaminophen or an NSAID should be avoided, and each medication should be prescribed separately to maximize non-opioid analgesic use and minimize opioid use to the lowest effective amount.

  Use of opioids for postoperative pain is discussed in detail separately. (See "Use of opioids for postoperative pain control" and "Management of acute pain in opioid naïve adults in the ambulatory setting".)

POSTOPERATIVE MONITORING FOR PAIN CONTROL AND SIDE EFFECTS

Assessment of pain — We suggest using a validated pain assessment tool to track effectiveness of treatment and adjust management (table 1) [11]. At the author's institution, patients are routinely assessed with numeric rating scales, as they are most commonly used by nurses. We use the Defense and Veterans Pain Rating Scale(DVPRS) to assess patients who require a balance of analgesia and functional goals (eg, after arthroplasty or spine surgery). (See 'Assessing function' below.)

- **Numeric scales** – The visual analog scale (VAS) and 11-point (0, no pain; 10, worst pain imaginable) numeric rating scale (NRS) are both validated assessment tools for pain intensity and have been shown to have a high level of agreement (figure 7) [59]. A limitation of the VAS is that it requires the patient to have vision, dexterity, and understanding if using a paper tool or slide ruler. VAS and NRS provide a patient's level

of pain intensity in that moment. When using either scale to estimate pain scores for a wider time frame (eg, prior 24 hours), the data collected are subject to bias.

For children and non-verbal adults, the faces pain rating scale is a validated tool that can be used instead of VAS or NRS (form 1) [60].

- **Pain at rest versus with movement –** A key tenet of enhanced recovery protocols is the provision of dynamic analgesia that facilitates early mobilization and rehabilitation [61]. Assessing only pain at rest will be unlikely to distinguish the effectiveness of acute pain interventions [59].

Assessing function — For many patients, it is important to assess functional outcomes concurrently with pain. For example, studies of the efficacy of continuous postoperative nerve blocks in patients who undergo knee arthroplasty (in whom postoperative ambulation is a functional goal) have shown relatively stable pain scores with movement while steadily progressing in total ambulation distance achieved, six-minute walking test distance, and knee flexion over a multi-day period [62,63].

Innovative pain assessment tools factor in pain interference. Examples include the Functional Pain Scale [64], Brief Pain Inventory (BPI) [65], specific domains in the Patient-Reported Outcomes Measurement Information System (PROMIS) [66], and DVPRS [67]. DVPRS integrates a numeric rating scale with faces, pain interference language to provide context to the numerical anchors, and four supplemental questions that assess the influence of pain on the patient's activity, sleep, mood, and stress [67].

ADJUSTING THE PLAN

Pain management may require modification for either lack of optimal efficacy or unacceptable side effects. The stepwise escalation of pain treatment interventions is intended to prevent opioid-related harm [58]. The validated assessment tools mentioned previously such as BPI, PROMIS, and DVPRS, which factor in pain interference, should be used for this purpose. For consistency, whichever tool is chosen should be used throughout the perioperative period for any given patient.

If patients require modification of the initial plan because of pain, first steps should include increases in or additions to nonopioid analgesia, as appropriate (eg, institution or modification of regional anesthesia techniques, additional nonopioid analgesics [ketamine, lidocaine]). If necessary after maximizing nonopioid strategies, opioids can be added, doses increased, or changed from as needed to regularly scheduled administration, or changed to intravenous administration. (See "Use of opioids for postoperative pain control", section on

'Oral dose adjustments' and "Use of opioids for postoperative pain control", section on 'PCA dose adjustments'.)

If patients develop unacceptable side effects, the offending drug or technique may be discontinued, doses reduced, or the technique modified. (See "Continuous epidural analgesia for postoperative pain: Technique and management" and "Use of opioids for postoperative pain control".)

Patients who continue to have greater than expected acute pain or a longer duration of pain or opioid use than expected despite multiple interventions should be referred to a pain medicine specialist, either a clinician specializing in chronic pain or a transitional pain service if available [11,68].

TRANSITIONING BETWEEN AND OFF ANALGESIC STRATEGIES

There should be a specific plan to de-escalate analgesic use, particularly for patients who have moderate to severe pain and receive opioids. The goal for these patients is to decrease opioids as pain resolves as soon as possible, guided by assessment of function and pain. Patients should be involved and aware of the plan, with clear expectations for adequate (not complete) analgesia and functional goals. There is no right way to make transitions, and the strategy must be individualized. Some reasonable guidance is provided here.

- **Discontinuing regional anesthesia techniques –** Continuous epidural or peripheral nerve blocks are typically used for a few days to a week, and are often discontinued when pain improves and is well controlled with oral analgesics. If there is any question, one option is to discontinue the infusion for several hours before removing the catheter. For patients with a perineural catheter in place at the time of planned discharge, we sometimes bolus the catheter prior to discharge. This may provide analgesia for the patient's first night at home.

- **Switch from IV to oral opioids –** Patients with severe pain often use PCA for several days, after which they should transition to oral opioids if able to take medications by mouth. (See "Use of opioids for postoperative pain control", section on 'Transition from IV to oral opioid'.)

- **Taper and discontinue oral opioids –** As pain improves, oral opioids may be tapered by increasing the dosing interval, decreasing the dose, or both, while continuing non-opioid analgesics. Another option is to switch from a full mu opioid agonist (eg, oxycodone) to tramadol, and then wean tramadol as for other opioids. (See "Use of opioids for postoperative pain control", section on 'Discontinuing opioids'.)

- **Nonopioid analgesics** – Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) are often used until hospital discharge, and are tapered and discontinued by the patient at home. Postoperative use and discontinuation of other non-opioid analgesics (eg, gabapentinoids, ketamine, lidocaine) are discussed separately. (See "Nonopioid pharmacotherapy for acute pain in adults".)

SPECIAL POPULATIONS

Patients with obesity and/or obstructive sleep apnea (OSA) — Similar to patients without obesity or OSA, multimodal opioid sparing analgesia should be routinely used for these patients. Postoperative pain management in patients with obesity and in patients with OSA is discussed separately. (See "Anesthesia for the patient with obesity", section on 'Management of postoperative pain' and "Postoperative management of adults with obstructive sleep apnea", section on 'Pain control'.) General considerations include the following:

- Regional anesthesia techniques may be more difficult in patients with obesity. There may be a higher incidence of peripheral, but not neuraxial, catheter related infections. (See "Anesthesia for the patient with obesity", section on 'Peripheral nerve blocks'.)

- Patients with OSA may have increased pain perception, and therefore increased analgesic requirements, compared with patients without OSA, as well as enhanced sensitivity to the respiratory depressant effects of opioids. These combined effects may predispose patients with OSA to postoperative respiratory depression, particularly in the first 24 hours after surgery. (See "Postoperative management of adults with obstructive sleep apnea", section on 'Pain control'.)

Patients who are opioid tolerant — For patients who take opioids chronically (for pain, for management of OUD, or due to illicit use), the general principles of acute pain management are to continue the baseline opioid, maximize nonopioid analgesic strategies, and add supplemental opioids only as necessary. These issues are discussed in detail separately. (See "Management of acute pain in adults with opioid use disorder" and "Management of acute pain in the patient chronically using opioids for non-cancer pain".)

Pregnant patients — Pain management after nonobstetric surgery in pregnant patients is similar to nonpregnant patients, with the possible exception of avoiding nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs should not be used routinely during pregnancy (particularly in the early first and late third trimesters) because of potential fetal effects, although a single dose for refractory postoperative pain in mid-gestation is likely safe. (See "Anesthesia for nonobstetric surgery during pregnancy", section on 'Postoperative care' and

"Safety of rheumatic disease medication use during pregnancy and lactation", section on 'NSAIDs'.)

Management of pain after cesarean delivery is discussed in detail separately. (See "Post-cesarean delivery analgesia".)

Patients who are breastfeeding — Anesthetic and nonopioid analgesic drugs are generally safe for use while breastfeeding, because they are transferred to breast milk in only very small amounts. For almost all drugs used perioperatively, there is no evidence of adverse effects on the breastfed infant. However, there is little or no information on the transfer of dexmedetomidine or ketamine to breast milk, and current recommendations are to avoid ketamine for breastfeeding women if possible. Opioids should be used with caution, especially after multiple doses and for mothers of infants <6 weeks old (table 5). (See "Preoperative evaluation for anesthesia for noncardiac surgery", section on 'Breastfeeding women'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Acute pain management".)

SUMMARY AND RECOMMENDATIONS

- **General approach**
  - Optimal perioperative analgesia may require balancing analgesia with achieving functional goals, while avoiding preventable complications. (See 'Goals and principles for acute pain management' above.)
  - We suggest a multimodal approach to analgesia for acute pain, rather than the use of opioids alone (**Grade 2C**), with nonpharmacologic techniques, regional anesthesia techniques as appropriate, nonopioid analgesics, and opioids as necessary (table 1). Multimodal analgesia decreases reliance on a single class of agents, reduces side effects, and can minimize the use of opioids. (See 'Use multimodal analgesia' above and 'Minimize opioids' above.)
- **Preoperative assessment**
  - Preoperative evaluation should include assessment of medical and psychological factors that may affect the plan for analgesia. (See 'Patient evaluation' above.)

- Complex patients (eg, those with chronic pain, opioid dependence, or opioid use disorder) may benefit from advanced preoperative multidisciplinary preparation. (See 'Early preoperative evaluation for some patients' above.)
- Patients should receive preoperative education on analgesic options and expected goals for pain relief. (See 'Shared decision-making, patient expectations and education' above.)

- **Basic strategy for all patients –** For all patients, perioperative pain management should include nonpharmacologic approaches, acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) and local or regional anesthesia/analgesia techniques when appropriate (algorithm 1 and table 2) (See 'Basic strategy for all patients' above.)

- **Strategy based on the expected degree of pain**

  - **Expected mild pain –** The basic strategy may be sufficient, without the addition of opioids. (See 'Expected mild pain' above.)

  - **Expected moderate pain –** In addition to the basic strategy, options include continuous regional anesthesia techniques, gabapentinoids for select patients, and as needed opioids (table 3) (See 'Expected moderate pain' above.)

  - **Expected severe pain –** In addition to the basic strategy, options include neuraxial analgesia techniques, continuous peripheral nerve blocks, gabapentinoids, ketamine or lidocaine infusions, and opioids on an as needed basis (oral or intravenous). (See 'Expected severe pain' above.)

- **Postoperative monitoring**

  - Patients should be monitored postoperatively for pain relief, functional status, and for side effects of analgesics, and the management plan adjusted accordingly. Pain should be assessed with a validated tool. (See 'Postoperative monitoring for pain control and side effects' above.)

- **Transition between and off analgesic strategies –** The tapering and discontinuation of components of multimodal analgesia should be individualized with a goal of reducing and stopping opioids as soon as possible. This usually involves continuing nonpharmacologic and nonopioid analgesics, while decreasing the dose and interval of opioids, and ultimately stopping opioids as pain improves. (See 'Transitioning between and off analgesic strategies' above.)

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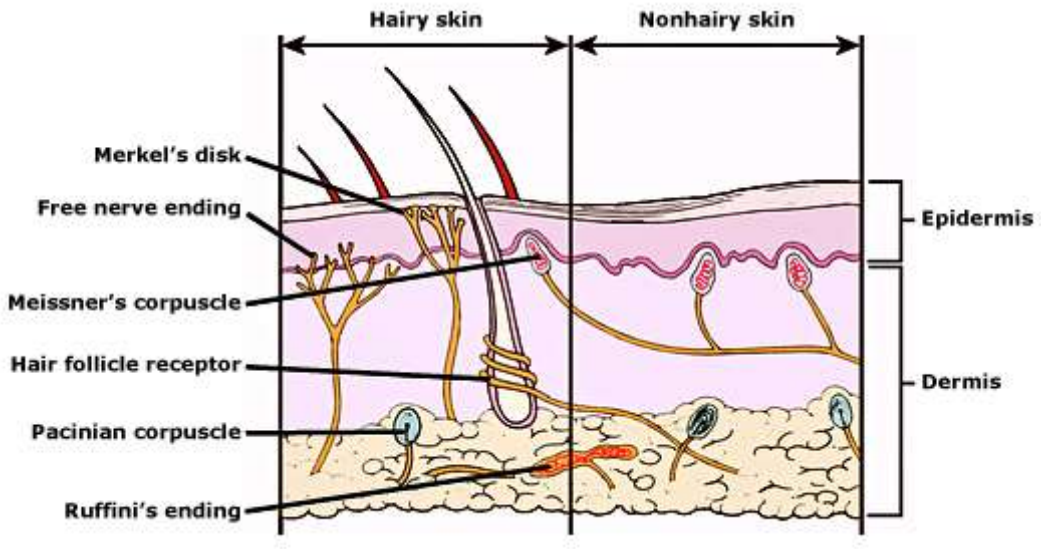
Topic 130312 Version 5.0

GRAPHICS

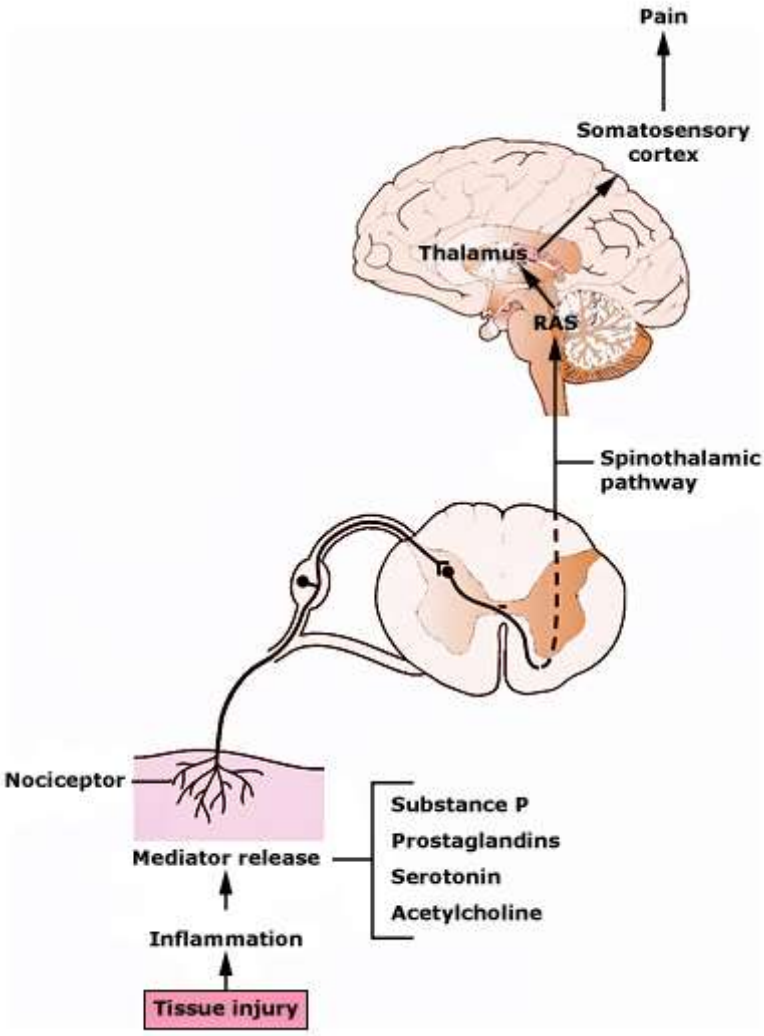
Somatic sensory receptors in the skin



Hairy and nonhairy skin have a variety of sensory receptors within the skin.

Graphic 56118 Version 4.0

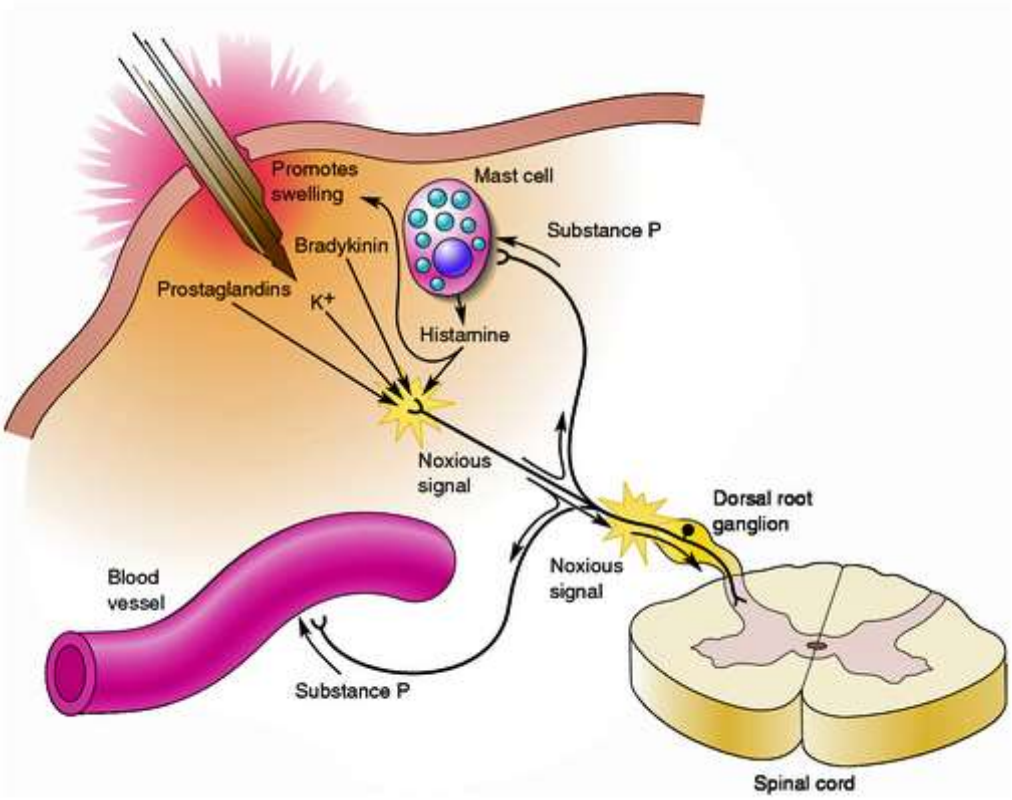
Mechanism of acute pain



Tissue injury leads to release of inflammatory mediators with subsequent nociceptor stimulation. Pain impulses are then transmitted to the dorsal horn of the spinal cord, where they make contact with second-order neurons that cross to the opposite side of the cord and ascend via the spinothalamic tract to the reticular activating system (RAS) and thalamus. The localization and meaning of pain occurs at the level of the somatosensory cortex.

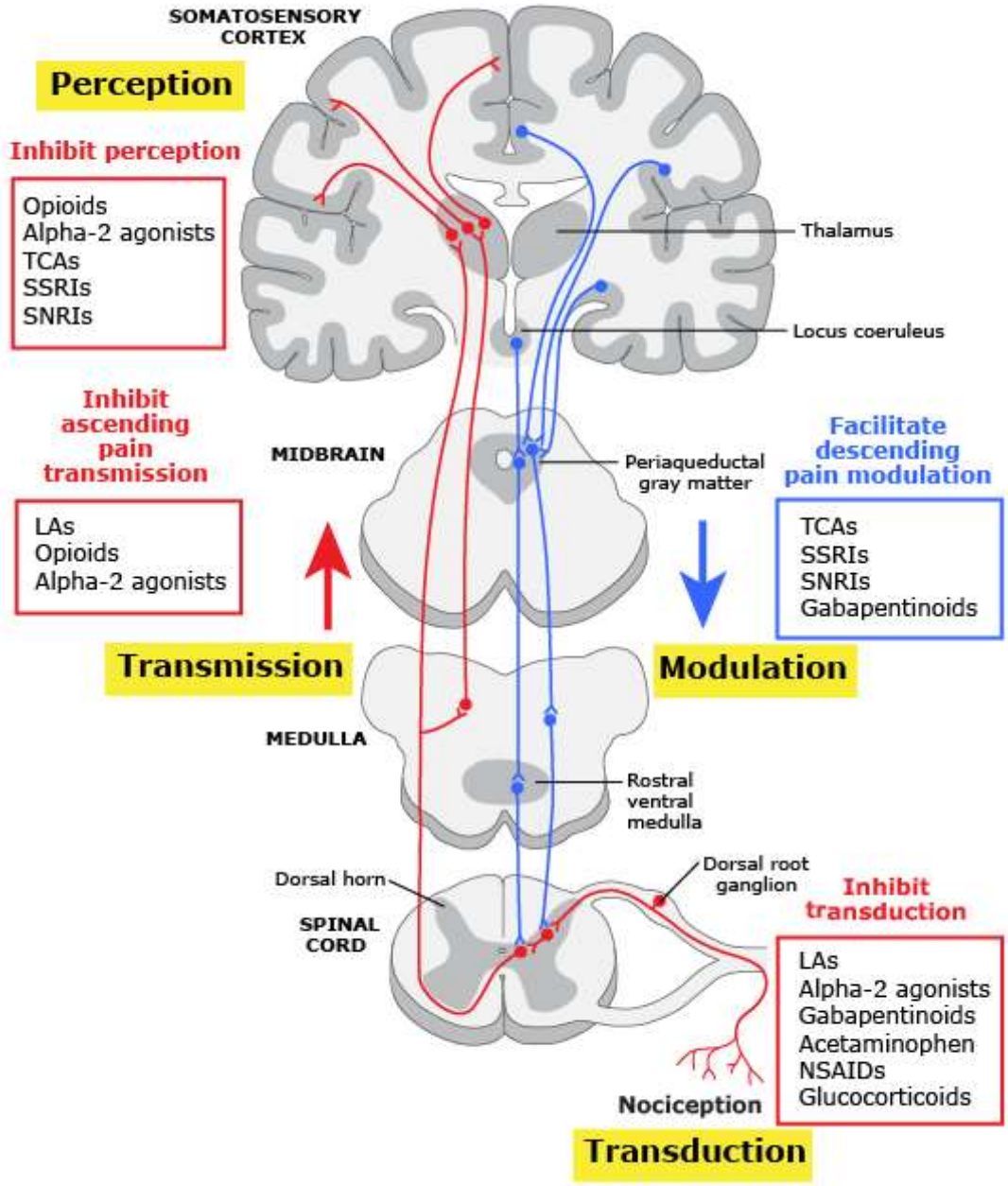
Graphic 74589 Version 4.0

Peripheral chemical mediators of pain and hyperalgesia



Graphic 53674 Version 5.0

Pain pathways and mechanisms

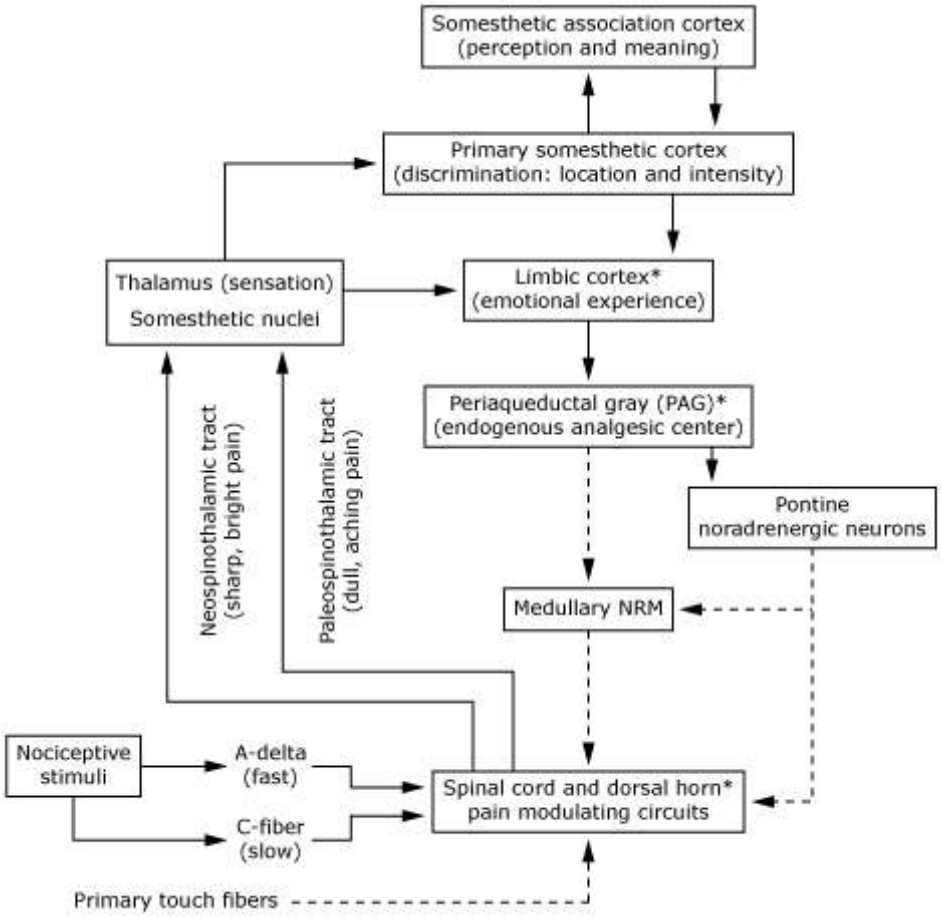


This graphic shows the four major processes of pain transmission and what are thought to be the primary sites of action of medications that affect those processes.

TCA: tricyclic antidepressant; SSRI: selective serotonin reuptake inhibitor; SNRI: serotonin-norepinephrine reuptake inhibitor; LA: local anesthetic; NSAID: nonsteroidal anti-inflammatory drug.

Graphic 140280 Version 1.0

Central perception of pain



The transmission of incoming nociceptive impulses is modulated by dorsal horn circuitry that receives input from peripheral touch receptors and from descending pathways that involve the limbic cortical systems (orbital frontal cortex, amygdala, and hypothalamus), periaqueductal endogenous analgesic center in the midbrain, pontine noradrenergic neurons, and the nucleus raphe magnus (NRM) in the medulla. Dashed lines indicate inhibition or modulation.

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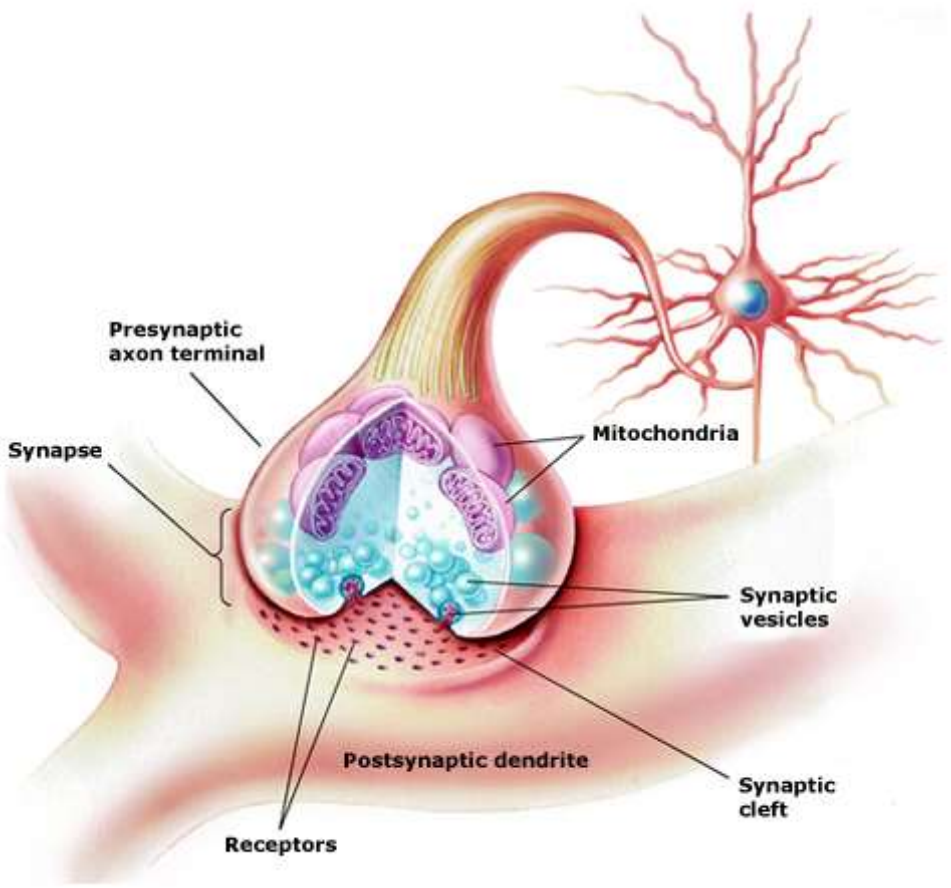
* Location of opioid receptors.

Graphic 60488 Version 1.0

The axon terminal and the synapse



Axon terminals form synapses with the dendrites or somata of other neurons. When a nerve impulse arrives in the presynaptic axon terminal, neurotransmitter molecules are released from synaptic vesicles into the synaptic cleft. Neurotransmitter then binds to specific receptor proteins, causing the generation of electrical or chemical signals in the postsynaptic cell.

Graphic 76587 Version 1.0

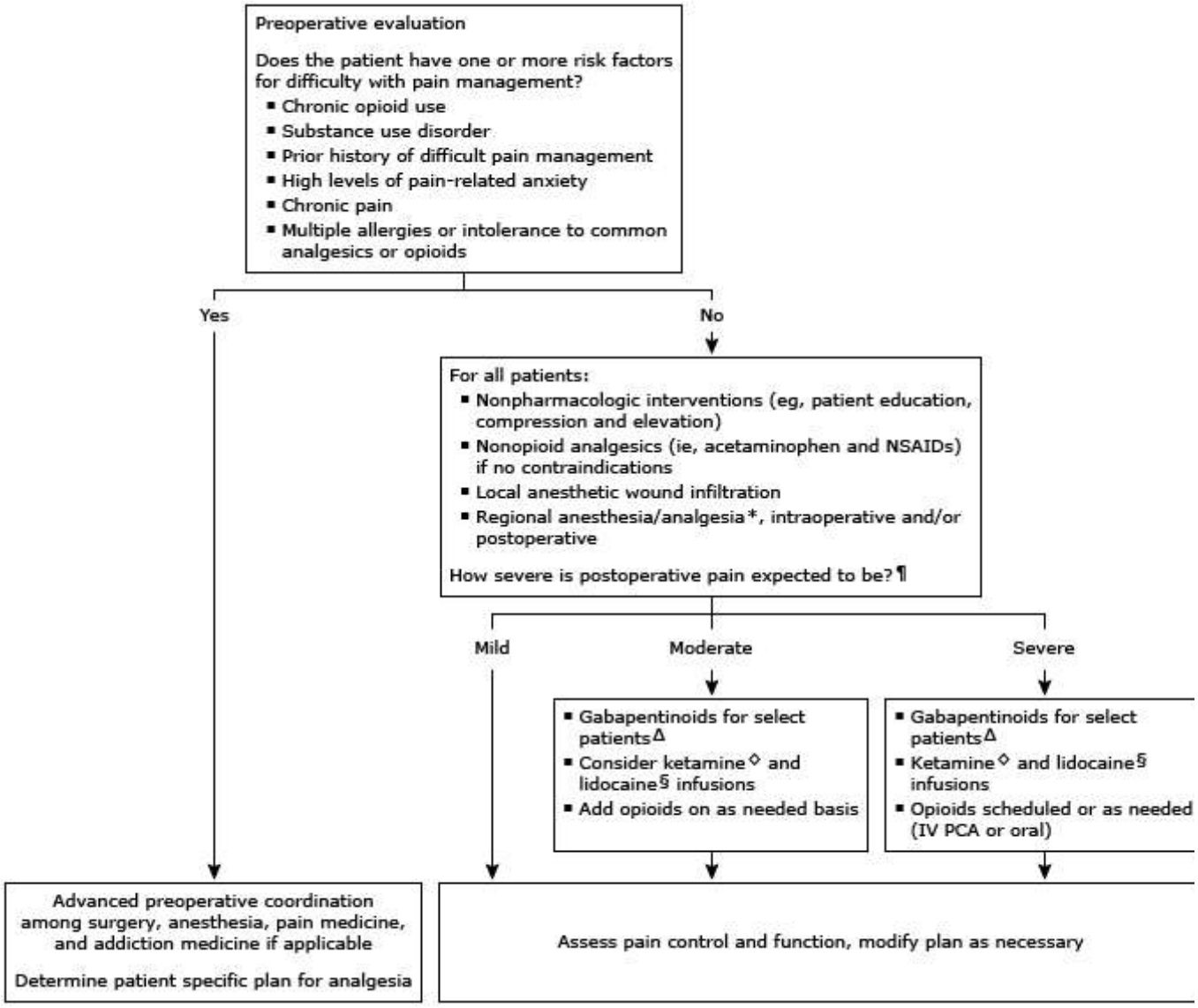
Guiding principles for acute perioperative pain management

Conduct a preoperative evaluation including assessment of medical and psychologic conditions, concomitant medications, history of chronic pain, substance abuse disorder, and previous postoperative treatment regimens and responses, to guide the perioperative pain management plan.
Use a validated pain assessment tool to track responses to postoperative pain treatments and adjust treatment plans accordingly.
Offer multimodal analgesia, or the use of a variety of analgesic medications and techniques combined with nonpharmacologic interventions, for the treatment of postoperative pain in adults.
Provide patient- and family-centered individually tailored education to the patient (and/or responsible caregiver), including information on treatment options for managing postoperative pain, and document the plan and goals for postoperative pain management.
Provide education to all patients (adult) and primary caregivers on the pain treatment plan, including proper storage and disposal of opioids and tapering of analgesics after hospital discharge.
Adjust the pain management plan based on adequacy of pain relief and presence of adverse events.
Have access to consultation with a pain specialist for patients who have inadequately controlled postoperative pain or are at high risk of inadequately controlled postoperative pain at their facilities (eg, long-term opioid therapy, history of substance use disorder).

This table shows the principles for perioperative pain management issued by the multidisciplinary Perioperative Pain Summit Consortium.

Graphic 133183 Version 1.0

Perioperative pain management in adults



This algorithm shows an overall approach to perioperative pain management with a multimodal opioid sparing strategy. It should be used in conjunction with UpToDate content on management of acute pain

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* Neuraxial or peripheral block with or without a catheter, wound infiltration, or wound infusion.

¶ The expected degree of pain and time course of resolution vary with both patient factors and the type of surgery, and may be difficult to predict. In general, peripheral superficial procedures (eg, carpal tunnel release) should result in mild pain of relatively short duration; moderate pain should be expected after most laparoscopic and other minimally invasive surgeries and most soft tissue surgeries; and severe pain occurs after major open surgery, spine surgery, and arthroplasty.

Δ Use of gabapentinoids for postoperative pain is controversial and practice varies. Consider gabapentinoids for patients <75 years of age who undergo moderately to severely painful surgery.

◇ Consider ketamine for patients who would benefit from maximal opioid avoidance (eg, patients who are opioid tolerant, with opioid use disorder, or who have obstructive sleep apnea).

§ Consider lidocaine for patients who undergo spine surgery or open abdominal surgery when epidural analgesia is not used.

Graphic 139595 Version 1.0

Nonopioid analgesics commonly used for perioperative pain in adults

Drug	Suggested dosing	Timing of administration	Comments
Acetaminophen (paracetamol)	Oral: 325 to 1000 mg every 4 to 6 hours; maximum dose 4 g per day IV: ▪ Weight ≥50 kg: 650 mg every 4 hours or 1000 mg every 6 hours, maximum dose 4 g per day ▪ Weight <50 kg or with chronic alcoholism, malnutrition, or dehydration: 12.5 mg/kg every 4 hours or 15 mg/kg every 6 hours, maximum 750 mg/dose, maximum 3.75 g/day	Preoperative, intraoperative, and postoperative	▪ Avoid regularly scheduled administration concomitantly with other medications that include acetaminophen (ie, combination drugs), to reduce risk of exceeding daily maximum dose ▪ No clinical advantage to IV form pre- and postoperatively in patients able to take oral form ▪ Avoid use in patients with alcoholic hepatitis, severe hepatic impairment, or severe active liver disease ▪ Oral acetaminophen at a reduced dose of 2 g per day is used safely in most patients with cirrhosis or advanced chronic liver disease ▪ Use acetaminophen cautiously in patients with mild to moderate hepatic impairment, (eg, limit to maximum 3g per day)
Nonsteroidal anti-inflammatory drugs (NSAIDs)			
Celecoxib	200 to 400 mg orally preoperatively; 200 mg orally every 12 to 24 hours postoperatively	Preoperative*, intraoperative, and postoperative until hospital discharge	▪ Use with caution or avoid in patients with kidney dysfunction, cardiovascular disease, or peptic ulcer disease ▪ Use with caution in those at high bleeding risk, especially

Diclofenac	50 mg orally every 6 to 12 hours, maximum 150 mg in 24 hours		those taking concomitant anticoagulants ▪ All NSAIDs have US FDA boxed warning for risk of cardiovascular thrombotic events including MI and stroke; risk may be higher for COX-2-selective NSAIDs (eg, celecoxib) ▪ NSAIDs are contraindicated for patients having coronary artery bypass surgery
Ibuprofen	600 to 800 mg orally or IV every 6 to 8 hours		
Ketoprofen	50 to 75 mg orally every 6 to 8 hours		
Naproxen (base)	500 mg orally every 12 hours		
Ketorolac[¶]	Weight ≥50 kg and age <65 years: 15 to 30 mg IV every 6 to 8 hours Weight <50 kg or age ≥65 years: 15 mg IV every 6 to 8 hours		
Meloxicam[Δ]	15 mg orally (conventional tablet) or 30 mg IV once per day		
Gabapentinoids			
Pregabalin	75 to 150 mg orally once (preoperatively); 75 mg orally every 12 hours (postoperatively)	Preoperative, postoperative until hospital discharge for patients with moderate to severe pain	▪ Synergistic respiratory depression when administered with opioids ▪ Evidence of perioperative benefit versus risk is uncertain, particularly for gabapentin ▪ Use reduced dose in kidney impairment ▪ Dose-dependent ataxia and somnolence; use reduced dose or avoid in older adults
Gabapentin	300 to 600 mg orally every 8 hours		
Ketamine	Intraoperative: Bolus 0.25 to 0.5 mg/kg IV (maximum 35 mg) followed by an infusion of 0.1 to 0.5 mg/kg/hour (2	Intraoperative; postoperative should be considered if local policy allows	▪ Reserve use for painful surgery in hospitalized patients ▪ Consider adding clonidine and low dose benzodiazepine as needed to mitigate adverse effects

	to 8 mcg/kg/minute)		(eg, emergence reaction, hypertension) ▪ Reduce or discontinue 45 to 60 minutes before end of surgery to avoid prolonged emergence ▪ Reduce dose in patients with liver disease
Lidocaine	Bolus: 1 mg/kg IBW IV near time of induction Infusion: 1 to 2 mg/kg IBW/hour intraoperatively	Intraoperative; postoperative may be considered if local policy allows and surgery is associated with high degree of inflammation (ie, abdominal surgery, breast, or spine surgery)	▪ Benefit likely limited to 24 hours postoperatively ▪ If titrating infusion outside of operating room patient should be in a monitored setting (eg, PACU or ICU) ▪ Not consistently shown to worsen cardiac conduction delays ▪ Reduce dose in patients with liver disease ▪ In underweight patients, use actual body weight to calculate dose
Dexamethasone	4 to 8 mg IV or orally every 8 hours	Preoperative, intraoperative, and postoperative	▪ May improve analgesia and reduce PONV; dosing at higher end of range may be needed for analgesia ▪ May prolong duration of peripheral nerve blocks ▪ Causes transient hyperglycemia, not associated with increased surgical complications
Alpha-2-receptor agonists			
Clonidine	IV: 1 to 4 mcg/kg once Oral: 200 to 300 mcg once Transdermal patch: 0.2 mg/24 hours for patients receiving ketamine infusions for multiple days	Preoperative and postoperative	▪ Used to mitigate adverse effects of ketamine, particularly when ketamine is administered for two days or more or at high doses

Dexmedetomidine	Loading dose, if hemodynamically stable (may be omitted): ≤0.5 mcg/kg IV over 10 to 15 minutes Infusion: 0.3 to 0.7 mcg/kg/hour	Intraoperative and postoperative	▪ Used for patients who undergo very painful surgery and who also have risk factors for emergence delirium (eg, prior history, alcohol abuse) ▪ Loading doses greater than 0.5 mcg/kg associated with bradycardia and/or hypotension ▪ Postoperative administration should be in a monitored setting (eg PACU); monitoring should continue for one hour after infusion stopped

For further information on management of acute pain, refer to UpToDate content on nonopioid pharmacotherapy for acute pain.

IBW: ideal body weight; IV: intravenous; US FDA: United States Food and Drug Administration; MI: myocardial infarction; COX-2: cyclooxygenase, isoform 2; PONV: postoperative nausea and vomiting; PACU: post anesthesia care unit; ICU: intensive care unit.

* For some surgical procedures, NSAIDs should not be administered until the surgeon confirms adequate intraoperative hemostasis.

¶ UpToDate contributors avoid ketorolac in patients with significant kidney impairment (ie, CrCl <60 mL/minutes) and those at increased risk for acute kidney injury.

Δ Due to its prolonged half-life (ie, ~24 hours) onset of full analgesic effect of meloxicam may be delayed relative to shorter-acting NSAIDs.

Graphic 139393 Version 6.0

Opioids commonly used for postoperative pain

Drug	Sample initial dose for opioid naïve adults*	Onset of analgesia	Elimination half life	Duration of analgesic effect¶	Metabolisr clearan
Parenteral					
Fentanyl	25 to 50 mcg IV for moderate pain or 50 to 100 mcg for more severe pain; repeat every 2 to 5 minutes as needed until adequate pain relief or side effects occur; then reassess pain control regimen	<1 minute; peak effect within several minutes	2 to 4 hours for bolus	30 to 60 minutes	▪ Metabolize CYP3A4 to inactive metabolite ▪ Metabolite excreted b kidney ▪ Short dura initial dose to redistrib
Morphine	1 to 3 mg IV; repeat every 5 to 10 minutes as needed until adequate pain relief; then 1 to 3 mg IV every 1 to	5 to 10 minutes; peak effect within 20 minutes	2 to 4 hours	3 to 5 hours	▪ Metabolize non-CYP e to morphir glucuronid (active ana and morph glucuronid

	4 hours as needed				(potential neurotoxin ▪ Metabolite excreted by kidney
Hydromorphone	0.2 to 0.5 mg IV; repeat every 5 minutes as needed until adequate pain relief, then 0.2 to 0.5 mg IV every 3 to 4 hours as needed	5 minutes; peak effect 10 to 20 minutes	2 to 3 hours	3 to 4 hours	▪ Metabolize glucuronid (ie, non-CY enzymes) t inactive hydromorp 3-glucuron (potentially neuroexcit ▪ Metabolite excreted by kidney
Oliceridine	Initial dose 1.5 mg IV; subsequent doses of 0.75 mg IV no more frequently than hourly◇; maximum total cumulative daily dose 27 mg IV	2 to 5 minutes	1.3 to 3 hours; increased in patients with hepatic dysfunction	1 to 3 hours	▪ Metabolize CYP3A4 an enzymes t inactive metabolite ▪ Metabolite excreted by kidney (70 fecally (30

Oral					
Oxycodone (immediate release)	5 to 10 mg orally every 3 to 4 hours as needed	10 to 15 minutes; peak effect 0.5 to 1 hour	3 to 4 hours; increased in kidney or hepatic dysfunction	3 to 6 hours	▪ Hepatic metabolisr CYP3A4 an CYP2D6 (m to active metabolite noroxycod and oxymorph and inactiv metabolite noroxymor alpha- and noroxycod alpha- and oxymorph ▪ Metabolite excreted b kidney
Hydromorphone (immediate release)	2 to 4 mg orally every 3 to 4 hours as needed	15 to 30 minutes; peak effect 30 to 60 minutes	2 to 3 hours	3 to 4 hours	▪ Metabolize glucuronid (ie, non-CY enzymes) t inactive hydromorp 3-glucuron (potentiall neuroexcit

					▪ Metabolite excreted b kidney
Hydrocodone (immediate release)	5 to 10 mg orally every 4 to 6 hours as needed	10 to 30 minutes; peak effect 60 minutes	~4 hours	4 to 8 hours	▪ Hepatic metabolisr CYP3A4 an CYP2D6 (m to active metabolite hydromorp and norhydroc
Morphine (immediate release)	10 to 15 mg orally every 3 to 4 hours as needed	~30 minutes	2 to 4 hours	3 to 5 hours	▪ Metabolize non-CYP er to morphir glucuronid (active ana and morph glucuronid (potential neurotoxir ▪ Metabolite excreted b kidney

Tramadol (immediate release)	50 to 100 mg orally every 4 to 6 hours as needed (maximum 400 mg per day)	Within 1 hour; peak effect 2 to 3 hours	6 to 9 hours (including active metabolite); increased in kidney or hepatic dysfunction	4 to 6 hours	▪ Hepatic metabolisr CYP3A4 an CYP2D6 (m to active metabolite desmethy tramadol ▪ Metabolite excreted b kidney

Tapentadol (immediate release)	50 to 100 mg orally every 4 to 6 hours as needed; maximum dose: ▪ First day: 700 mg per day ▪ Day 2 and subsequent days: 600 mg per day	Within 1 hour; peak effect 1.25 hours	4 hours; increased in kidney or hepatic dysfunction	4 to 6 hours	▪ Hepatic metabolisr primarily v glucuronid (non-CYP) t inactive metabolite tapentadol glucuronid ▪ Metabolite excreted b kidney (70
Codeine (immediate release)	15 to 60 mg orally every 4 to 6 hours as needed	0.5 to 1 hour; peak effect 1 to 1.5 hours (variable; refer to comment)	~3 hours	4 to 6 hours	▪ Hepatic metabolisr CYP2D6 to morphine and via CYI norcodeine (inactive) ▪ Metabolite excreted b

					kidney (90
Methadone	2.5 to 5 mg orally every 8 to 12 hours	0.5 to 1 hour	8 to ≥59 hours	4 to 8 hours for single dose, increases to 8 to 12 hours with repeated doses	▪ Hepatic metabolisr CYP3A4, 2[other CYP enzymes t(inactive metabolite ▪ Complex pharmacol resulting ir widely vari effects witl compared repeated d ▪ Significant accumulati with repea doses and titrating

IV: intravenous; SSRI: selective serotonin reuptake inhibitor; SNRI: serotonin-norepinephrine reuptake inhibitor; TCA: tricyclic antidepressants; CrCl: creatinine clearance; AUC_{0-24}: area under plasma concentration versus time at 0-24 hours after dose; NMDA: N-methyl-D-aspartate; MAO-I: monoamine oxidase inhibitor; P-gp: P-glycoprotein.

* Lower doses may be effective for patients who simultaneously receive nonopioid analgesics. A dose reduction of approximately 50% and a reduced frequency is warranted for older or debilitated adults or patients with impaired liver or kidney functioning, low cardiac output, or respiratory compromise.

¶ The duration of action is highly variable among individuals and is influenced by the dose, variations in metabolism, subjective patient experience, and combination with other therapies. As such, the expected duration of action for each type of opioid is only a rough estimate.

Δ Opioids metabolized by CYP pathways or substrates of P-gp-mediated efflux may be subject to interaction with drugs that either inhibit or accelerate CYP metabolism or P-gp-mediated efflux. Lists of drugs that alter CYP3A4, 2D6, and P-gp-mediated efflux are available as separate tables in UpToDate. In addition, patients may have polymorphisms of cytochrome P450 (CYP) genes that affect drug metabolism. Polymorphisms may contribute to either diminished or absent metabolic enzymes or excessive metabolism, either of which can change the clinical effect of a given dose of opioid. Poor, intermediate, extensive, and ultrarapid CYP2D6 function types have been well characterized. Significant drug interactions may be identified by use of the Lexicomp drug interaction program available through UpToDate.

◇ After initial two doses, oliceridine dose may be titrated, if needed, based on tolerability and response up to a maximum of 3 mg per dose, at intervals of one hour or more; maximum cumulative dose is 27 mg per day.

§ Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) are usually administered on a regular basis as part of multimodal therapy. Avoiding combination preparations (ie, opioid plus nonopioid) allows fixed schedule administration of the nonopioid medication regardless of the patient's opioid utilization, without limitation by the maximum daily dose of the nonopioid.

Graphic 140310 Version 4.0

Example of PCA regimens for opioid naïve adults

Drug	Concentration	Demand dose range	Lockout interval	Maximum demands per hour	Maximum 4 hour dose
Hydromorphone	0.2 mg/mL	0.1 to 0.3 mg	10 to 20 minutes	6	6 mg
Morphine	1 mg/mL	0.5 to 2 mg	10 to 20 minutes	6	30 mg
Fentanyl	10 mcg/mL	5 to 20 mcg	5 to 10 minutes	10	300 mcg
Oliceridine	1 mg/mL	0.35 to 0.5 mg	6 to 12 minutes	8	4.5 mg*

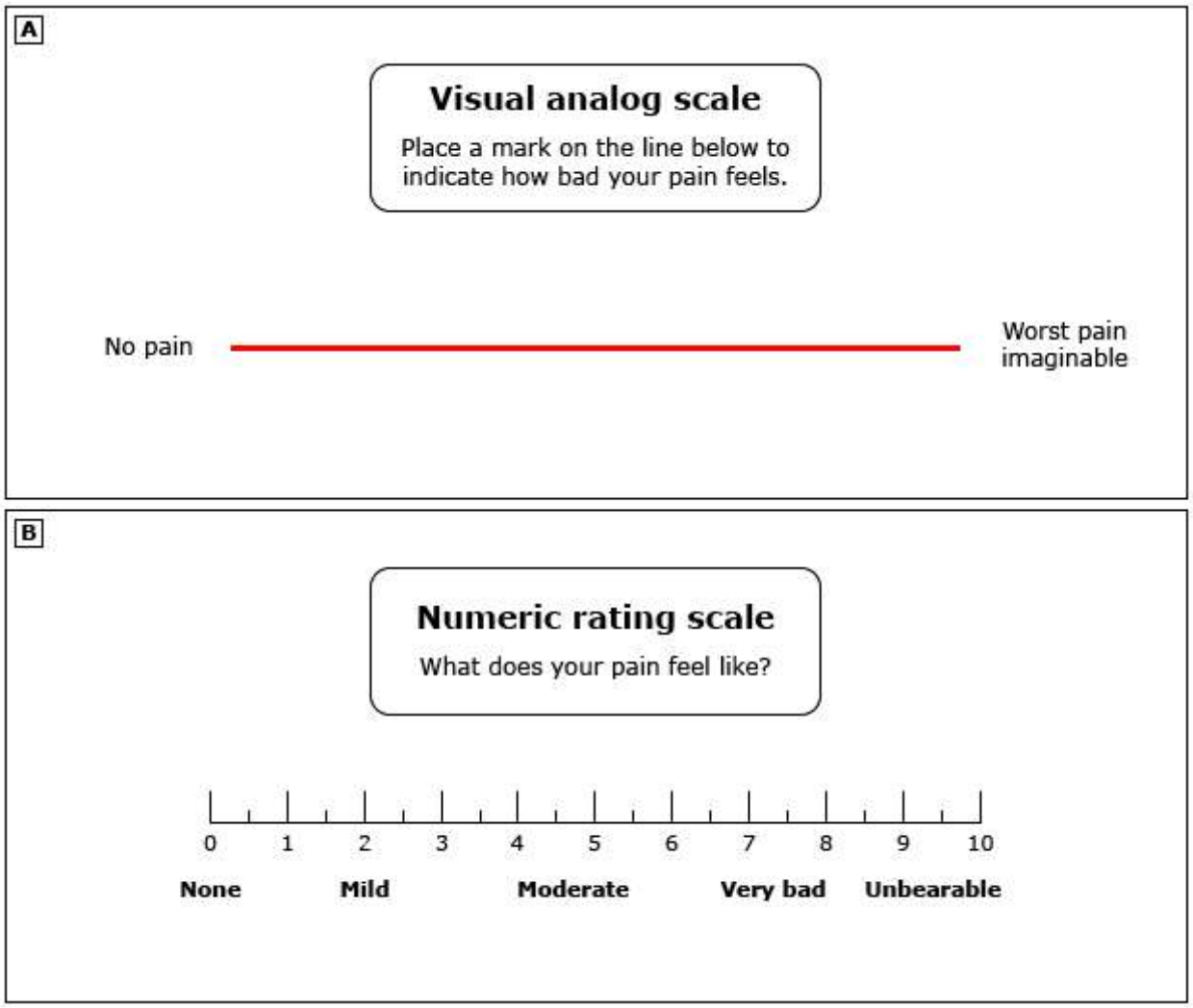
There is wide inter-institution variability in PCA pump settings. This table shows an example of one protocol.

PCA: patient controlled analgesia.

* Maximum allowable dose of 27 mg in 24 hours.

Graphic 140312 Version 2.0

Visual analog and numeric rating pain scales



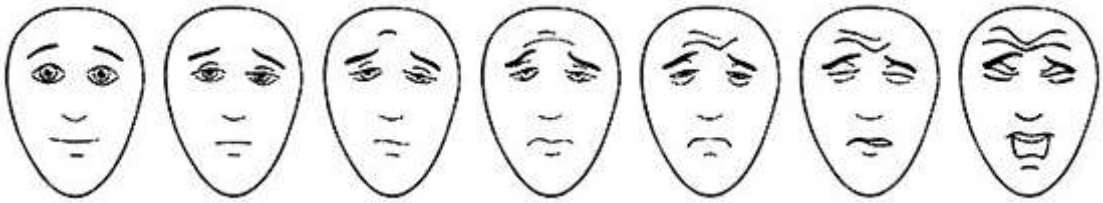
(A) When using a VAS, the patient is asked to mark a 10 cm line at a point that corresponds to the degree of pain. The VAS score is the distance in millimeters from the left end of the line to the patient's mark.

(B) When using an NRS, the patient indicates the number that corresponds to pain severity, either verbally or by marking the scale.

VAS: visual analog scale; NRS: numeric rating scale.

Graphic 62346 Version 7.0

Faces pain scale



Schematic representation of the faces pain scale, rated from 0 to 6 left to right.

Graphic 67351 Version 5.0

General principles for anesthesia and perioperative management for a patient who is breastfeeding[1-3]

Preoperative planning	
Ask all women with infants <2 years of age if they are breastfeeding. For those who are breastfeeding: ▪ Where possible, day surgery is preferable to avoid disrupting normal feeding routines. ▪ If the mother will be separated from the infant for more than a few hours perioperatively, encourage her to express and store breast milk preoperatively to feed the infant during that time. ▪ If the infant has not been fed from a bottle, encourage the mother to introduce bottle feeding prior to surgery.	
Selection of drugs	
General principles:	▪ Anesthetic and nonopioid analgesic drugs are generally safe for use while breastfeeding*, because they are transferred to breast milk in only very small amounts. For almost all drugs used perioperatively, there is no evidence of adverse effects on the breastfed infant.
Optimal choices:	▪ Opioid-sparing techniques are preferable for the breastfeeding woman. Local and regional anesthesia have benefits in this regard, and also interfere the least with the woman's ability to care for her infant.
Use with caution:	▪ Ketamine should be avoided if possible and should be used with careful monitoring of the infant during breastfeeding*. ▪ Opioids and benzodiazepines should be used with caution¶, especially after multiple doses and in infants <6 weeks old (corrected for gestational age). In this situation, the infant should be observed for signs of abnormal drowsiness and ventilatory depression, especially if the woman is also showing signs of sedation.
Avoid:	▪ Codeine should not be used by breastfeeding women due to concerns of excessive sedation in some infants, related to differences in metabolism.
Postoperative management	
▪ Women should be encouraged to breastfeed as normal following surgery. ▪ There is no need to express and discard breast milk ("pump and dump") after anesthesia. ▪ A woman having day surgery should have a responsible adult stay with her for the first 24 hours postoperatively. She should be cautious with cosleeping, and be careful not to fall asleep while feeding the infant, as she may not be as responsive as normal. ▪ Breastfeeding support should be accessible for lactating women undergoing surgical and medical procedures.	

For most women it is safe to breastfeed as usual after anesthesia and surgery, without the need to pump and discard breast milk. If a medication could otherwise be prescribed to the infant for

a medical condition, it is generally considered safe for the mother to take while breastfeeding. For further information, consult the Lactmed database.

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* There are limited or no data on transfer of some drugs used perioperatively to breast milk (eg, ketamine, dexmedetomidine).

¶ Small doses of opioids and benzodiazepines are safe to use for most patients.

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