



The Pain Management Dilemma*

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Learning Objectives:

1. To develop a treatment strategy for management of non-acute persistent pain.
2. To identify mechanisms for monitoring opioid use in the treatment of pain.
3. To describe the shifting paradigm in pain management goals for palliative care.

Healthcare practitioners see patients with persistent pain on a daily basis. Practitioners may first recommend nonpharmacologic interventions such as physical therapy, behavioral management, and localized treatments (eg, heat/cold, acupuncture). The use of non-opioid medications and regional anesthetic approaches may be the next addition to the therapeutic regimen. However, practitioners will find that a certain percentage of patients will also require opioid medications as part of the treatment plan. The dilemma occurs with recognition of the ethical, moral, and professional obligation to treat pain in the face of concerns regarding the prescription of opioids: possible abuse/misuse of the medication, the impact of drug abuse on the community at large, and regulatory issues. To unravel these complex and sometimes conflicting issues, this article discusses the goals of pain management, various pain treatment strategies, and risk management—so that practitioners will have greater comfort in treating patients with persistent pain and so that patients will derive greater symptomatic relief. The article also includes a section on the use of opioid medications in palliative care.

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The National Center for Health Statistics reports that pain afflicts a higher number of US adults than do diabetes, cancer, coronary heart disease, and stroke.¹ Furthermore, about 76.5 million US adults aged 20 years or older have reported experiencing non-acute pain lasting more than 24 hours, with more than 40% of them reporting a duration greater than 1 year.² In addition, approximately 70% of patients with cancer experience pain, but only half of these pain sufferers receive adequate analgesic treatment.^{3,4} The elderly also experience a great deal of pain, with 25% to 50% of elders in the community experiencing pain and 71% to 83% of institutionalized elders reporting one or more pain problems.⁵

According to the National Institute of Health Statistics, the most common types of pain are back pain (27%), severe headache/migraine (15%), neck pain (15%), and facial pain (4%).⁶ Furthermore, many patients with persistent low back pain have multiple physical and psychological health problems secondary to the persistent pain condition.⁶ The amount of time patients wait to have persistent pain treated also has an impact. In a review of 24 studies, researchers found that a wait of 6 months or longer contributed to a deterioration of health with regard to quality of life (QoL) and psychological distress.⁷ This finding is alarming, given the fact that 50% of patients report that a full year elapses before they achieve adequate pain control.⁸

Many patients with persistent pain experience disturbances of sleep, function, and mood. Therefore, to effectively treat pain, practitioners need to evaluate not only the history, triggers, intensity, duration, and frequency of the pain, but also the effects that the pain is having on a patient's daily life. Treatment of pain entails reducing the pain, improving function, recapturing restorative sleep patterns, and stabilizing mood. To achieve these goals, practitioners need to implement multimodal treatment. Oftentimes, these treatments need to be administered in concert rather than sequentially. Although the main purpose of this article is to discuss the pharmacologic treatment of pain, practitioners should not overlook the importance of rehabilitative approaches (eg, physical therapy [PT], occupational therapy) and behavioral pain management. Pharmacotherapy alone will rarely allow patients to meet pain treatment goals.

Pharmacologic Management

Pharmacologic management of persistent pain depends on the specific diagnosis of the pain problem. In addition, practitioners must determine whether the origin of the pain is neuropathic, nociceptive, or a mixture of both. *Neuropathic pain* begins as a result of a primary lesion or dysfunction in the central nervous system (CNS) or peripheral nervous system. Examples of neuropathic pain include diabetic peripheral neuropathy (DPN), trigeminal neuralgia (TN), post-herpetic neuralgia (PHN), and sciatica. *Nociceptive pain* occurs as a result of the activation of the primary afferents because of a noxious stimulus (eg, tissue damage as a result of a bruise, burn, sprain, or fracture; inflammation; obstruction). Some conditions appear to have a combination of neuropathic and nociceptive features (eg, migraine, lumbar/cervical radiculopathy). Once the origin of pain is determined, pharmacologic interventions can be initiated.

Neuropathic pain and mixed neuropathic/nociceptive pain are often treated with adjuvant analgesics such as tricyclic antidepressants (TCAs), antiepileptic drugs (AEDs), or local anesthetics, possibly with the addition of an opioid analgesic. Treatment of nociceptive pain and mixed nociceptive/neuropathic pain usually begins with a non-opioid analgesic, followed by an opioid and the possible addition of an adjuvant analgesic. Of note, some of these adjuvant drugs are approved by the US Food and Drug Administration (FDA) to treat conditions other than pain, so when they are prescribed for patients with pain conditions, they are being given off label. These adjuvants may be used alone or in combination with opioids, depending on patient response.

Non-opioid Analgesics

Acetaminophen (APAP; Tylenol® and others) and nonsteroidal anti-inflammatory drugs (NSAIDs) are first-line non-opioid analgesics. APAP is used to treat mild to moderate musculoskeletal pain. APAP's mechanism of action is thought to be mediated through central mechanisms at the spinal cord level. However, APAP has only a negligible anti-inflammatory effect. To limit hepatotoxic effects, the daily dose of APAP should not exceed 4 g (2 g in the elderly).

All NSAIDs relieve mild pain, but certain NSAIDs (eg, piroxicam [Feldene®], meloxicam [Mobic®], diclofenac [Voltaren®]) may relieve pain of up to moderate severity. The COX-2 inhibitor celecoxib (Celebrex®) is also effective



in alleviating pain of moderate severity. NSAIDs' primary mechanism of action is inhibition of the enzyme cyclooxygenase (COX), which results in blockade of prostaglandin synthesis. These agents have anti-inflammatory, antipyretic, and analgesic effects, and they can ease persistent pain associated with osteoarthritis, as well as muscle, joint, bone, dental, and inflammatory pain. Long-term use of NSAIDs requires careful evaluation in terms of risks and benefits.

NSAIDs are among the most frequently prescribed drug class and account for more than half of the adverse drug reactions reported to the FDA.⁹ Elderly patients in particular are at high risk for adverse effects such as gastrointestinal (GI) bleeding, renal impairment, drug–drug interactions, and drug–disease interactions.⁹ Use of antacids, proton pump inhibitors, histamine-2-receptor antagonists, and misoprostol (Cytotec[®]) can provide some degree of GI protection in NSAID users.¹⁰

Antidepressants—TCAs are prescribed off label to treat neuropathic pain. TCAs' analgesic effect is due in part to the blocking of serotonin and norepinephrine reuptake in the CNS. Most TCAs are started at a dosage as low as 10 mg daily and then escalated slowly to effect. Most patients should take this medication in the early evening, especially if the goal is to achieve both analgesic effects and improved restorative sleep patterns. Common TCA side effects are sedation, anticholinergic effects, and orthostatic hypotension. Compared with other agents in its class, amitriptyline (Elavil[®]) is associated with more sedative and anticholinergic effects. Thus, practitioners should consider prescribing nortriptyline (Pamelor[®]) instead, particularly in elderly patients, who are more vulnerable to these side effects. Because TCAs can induce arrhythmias in susceptible individuals, patients in whom TCA therapy is being considered should have an electrocardiogram for evaluation of the QT interval. TCA use is contraindicated in patients with known conduction abnormalities.

Duloxetine (Cymbalta[®]), a selective serotonin and norepinephrine reuptake inhibitor, has been shown to be effective in alleviating neuropathic pain conditions such as DPN (FDA approved for this indication), PHN, pain symptoms associated with depression, and possibly fibromyalgia.

Antiepileptic Drugs—AEDs such as phenytoin (Dilantin[®]), divalproex sodium (Depakote[®]), carbamazepine (Tegretol[®]), gabapentin (Neurontin[®]), lamotrigine (Lamictal[®]), topiramate (Topamax[®]), and pregabalin (Lyrica[®]) may be used for neuropathic pain treatment or for migraine prophylaxis, particularly in patients who describe migraine pain as lancinating, stabbing, or knife-like. Although the exact mechanism whereby AEDs exert their analgesic effects is unknown, these agents are thought to work, at least in part, by decreasing cell membrane excitability and abnormal discharges in the neurons. Some AEDs are prescribed off label to treat neuropathic pain, whereas other AEDs are FDA approved, as follows: gabapentin for PHN, carbamazepine for TN, topiramate for migraine prophylaxis, and pregabalin for fibromyalgia.

AED dosing is individualized. As with TCAs, AED dosing starts low and is gradually increased until the analgesic effect is achieved. Side effects include sedation, dizziness, mental clouding, and nausea. The older AEDs (eg, phenytoin, divalproex sodium) are associated with liver dysfunction, hematologic abnormalities, and rash. Newer AEDs (eg, gabapentin) require less monitoring.

Opioid Analgesics

Opioids, alone or in combination with non-opioids and/or adjuvant drugs, may be used to treat moderate to severe pain. Nociceptive pain is primarily treated with opioids after the failure of non-opioid treatment. Opioids are also effective in treating neuropathic pain but are often added to the adjuvant analgesic regimen. In patients with mixed nociceptive/neuropathic pain, both an opioid and an adjuvant may be needed. Opioids bind to opioid receptors in the CNS, where they inhibit nociceptive input from the periphery as well as activate descending inhibitory pathways that modulate pain in the spinal cord. Furthermore, opioids stimulate receptors inside the limbic system.

Practitioners should consider the use of opioids in patients with persistent pain when conservative treatment fails to adequately treat the pain, when opioids are the best option for aggressive treatment, and/or when treatment options are limited—for example, in individuals with multi-level disk problems in whom surgical outcome for treatment



success is likely poor. Patients for whom opioids are prescribed should be carefully screened and closely supervised, as discussed later in the article.

Drug Selection and Dosage—Opioids are commonly used in the treatment of moderate to severe pain.⁸ No single opioid is preferred over another, although practitioners should avoid prescribing meperidine (Demerol[®]) and propoxyphene (Darvon[®]) in the treatment of persistent pain.¹¹ Long-term use of meperidine can cause seizures (related to the drug’s active metabolite normeperidine) and long-term use of propoxyphene can cause hepatic and renal injury, myopathy, and cardiotoxicity. “Opioids Commonly Used to Treat Moderate to Severe Pain,” is a useful guide for opioid use (see Box at the end of the article). Included in this guide are indications for use, dosing intervals, routes of administration, and side effects.

Drug choice is based on patient characteristics such as pain intensity, pain pattern, and patient age. In addition, unique drug characteristics such as duration of action and active metabolites should be considered. For example, patients with intermittent pain can use a short-acting (immediate-release) opioid formulation, whereas patients with persistent pain that occurs daily and lasts through most of the day will likely do better with an extended-release preparation.

The general recommendation for initiating opioid treatment is to start at a low dosage and slowly titrate to effect. Two types of charts are available to aid in estimating the starting dose of a given opioid. The equianalgesic dose chart provides a list of opioids in both oral and parenteral doses that are approximately equal in potency (Table 1).^{12,13} This chart, based on single-dose studies conducted on opioid-naïve patients, is particularly helpful if conversion from one administration route to another is needed. When making an opioid switch in patients who have been on an opioid for an extended period of time, practitioners should decrease the equianalgesic dose by 50% because of the lack of cross-tolerance of drugs. To optimize their benefits, opioids need to be titrated slowly to effect.

TABLE 1 EQUIANALGESIC OPIOID DOSING^{12,13}

Opioid Medication	Starting Dosage (mg) (Adults ≥50 kg) [†]		Starting Dosage (mg/kg) (Adults <50 kg) [†]		Equianalgesic Oral Dosage (mg)	Equianalgesic Parenteral Dosage (mg)
	Oral	Parenteral	Oral	Parenteral		
Morphine*	15-30 q3-4h	10 q3-4h	0.3 q3-4h	0.1 q3-4h	30	10
Hydromorphone*	4-8 q3-4h	1.5 q3-4h	0.06	0.02	7.5	1.5
Oxycodone	10-30 q4h	NA	I	NA	20	NA
Meperidine	NR	NR	NR	NR	300	75
Hydrocodone (in combination formulations)	5-10 q3-4h	NA	0.135 q3-4h	NA	NA	NA
Codeine* (with aspirin or acetaminophen)	30-60 q3-4h	NA	0.5-1.0 q3-4h	NA	NA	NA

*For morphine and hydromorphone, rectal administration is an alternate route for patients unable to take oral medications, but equianalgesic dosages may differ from oral and parenteral dosages because of pharmacokinetic differences.

[†]**Caution:** Dosages of aspirin and acetaminophen in combination opioid/NSAID preparations must also be adjusted to patients’ body weight.

[‡]**Caution:** In many cases, codeine doses >65 mg are not appropriate because of diminishing incremental analgesia with increasing doses but continually increasing constipation and other side effects.

NSAID = nonsteroidal anti-inflammatory drug; NA = not available; I = individualized; NR = not recommended.



The second type of chart is a conversion chart for opioids. Recommended dosing on these charts comes from the manufacturer of each particular agent. These charts provide conservative estimates of approximate starting dosages for each agent. Practitioners should note that conversion charts are often in “one direction” and may not be used in reversing direction to place a patient on a different drug. To do so may cause an overdose. Because the starting dose in these charts is generally conservative, patients may require slow upward titration to achieve adequate analgesic effect.

Breakthrough Medication—Opioids may be provided for breakthrough pain in long-term opioid users. In most cases, an immediate-release (short-acting) opioid is used for rescue treatment. When possible, the opioid medication used for breakthrough pain should be the same as that used as the baseline drug. Use of breakthrough medication in patients with non-life-threatening disorders should be limited to small quantities (eg, 30 tablets/month). If patients are experiencing substantially more intense pain or pain prior to the next dose of analgesic administration, an increase in dosage of the baseline opioid may be appropriate.

Side-Effect Management—Side effects may occur regardless of the particular opioid and dose. The most common side effects of opioids are constipation, nausea, headache, cognitive dysfunction (sedation, mental confusion or clouding), pruritus, urinary retention, and diaphoresis. The most serious side effect, respiratory depression, is rare but is more likely to occur in opioid-naïve patients. Bowel regimens for constipation should be planned or initiated upon initiation of an opioid regimen. Untreated constipation can lead to bowel obstruction, a life-threatening health emergency. Bowel regimens may be as simple as an alteration of diet, including increased intakes of fluids, fruits, and vegetables, or they may entail use of a stool softener or laxative. Nausea may be a self-limited problem in the first 2 weeks of opioid therapy. A 2-week course of an antiemetic prior to initiation of the analgesic will often avoid this problem. Opioid-associated pruritus may be transient or long term, and may be ameliorated by the concurrent use of antihistamines for several weeks. Cognitive dysfunction may be mitigated by lowering the opioid dosage and/or evaluating patients’ other medications and lowering their dosage or discontinuing them.

Monitoring Patients on Opioids—As with all treatments, regardless of the disease/disorder or symptom, monitoring of efficacy and side effects is part of the process. Practitioners need to assess for (1) lack of sufficient efficacy, (2) lack of improvement in function and QoL, (3) unacceptable or intolerable side effects, and (4) abuse/addiction. Practitioners should take a universal precaution approach in prescribing analgesics, as shown in Table 2.¹⁴ All practitioners and office staff members must develop a standard manner of monitoring patients on opioids. Consistency and agreement in office practice will yield better outcomes.

TABLE 2 UNIVERSAL PRECAUTIONS IN PAIN PHARMACOTHERAPY¹⁴

- Make a diagnosis (with other elements of the differential diagnosis ruled out).
- Perform a psychological assessment, including risk of an addictive disorder.
- Obtain informed consent.
- Create and have patient sign a treatment agreement.
- Assess pre-treatment and post-intervention pain level and function.
- Initiate an appropriate trial of opioid therapy ± adjunctive medication.
- Reassess pain score and level of function on a periodic basis.
- Regularly assess the “four A’s” of pain pharmacotherapy: analgesia, activities of daily living, adverse side effects, and aberrant drug taking.
- Periodically review the pain diagnosis and comorbid conditions, including addictive disorders.
- Document all interventions and patient responses in health record.



Pretreatment Assessment—Before initiation of opioid therapy, patients should be assessed and evaluated in terms of diagnosis, function, QoL, mental health risk, and addiction risk. Evaluation of these parameters provides the framework for appropriate monitoring of pain treatment. If practitioners determine that opioids are not appropriate for a particular patient, then an alternate plan to treat the pain should be sought or the patient should be referred to a clinician with the expertise to manage the case.

Making an accurate diagnosis regarding the cause of a patient's pain, based on a comprehensive history, physical examination, and appropriate diagnostic testing, as well as ruling out other entities on the differential diagnosis, allows practitioners to provide a framework for the proper treatment plan. As with all diagnoses, appropriate standards of care must be applied. Use of opioids may be appropriate in patients in whom a diagnosis congruent with moderate to severe pain is made. This recommendation is not to be misconstrued as suggesting that all patients with moderate to severe pain should be placed on opioids, but, rather, that patients who have failed conservative management should be considered candidates for opioid treatment. Patients whose pain complaint seems to exceed the bounds expected for the underlying diagnosis may be referred to a pain treatment program.

Many evaluation tools are available in the public and private domains for patients presenting with persistent pain. One step in the evaluation should be the assessment for depression, which underlies many pain syndromes. Depression evaluation may be performed by using the Zung Self-Rating Depression Scale and Beck's Depression Inventory.^{15,16} Practitioners should also assess for the presence of an underlying anxiety disorder by using the Hamilton Anxiety Scale or Zung Self-Rating Anxiety Scale.^{17,18}

Functional and pain disability indexes allow practitioners to evaluate the current status of patients' function at treatment onset and periodically mid-course. The Pain Disability Index is one such tool.¹⁹ QoL scales measure social, occupational, mental, and physical health (ie, patients' overall function). The American Chronic Pain Association provides a QoL measure that is available at www.theacpa.org/documents/Quality_of_Life_Scale.pdf²⁰

To better predict or identify individuals with a substance abuse problem, practitioners can use screening tools for substance abuse. These tools should be used before initiation of therapy along with a structured interview that identifies previous or current abuse problems, family history of substance abuse problems, and mental health conditions that may contribute to substance abuse concerns. A few examples of addiction screening tools are the Cage questionnaire,²¹ the Drug Abuse Screening Test,²² the Screening Instrument for Substance Abuse Potential,²³ and the Screener and Opioid Assessment for Patients with Pain.²⁴

Monitoring Opioid Users—Although screening tools may help identify many patients at risk for addiction problems, they do not identify all patients who could or would ultimately develop such problems. Monitoring of aberrant behaviors, along with the implementation of opioid management agreement and consent forms, urine toxicology tests, pill counts, and patient education efforts, can further reduce misuse/abuse of these agents.²⁵

Before initiation of opioid treatment, practitioners need to discuss issues of concern with patients. Items of discussion include treatment goals, the purpose of the proper use of medication, the risk–benefit ratio, and rules regarding practice protocols. Implementation of medication management agreements and opioid consent forms ensures that the information is consistently provided to each patient and establishes a standard within the practice. These agreements are used for all patients using opioids; in cases in which patients cannot provide informed consent, arrangements should be made with the caretaker and/or legal guardian. Examples of opioid management agreements are available through the American Academy of Pain Medicine and the American Academy of Family Medicine (see references 26 and 27 for Web addresses).^{26,27}

If possible, urine drug toxicology (UDT) screening should be performed before the initiation of therapy and randomly thereafter. UDT testing can detect the presence of the prescribed opioid, the presence of a prescription drug not ordered by the practitioner, and the presence of an illicit substance. Testing should be carried out to assess adherence, as well as substance misuse or addiction, but it does not replace good clinical evaluation and judgment.

The most commonly screened drugs and their metabolites include opioids (although not all opioids are tested), benzodiazepines, amphetamines, barbiturates, and illicit substances such as heroin, cocaine, marijuana, and phencyclidine (PCP). Gas chromatography/mass spectrometry is a more specific technique used in UDT screening.



Laboratories differ, so practitioners need to know their lab's standards to prevent errors in interpreting the results and, thus, in making clinical decisions. Practitioners also need to know the specific drugs tested by the screen, cross-reactivity patterns, and cutoff concentrations, as well as drugs that can interfere with the results. Questionable results are further validated with a knowledgeable consultant within the toxicology lab.

To accurately interpret a patient's UDT test findings, practitioners need to take a detailed history of medications used, including over-the-counter and herbal preparations, and the time of the most recent use of these medications. Random urine collection at the office is ideal. Collection of urine can be unsupervised, but patients should leave personal belongings outside the collection area. Patients should be given a labeled collection container that they agree is labeled with their correct name. Temperature of the urine sample should be attained within 4 minutes of voiding and should range between 90°F and 100°F. Laboratories should evaluate urinary creatinine and pH as well. These measures provide some assurance that the sample was not brought in from an outside source or diluted.

In addition to the use of opioid user consent and agreement forms and UDT testing, patients should be monitored further. Treatment should be evaluated with regard to adherence to nonpharmacologic regimens such as PT and behavioral pain management. In addition, patients are expected to keep their designated office appointments and bring their medication bottles for verification of fill dates, pill counts, and consistency of pharmacies. At first, patients should be monitored and re-evaluated frequently to ensure adherence, efficacy of the analgesic regimen, and side-effect management. Appropriate re-evaluations are spaced on an individual basis; needs for opioid users vary from daily to monthly to every 3 months.

Addiction/Abuse/Misuse of Opioids—Addiction is characterized by behaviors of impaired and compulsive use of drugs for non-medical purposes and continued use despite harm. Complicating the picture are patients who appear to display aberrant drug-related behaviors but are really experiencing undertreatment of the pain (pseudoaddiction). Aberrant behaviors that may suggest substance abuse/misuse include reported “loss” of the prescription, multiple unauthorized escalations of the opioid dosage despite repeated warnings from the practitioner, resistance to a change of opioid despite inadequate analgesia, and concurrent use of illicit drugs.²⁸ No single behavior is a better predictor than another in terms of helping to identify opioid addiction/abuse/misuse; in many cases, practitioners come to the realization that a patient is having trouble over a period of time. The prevalence of prescription opioid abuse in patients being treated for persistent pain is unknown. Therefore, all patients should be monitored.

What should practitioners do if they suspect that a given patient is addicted to, abusing, or misusing opioids? No standard protocol for handling such cases exists. Regardless of whether a patient has an abnormal or unexpected UDT test result or is displaying aberrant drug-related behaviors, practitioners must discuss the situation with the patient in person. If the discussion does not result in an improvement in the problem, other options besides discharging the patient from the practice are available. One option is for the patient to be evaluated by a substance-abuse clinician, who will collaborate with the practitioner in terms of treating the addiction and the pain. If a patient is unwilling to undergo a substance-abuse evaluation and follow up with a substance-abuse counselor or, despite treatment, if a patient is unable or willing to change the behavior, then the practitioner may need to discharge the patient.

Documentation—In prescribing opioids, a crucial element from a medicolegal standpoint is careful and complete documentation. Documentation should clearly identify the diagnosis of the pain problem, the treatment plan (including the goals), and the efficacy and side effects of treatment. Patients' progress is noted not only in terms of pain relief but also in terms of function and QoL. If a monitoring program is a standard of care in the practice, this program must be followed consistently and be well documented.

Novel Abuse-deterrent Technologies—New formulations are being developed within the pharmaceutical arena to deter abuse of prescription opioids.²⁹ Technologies under development incorporate the use of physical barrier designs, addition of an aversive component, and pharmacologic property alterations. Physical barrier designs aim to prevent the drug from being altered by crushing, dissolving, or extracting it from the manufactured formulation. Aversive technologies allow a sequestered drug such as capsaicin, ipecac, denatrimon benzoate, or naloxone to be released



when the product is tampered with. Pharmacologic property changes under investigation use a prodrug, which is a compound that must undergo chemical conversion through a metabolic process once it is administered. Now under development are prodrugs that require enzymatic cleavage in the GI tract for the active metabolite of the opioid to be produced.

Palliative Care

The primary goals of palliative care are to prevent and relieve suffering and to promote the best QoL possible for patients and their families. Palliative care may include traditional management of the underlying condition/disease/disorder in combination with treatment to minimize pain and other symptoms, as well as the provision of psychosocial and spiritual care. Palliative care is a component of the hospice model but differs in that active management aimed at curing or mitigating the underlying disease may be still a goal of treatment. Palliative care assessment and evaluation tools are available at <http://palliative.info/pages/Tools.htm>³⁰

Pain management is an important component of palliative care. Strategies for managing pain in this setting are similar to those previously mentioned—with several key differences, including closer follow-up, more aggressive titration of medications, and more liberal dosing for breakthrough pain. In end-of-life cases, practitioners can focus less on addiction concerns and more on providing true pain relief (Table 3).

TABLE 3 PAIN MANAGEMENT IN ADVANCED DISEASE

- Pain is common in the advanced stage of many illnesses such as cancer, AIDS, congestive heart failure, and chronic obstructive pulmonary disease.
- Although death is inevitable, a painful death is not.
- Fear of inflicting harm or hastening death prevents practitioners from treating uncontrolled pain.
- Pain management is provided from broad constructs of suffering, quality of life, and goals of care.
- Assess patients for anxiety and depression and provide treatment as needed. Remember that reports of pain may represent a mood disorder.

Patients may require daily follow-up to gain quicker control of their pain. The baseline opioid (exception for methadone) can be safely titrated every 3 days or even more often under closely controlled and monitored situations. Practitioners can determine dosing increments based on the amount of breakthrough medication a patient is using. For example, if a patient receiving extended-release morphine (KADIAN® and others) 60 mg every 12 hours is given 15 mg of immediate-release morphine 4 times daily and uses all four doses of rescue medication (total daily dose, 180 mg), the new dose of extended-release morphine would be increased to 90 mg every 12 hours (total daily dose, 180 mg). This patient would still be able to use immediate-release morphine for breakthrough pain; the total daily dose of breakthrough medication should be approximately one third of the total daily extended-release morphine dose. Focus on addiction during end-of-life cases is minimal. For a patient who is dying, the main focus is on relieving pain. This is the essence of palliative care—even in persons known to have an addiction problem.

Conclusion

Millions of US adults experience persistent pain. Practitioners have an ethical, moral, and professional responsibility to ensure that patients with persistent pain receive adequate analgesic treatment. Further, safe pain management



mandates that patients be monitored closely for efficacy, side effects, and adherence. Practitioners also need to keep in mind patients' potential for addiction, abuse, and misuse of opioids but not unnecessarily withhold needed medication for patients with moderate to severe persistent pain and for those receiving palliative care. In this way, practitioners, can have a beneficial impact on patients' QoL. ■

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OPIOIDS COMMONLY USED TO TREAT MODERATE TO SEVERE PAIN⁸

Generic Name/ Trade Name	Indications	Usual Dosing Interval	Routes of Administration/ Dosing Forms	Potential Side Effects	Comments
Morphine (KADIAN [®] , MSIR [®] , MS Contin [®] , and others)	Severe acute pain (eg, trauma, postoperative pain, MI), cancer pain, persistent pain	Varies with IR and CR	PO (IR and CR), PR, IV, SC, IM, EA, IA, SL	Mu agonist class side effects, precautions, warnings, and contraindications*; metabolite can accumulate in setting of renal or hepatic dysfunction	Used as a standard of comparison for all opioids; can stimulate histamine release; IR and CR oral preparations available; CR tablets are taken whole and must not be broken, chewed, or crushed (to prevent potential toxic dose)
Hydromorphone (Dilaudid [®])	Oral: management of pain where opioid therapy is appropriate; parenteral: moderate to severe pain (eg, trauma, MI, surgery, burns, renal colic, biliary colic, cancer)	4-6 hours for oral and parenteral; 6-8 hours for rectal	PO, PR, IV, SC, EA, IA	Mu agonist class side effects, precautions, warnings, and contraindications*	Useful alternative to morphine; available in high-potency injectable that facilitates SC administration
Fentanyl (Duragesic [®])	Severe acute pain, cancer pain, CNCP; TD fentanyl is indicated only for treatment of persistent pain that requires continuous administration and cannot be managed by less aggressive means	Varies with RoA and form; 72 hours for TD fentanyl	IV, EA, IA, TD, OTFC	Mu agonist class side effects, precautions, warnings, and contraindications*; TD fentanyl is contraindicated for acute pain, postoperative pain, or intermittent pain responsive to PRN or non- opioid therapy, and at doses >25 [Greek mu]g/hour at the initiation of opioid therapy; TD fentanyl should not be used in children <12 years or in patients <18 years who weigh <110 lb, except in research setting	TD and oral transmucosal formulations available, including OTFC; IV fentanyl is fast-acting and is frequently combined with benzodiazepines for procedural analgesia and sedation; TD fentanyl is long-acting and can control pain for up to 72 hours, but a small number of patients may require q48h dosing; ensure patients follow the correct patch application procedures for TD fentanyl and avoid direct exposure of application site to heat



OPIOIDS COMMONLY USED TO TREAT MODERATE TO SEVERE PAIN⁸

Generic Name/ Trade Name	Indications	Usual Dosing Interval	Routes of Administration/ Dosing Forms	Potential Side Effects	Comments
Oxycodone (OxyContin [®] and others) [†]	Moderate to moderately severe pain (eg, trauma, postoperative pain, musculoskeletal disorders, abdominal pain, dental pain, cancer pain); CR formulation for moderate to severe pain wherein opioid is required for an extended period of time	Varies with IR and CR	PO (IR and CR)	Mu agonist class side effects, precautions, warnings, and contraindications*; CR tablets are to be taken whole and must not be broken, chewed, or crushed, to prevent potential toxic dose; CR 80 mg tablets for use in opioid-tolerant patients only	IR and CR preparations; available as single entity and in combination with a non-opioid; can be used like oral morphine for severe pain; frequently combined with a non-opioid for moderate pain
Hydrocodone [‡]	Moderate to severe pain (eg, trauma, back pain, postoperative pain, abdominal pain, dental pain)	4-6 hours	PO	Mu agonist class side effects, precautions, warnings, and contraindications*; hydrocodone/ibuprofen NR for OA or RA or for patients with NSAID hypersensitivity or other contraindications to NSAIDs	Available in combination with non-opioids: hydrocodone/acetaminophen for moderate or moderately severe pain; hydrocodone/ibuprofen for short-term (<10 days) management of acute pain (eg, trauma, musculoskeletal and back pain, postoperative pain, abdominal pain, dental pain)
Codeine [§]	Mild to moderately severe pain	4 hours	PO, SC	Mu agonist class side effects, precautions, warnings, and contraindications*; the most common side effects are lightheadedness, dizziness, SoB, sedation, and N/V	Used orally for mild to moderate pain, with limited use for severe pain; usually used in combination with non-opioid, which has an analgesic ceiling; codeine is a prodrug—10% of patients lack the enzyme needed to make codeine active; may cause more nausea and constipation per unit of analgesia than other mu agonist opioids

*Mu agonist class side effects include sedation, mental clouding or confusion, respiratory depression, nausea, vomiting, constipation, pruritus (itching), and urinary retention. With the exception of constipation, these side effects tend to subside over time. Most opioids should be used with caution in patients with impaired ventilation, bronchial asthma, liver failure, or increased intracranial pressure. Opioid-induced respiratory depression is usually short lived, antagonized by pain, and most common in opioid-naïve patients.

[†]Also available in combination with non-opioid analgesics (eg, oxycodone/aspirin [eg, Percodan]).

[‡]Available in combination with non-opioid analgesics (eg, hydrocodone/acetaminophen [eg, Vicodin]).

[§]Also available in combination with non-opioid analgesics (eg, codeine/acetaminophen [Tylenol w/ Codeine]).

MI = myocardial infarction; IR = immediate release; CR = controlled release; PO = orally; PR = rectally; IV = intravenously; SC = subcutaneously; IM = intramuscularly; EA = epidural administration; IA = intrathecal administration; SL = sublingually; CNCP = chronic non-cancer pain; TD = transdermal; RoA = route of administration; OTFC = oral transmucosal fentanyl citrate; PRN = as needed; CNS = central nervous system; NR = not recommended; OA = osteoarthritis; RA = rheumatoid arthritis; NSAID = nonsteroidal anti-inflammatory drug; SoB = shortness of breath; N/V = nausea/vomiting.