The relief of pain and suffering has always been one of the most important and elusive goals in the practice of medicine. Though many tools for safe and effective management of pain became available in the 20th century, pain is often not treated optimally. In the last 20 years, national and international organizations have issued clinical practice guidelines that address acute pain and the physical pain associated with terminal illnesses such as cancer; more recently, guidelines have emerged for the management of chronic nonmalignant pain, which is perhaps the most prevalent form of pain in the world today.

THE PREVALENCE OF CHRONIC PAIN AND ITS UNDERTREATMENT

Chronic pain is one of the most common reasons people seek medical help. In a comprehensive cross-sectional study of 29,474 US households conducted by the American Pain Society (APS), 9% of adult Americans reported moderate-to-severe (≥5 on a 10-point scale) chronic nonmalignant pain. The majority (57%) of chronic pain sufferers in the APS survey reported severe or very severe pain, and in more than one half (56%) the pain had persisted for at least 5 years, either as constant pain or frequent flares, significantly affecting their quality of life.

Most chronic pain sufferers—51% in the APS survey—said they were seeing a primary care physician (family physician or internist) for pain treatment, while 15% were being treated by orthopedic surgeons, 10% by rheumatologists, 8% by neurologists, and 5% by chiropractors. Yet, a large proportion of respondents reported difficulty getting adequate care for chronic nonmalignant pain. Only 55% considered their pain to be “under control.” Nearly all reported functional limitations as a result of their pain, including difficulty sleeping (68%), walking (53%), having sex (50%), concentrating (42%), working (34%), and socializing (26%). Depression was experienced by 18% of respondents.

Many pain sufferers were dissatisfied with their physicians: 47% had changed doctors at least once, and 22% had changed doctors at least 3 times in the pursuit of pain relief. Similar data have been reported elsewhere.

Dr Potter is Associate Clinical Professor, Department of Family and Community Medicine, University of California, San Francisco School of Medicine. Dr Potter reports having no financial or advisory relationships with corporate organizations related to this activity.

Off-Label Product Discussion: The author discusses off-label use of amitriptyline, desipramine, fluoxetine, nortriptyline, paroxetine, venlafaxine; carbamazepine, clonazepam, divalproex sodium, gabapentin, phenytoin, valproic acid; chondroitin, glucosamine sulfate; and tizanidine for chronic pain.

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The most common reasons patients cited for changing physicians were difficulties finding physicians who were sufficiently knowledgeable about pain management, were willing to listen and take their pain seriously, and were willing to treat their pain aggressively. While there is still a great need for improved therapies for pain, it is clear that there is ample room for the medical community to do a better job of pain management using existing tools.

Etiology and General Approach to Chronic Nonmalignant Pain

Chronic nonmalignant pain is mediated primarily by 2 pathogenic mechanisms: nociceptive and neuropathic. Somatic pain, which accounts for the vast majority of chronic pain syndromes, arises by activation of nociceptors in the skin and musculoskeletal tissue. It is initiated and maintained by chemical proinflammatory mediators and is usually the result of trauma, surgery, or cancer. Common sources of chronic somatic pain include low back pain and degenerative joint disease. Neuropathic pain is caused by an injury or a disease process that damages peripheral sensory nerves or their ganglia in the central nervous system. Examples of chronic pain syndromes of neuropathic origin include postherpetic neuralgia and diabetic neuropathy.

The treatment of chronic pain begins with establishing a thorough understanding of what the patient is experiencing. This includes taking a complete history of events that triggered the pain, reviewing prior diagnostic evaluations and treatment, determining the level of pain, and ascertaining how the pain interferes with the patient's daily functioning and quality of life. It is important when assessing pain to remember that it is ultimately a subjective experience for the patient. While physical examination can be helpful in making a diagnosis, it should not be relied upon to confirm the level of pain that the patient is experiencing.

While it is important to diagnose and treat the underlying cause of the pain whenever possible, it is equally important to treat the pain itself, even when the diagnosis remains in doubt. Regardless of etiology, early and aggressive treatment of pain symptoms reduces the risk of developing a chronic pain syndrome. Functional limitations arising as a result of chronic pain, which can be both physical and psychological, are also important to address explicitly. Depression in particular is one of the most common sequelae of chronic pain and should be addressed aggressively.

Regardless of etiology, a wide range of pharmacologic and nonpharmacologic approaches may need to be tried before chronic pain is adequately controlled. Because sorting through the various treatment options can be difficult and time consuming, the physician should always attempt to begin by forming a partnership with the patient that is marked by mutual trust and understanding. The physician should also provide the patient with realistic expectations from the outset by noting that while chronic pain can usually be controlled, it is less often cured. The key to long-term success is to create a therapeutic alliance that will last through the many trials and errors of treatment, until the pain can be successfully controlled.

Overview of Pain Management

World Health Organization Analgesic Ladder

One of the foundations of modern analgesia is the 3-step analgesic ladder developed by the World Health Organization (WHO) to assist clinicians caring for patients with cancer pain or pain related to cancer treatment (Figure 1). Mild pain (step 1) is
best treated with a nonopioid analgesic (eg, acetaminophen or nonsteroidal anti-inflammatory drug [NSAID]), with or without adjuvant medications (eg, antidepressant or anticonvulsant). For mild-to-moderate pain (step 2), a mild opioid is recommended (eg, codeine), with or without a nonopioid analgesic and/or an adjuvant. Moderate-to-severe pain (step 3) is best treated with a potent opioid (eg, morphine), with or without a nonopioid analgesic and/or an adjuvant. It has been suggested that this same approach is appropriate for pain treatment regardless of the source.\textsuperscript{2,12} The WHO analgesic ladder does not address many of the important issues in chronic pain management, but it does provide a useful framework for considering the broad array of pharmacologic therapies commonly used to control chronic pain.

**Acetaminophen**

Acetaminophen is an effective analgesic for many patients. Although acetaminophen lacks anti-inflammatory properties, when used at maximal doses it can be as effective as an NSAID for arthritis pain and is recommended as first-line treatment for arthritis by the American College of Rheumatology and the APS.\textsuperscript{13,15} Acetaminophen is often underused and may need to be taken at doses of 1000 mg 4 times daily for a month or more to establish maximal efficacy. The risk of hepatotoxicity, however, increases when patients are prescribed more than 4 g daily on an ongoing basis. Individuals with underlying liver dysfunction may not be able to tolerate more than 2 g to 3 g daily in divided doses, and liver function should be monitored in patients for whom acetaminophen has been prescribed. Patients who take acetaminophen at maximum doses should be warned that it is often contained as an ingredient in many over-the-counter preparations. Acetaminophen toxicity is a potentially devastating complication in patients who unwittingly take large doses of acetaminophen by combining multiple over-the-counter preparations containing the drug.

**NSAIDs and COX-2 Inhibitors**

NSAIDs exert their therapeutic effect by inhibiting an enzyme known as cyclooxygenase 2 (COX-2), the enzyme responsible for producing pro-inflammatory prostaglandins. The therapeutic window of first-generation NSAIDs is frequently limited by the fact that these drugs also inhibit cyclooxygenase 1 (COX-1), which plays an important role in maintaining the protective lining of the stomach.\textsuperscript{12,16} As a result, gastritis and peptic ulcers are relatively common side effects of the nonselective first-generation NSAIDs. These drugs include salicylates, propionic acids, acetic acids, oxicams, naphthyalkalones, and fenamates.\textsuperscript{18} Nonetheless, pain responds well to relatively low doses of NSAIDs (eg, 400 mg ibuprofen 3 times daily) and many patients also tolerate larger doses (eg, 800 mg ibuprofen 3 times daily) with minimal side effects. Responses may vary from drug to drug, so failure to achieve therapeutic benefit with one NSAID does not rule out trying another drug from this class.

**Key Points 1**

1. Pain management should encompass a comprehensive evaluation of the cause of pain, the level of pain, and the functional status of the patient.
2. A diagnostic and treatment plan should be developed that addresses all 3 of these issues.
3. Successful chronic pain management usually involves a collaborative, trusting relationship between the primary care physician and patient.
4. A combination of therapies and a multidisciplinary team approach are often necessary to achieve adequate pain control.
5. Evaluation and treatment of associated depression and anxiety are important.

The development of NSAIDs that selectively inhibit COX-2 has held the promise of pain relief equivalent to that of nonselective NSAIDs but with diminished gastric side effects.\textsuperscript{19} The use of COX-2 inhibitors instead of traditional NSAIDs in elderly patients with chronic inflammatory pain has recently been endorsed by the American Geriatric Society, and the APS recommends the use of COX-2 inhibitors for moderate-to-severe osteoarthritis or rheumatoid arthritis pain that is unresponsive to acetaminophen.\textsuperscript{13,16} The extent of additional gastric protection afforded by COX-2 inhibitors continues to be hotly debated because they may cause gastrointestinal toxicity in some patients. Consequently, in many patients COX-2 inhibitors should often be coadministered with a gastroprotective agent, such as a proton pump inhibitor, and should probably be avoided altogether in patients at high risk of gastric toxicity.

COX-2 inhibitors are just as nephrotoxic as traditional NSAIDs, and routine monitoring of renal function is advised in patients at risk of renal deterioration, particularly the elderly.\textsuperscript{12} Also, NSAIDs and COX-2 inhibitors may cause blood pressure to increase by a few points. The use of NSAIDs or COX-2 inhibitors does not preclude the need for aspirin therapy in patients with cardiovascular disease.

**Glucosamine Sulfate**

Glucosamine sulfate has been touted as an arthritis treatment that may be disease modifying.
and as effective as acetaminophen or NSAIDs for relief of osteoarthritis pain, but efficacy remains to be evaluated in definitive clinical trials.\(^{18}\) Many patients are turning to this readily available over-the-counter medication, especially those who fail to find relief or are at risk of adverse effects from acetaminophen or NSAIDs.

Few adverse effects have been reported with glucosamine; however, it is not regulated by the Food and Drug Administration. Since some glucosamine products are made from shellfish, patients with allergies to shellfish should be cautioned about taking glucosamine. In addition, there has been some concern that glucosamine may increase the risk of insulin resistance in some patients.

Glucosamine hydrochloride and n-acetyl glucosamine are two other glucosamine compounds that are even less well studied than glucosamine sulfate. Chondroitin is often added to various glucosamine preparations, again with very little evidence to support its efficacy in the treatment of arthritis pain. Therefore, it is reasonable for patients who wish to try one of these products to use the glucosamine sulfate products until more data are available.

**Adjuvant Analgesics**

Adjuvant analgesics are a diverse group of drugs that have primary indications other than chronic pain and exert analgesic effects in certain circumstances. Those relevant to chronic musculoskeletal and neuropathic pain are discussed below.

**Adjuvant Medications for Musculoskeletal Pain.** Muscle relaxants (eg, baclofen, carisoprodol, chlorzoxazone, cyclobenzaprine, metaxalone, methocarbamol, tizanidine) are among the most prescribed adjuvants for chronic musculoskeletal pain, especially back pain and muscle spasms that affect the neck and shoulders. They comprise a wide spectrum of structurally unrelated agents with diverse actions, although most are thought to modify central perception without affecting peripheral pain reflexes or motor function. The efficacy of these agents is usually modest, and evidence to support the superiority of any one over the others is lacking. These adjuvant therapies may be helpful, however, in some patients who have poorly controlled somatic pain or are unable to tolerate other therapies. Failure with one of these agents does not mean that a trial with another might not be of benefit. As a group, most of these drugs are well tolerated and have a relatively low toxicity profile.\(^{17}\) However, somnolence is a common adverse effect associated with many of these drugs. A few of these drugs have also been reported to induce drug-seeking behavior in some people.

**Adjuvant Medications for Neuropathic Pain.** The most studied adjuvants for neuropathic pain include antidepressants, anticonvulsants, \(\alpha_2\)-adrenergic agonists, and other drugs designed specifically to target neuropathic pain.\(^{16}\) The analgesic effect of antidepressants is independent of their antidepressant activity and occurs at a much lower dosage.\(^{20-22}\) Yet, because chronic pain is frequently accompanied by depression, many chronic pain patients, regardless of the etiology of their pain, can benefit from treatment with an antidepressant.\(^{23}\) Among the tricyclic antidepressants, desipramine and nortriptyline are usually favored over amitriptyline because of their comparatively better anticholinergic adverse effect profiles.\(^{23,24}\) Some selective serotonin reuptake inhibitors (SSRIs) (eg, fluoxetine, paroxetine, venlafaxine) may reduce neuropathic pain with fewer side effects.\(^{23,26}\) SSRIs, however, are more expensive, and there is no evidence that they are more effective than the tricyclic antidepressants.

Anticonvulsants can be effective in relieving the burning, lancinating, or dysesthetic pain of diabetic neuropathy and postherpetic neuralgia. Compared with antidepressants, they have similar rates of efficacy and adverse effects.\(^{28}\) Anticonvulsants (eg, carbamazepine, clonazepam, divalproex sodium, gabapentin, phenytoin, valproic acid) act by suppressing ectopic neuronal discharges that occur following nerve injury and, in patients with neuropathic pain, possibly via \(\gamma\)-aminobutyric acid inhibition.\(^{18,22}\) The off-label use of gabapentin has become a popular therapy for neuropathic pain in the United States; however, it has not been conclusively shown to be more effective than other therapies.\(^{15,26,27}\)

**Key Points 2**

1. Make sure that the underlying causes of pain are being aggressively evaluated and treated through diagnostic testing and/or specialty referral, if appropriate.
2. Understand and explain to patients the difference between addiction, physical dependence, and tolerance.
3. Warn patients about the risk of sedation, and reassure them that it usually resolves within a week of achieving a stable dose of medication.
4. Anticipate common adverse effects, such as nausea and constipation, and provide prophylactic treatments to improve outcomes and adherence to therapy.
5. Warn patients about the risks of acetaminophen toxicity when short-acting acetaminophen-containing opioids are used inappropriately.
6. Be clear with patients from the outset about the rules for the use and misuse of opioids in your practice.
7. Consider random urine drug testing in some patients.
8. Refer patients to a pain specialist if they have a past or present history of substance abuse, if they exhibit aberrant behavior when prescribed opioids, or if they require large doses of opioids to control their pain.
9. Document the care you provide according to Federation of State Medical Boards (FSMB) guidelines.
Topical analgesics may also be useful for treating neuropathic pain. Capsaicin, an irritant derived from chili peppers, has been used topically with some success for a variety of conditions, including diabetic neuropathy, postherpetic neuralgia, and cluster headaches. When used repetitively over a period of time, capsaicin depletes C-fibers of substance P, thereby diminishing the transmission and perception of pain. Another available topical analgesic is lidocaine, which can be administered as a gel or via a patch and has been advocated as an effective therapy particularly for postherpetic neuralgia.

Opioids for Moderate-to-Severe Musculoskeletal or Neuropathic Pain

Opioids, often viewed as a last resort for the relief of chronic pain, are nonetheless the mainstay of treatment for chronic somatic and neuropathic pain refractory to other analgesics. There is a wide range of agents available with varying potencies and delivery systems that optimize convenience, pain relief, and management of side effects (Table). Opioids represent a family of alkaloids that are either purified directly from the opium poppy (eg, codeine, morphine, thebaine), semisynthetic derivatives of opium (eg, hydrocodone, oxycodone, hydromorphone, oxymorphone, buprenorphine), or structurally related agents that are completely synthetic (eg, meperidine, fentanyl, propoxyphene, methadone). The efficacy and risk of adverse effects are similar for these drugs; however, meperidine and propoxyphene are no longer recommended for the treatment of acute or chronic pain because their toxic metabolites can accumulate in individuals with compromised renal function, leading to neurotoxicity.

Short-Acting Opioids. Short-acting opioid preparations can be useful for treating chronic pain that is sporadic or intermittent. For persistent pain that requires around-the-clock relief, short-acting opioids can also be very useful initially, ie, when titrating to achieve the maximum response to therapy. However, once a stable dose of opioid is achieved, it is usually best to switch to a long-acting opioid that requires less frequent dosing and that results in fewer peaks and troughs in drug levels. When switching to long-acting opioids, the short-acting opioids should be tapered, while the long-acting preparations are gradually introduced. However, to treat breakthrough pain, smaller amounts of a short-acting opioid can also be prescribed for use as needed. If short-acting opioids containing acetaminophen are prescribed, patients should be cautioned about the risk of acetaminophen toxicity if these medications are combined with other over-the-counter preparations that contain acetaminophen.

Long-Acting Opioids. The most commonly used long-acting opioids are sustained-release morphine and oxycodone. Particular caution should be used when titrating the fentanyl patch in opioid-naïve patients, since drug levels gradually increase over 3 days. Methadone has a variable half-life and also should be titrated carefully over several days when it is initiated. Despite these potential risks, long-acting opioids are generally safe and effective when used appropriately. Many patients appreciate the convenience of the fentanyl patch, and others appreciate the relatively low cost of methadone. Delivery of opioids near the spine, either epidurally or intrathecally via an implantable pump, has been another effective way to dispense morphine in ambulatory patients with intractable chronic nonmalignant pain, particularly back pain.

Tramadol. Tramadol is a synthetic opioid with a relatively low affinity for opioid receptors. It has the potential added benefit of inhibiting reuptake of serotonin and norepinephrine. It is particularly effective in patients with moderate-to-severe chronic arthritis pain who are either unresponsive to acetaminophen or NSAIDs or cannot tolerate them. It is also effective in patients with chronic low back pain. The need for frequent dosing (4 times daily) may limit the utility of tramadol in patients who need around-the-clock pain relief.

Potential Adverse Effects of Opioids

When prescribing opioids, physicians should make sure that patients are well informed so they will

<table>
<thead>
<tr>
<th>Opioids</th>
<th>Approximate Equianalgesic Oral Dose</th>
<th>Usual Starting Dose for Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30 mg q 4 hours</td>
<td>15 mg q 4 hours</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>30 mg q 4 hours</td>
<td>10 mg q 4 hours</td>
</tr>
<tr>
<td>Codeine</td>
<td>120 mg q 4 hours</td>
<td>60 mg q 4 hours</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>7.5 mg q 4 hours</td>
<td>6 mg q 4 hours</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>30 mg q 4 hours</td>
<td>5 mg q 4 hours</td>
</tr>
<tr>
<td>Morphine SR</td>
<td>30 mg q 8 hours</td>
<td>30 mg q 8 hours</td>
</tr>
<tr>
<td>Methadone</td>
<td>20 mg q 8 hours</td>
<td>10 mg q 8 hours</td>
</tr>
<tr>
<td>Oxycodone CR</td>
<td>60 mg q 8 hours</td>
<td>10 mg q 8 hours</td>
</tr>
<tr>
<td>Fentanyl patch</td>
<td>NA</td>
<td>25 mcg/hour patch, q 72 hours</td>
</tr>
</tbody>
</table>

q = every; SR = sustained release; CR = controlled release.

* Long-acting opioids are preferred for pain that is around-the-clock. Short-acting opioids should be used when titrating initial therapy and then administered only as needed for intermittent or breakthrough pain.
be able to respond appropriately if adverse effects occur and will not abandon therapy prematurely. While sedation is common when opioids are initiated, the symptoms usually dissipate within a week after a stable dose is achieved. Most patients are able to engage in their usual activities, including driving, after adjusting to a stable dose. 40,41 Because chronic sedation can occur, opioid therapy may have to be withdrawn in some patients. However, patients with refractory pain, who are having difficulty tolerating opioids due to somnolence that does not resolve after several days or weeks, may sometimes be successfully treated with methylphenidate or donepezil.

When used in very high doses, opioids can also cause neurotoxic effects, such as delirium and/or hyperalgesia. However, these risks can usually be avoided when the opioid is titrated slowly and carefully, and if the primary care physician consults a pain specialist when dosing increases to 250 mg of morphine equivalents per day.

Respiratory suppression is very rare in ambulatory patients who are taking opioids at recommended starting doses and whose medication has been titrated appropriately. Nausea is a relatively common early adverse effect, but it can be treated with medications, such as metoclopramide or promethazine; the nausea usually is temporary and diminishes over time. Constipation is probably the most common adverse effect of opioid therapy; it can lead to serious complications if not treated aggressively. Most experts recommend the use of a gentle laxative, such as senna, in combination with a stool softener, such as docusate sodium, to prevent chronic constipation whenever opioids are prescribed for more than a few days. Fiber-based bowel preparations, however, should be avoided because they may increase the bulkiness of stools without promoting bowel motility, resulting in an increased risk of bowel obstruction. 22,33

Some opioid, nonopioid, and adjuvant analgesics produce superior results when used in combination. For example, muscle relaxants are frequently prescribed with NSAIDs or acetaminophen. The combination of acetaminophen with opioids, such as codeine or hydrocodone, is effective for osteoarthritis pain. 22 NSAIDs used in combination with tramadol or codeine effectively relieve osteoarthritis pain and chronic low back pain. 42,43

The Risk of Addiction. Research and clinical experience during the last decade have demonstrated that addiction to prescribed opioids among patients with chronic pain who have no prior history of substance abuse is very uncommon. 32 Clearly, patients with a history of past or current substance abuse warrant careful evaluation by a specialist and very close monitoring if opioids are considered as a treatment. Because not all patients are likely to be forthcoming about a history of substance abuse, physicians should watch for aberrant behaviors in all patients who are taking opioids. However, patients who exhibit drug-seeking behavior may just as likely be suffering from an iatrogenic condition termed pseudoaddiction, which is due to inadequate treatment. 44 Physicians should therefore consider their own biases, as well as the adequacy of the therapy they are providing, before dismissing a patient with chronic pain as an addict who does not deserve opioid therapy. Making the distinction between true addiction and pseudoaddiction may be difficult and will often require consulting with a pain specialist. Finally, it is important for physicians and patients to distinguish physical dependence and/or tolerance from addiction. Physical dependence, a reaction to abrupt withdrawal of medication, occurs with many drug classes and may occur with opioid use, but is not a contraindication to treatment with opioids. Many commonly used drugs, such as paroxetine, clonidine, or beta-blockers, can also cause physical dependence. The accepted approach is to continue these drugs if needed, and to withdraw them gradually when no longer needed. The same is true for patients taking opioids around-the-clock. Tolerance

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**Definitions Issued by Consensus of the American Academy of Pain Medicine, American Pain Society, and American Society of Addiction Medicine.**

**Addiction:** a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. Addiction in the course of opioid therapy of pain can best be assessed after the pain has been brought under adequate control. Behaviors suggestive of addiction may include: inability to take medications according to an agreed upon schedule, taking multiple doses together, frequent reports of lost or stolen prescriptions, doctor shopping, isolation from family and friends, and/or use of psychoactive drugs not prescribed in addition to prescribed medications.

**Physical Dependence:** a state of adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.

**Tolerance:** a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.

**Pseudoaddiction:** term that has been used to describe patient behaviors that may occur when pain is undertreated. Patients with unrelieved pain may become focused on obtaining medications, may “clock watch,” and may otherwise seem inappropriately “drug seeking.” Even such behaviors as illicit drug use and deception can occur in the patient’s efforts to obtain relief. Pseudoaddiction can be distinguished from true addiction in that the behaviors resolve when pain is effectively treated.

The consensus statement is available at www.ampainsoc.org/advocacy/opioids2.htm
to opioids may occur, requiring increased doses to achieve therapeutic benefit. However, most patients with chronic pain do not experience tolerance once they have achieved a stable dose. Diminished response to a given dose of opioid medication over time is less likely to be due to tolerance than it is to a worsening of the underlying condition that is causing the pain.\textsuperscript{45,46}

**Nonpharmacologic Therapies**

Clearly, there is an important role for nonpharmacologic therapy in the management of most patients who experience chronic pain. In fact, many patients will prefer nonpharmacologic therapies as a first-line treatment for pain, and anecdotal evidence suggests that these treatments can be as effective as first-line therapy for chronic pain in many cases. These treatments can include acupuncture; biofeedback; bodywork; chiropractics; cognitive-behavioral therapy; homeopathy; hypnosis; relaxation techniques; and physical therapy methods that use heat, ice, massage, or transcutaneous electrical nerve stimulation. Attempts to standardize these approaches have been made by the National Center of Complementary and Alternative Medicine of the National Institutes of Health.\textsuperscript{47} While very few studies have conclusively shown improved outcomes with nonpharmacologic modes of treatment, 3 techniques offered by most pain clinics (biofeedback, relaxation, and cognitive-behavioral therapy) have a large body of literature to support their effectiveness.

**Issues When Prescribing Opioids for Chronic Pain in Primary Care**

The management of chronic pain has become mired in controversy. The recent concern about undertreatment has been well publicized and has recently led to a number of successful lawsuits by patients who sought damages for inadequate pain treatment. The passage of the Pain Patient’s Bill of Rights in California has only added to this controversy.\textsuperscript{48} At the same time, many clinicians continue to be concerned about the risk of addiction, physical dependence, tolerance, and potentially dangerous adverse effects when prescribing the most potent opioid pain relievers. In addition, most clinicians are aware of at least one case in which a colleague was inappropriately investigated by legal authorities for overprescribing opioids. This paradox is unfortunate. However, it is imperative that physicians know how to evaluate pain, be aware of the full range of treatments, and be willing to prescribe appropriate treatments including opioids when indicated.

Physicians can take steps to protect both themselves and their patients who require opioid analgesics for chronic pain, and to enhance their comfort with prescribing analgesics.\textsuperscript{49-51} The Federation of State Medical Boards (FSMB) has published guidelines endorsed by many state medical boards to assist physicians with the safe administration of controlled substances, such as opioids for chronic pain.\textsuperscript{52,53} The FSMB guidelines recommend 7 important elements of evaluating the use of controlled substances for pain control: patient evaluation, treatment plan, informed consent and agreement for treatment, periodic

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**Excerpts from the California Pain Patient’s Bill of Rights**

- A patient suffering from severe chronic intractable pain has the option to request or reject the use of any or all modalities to relieve his or her severe chronic intractable pain.
- A patient who suffers from severe chronic intractable pain has the option to choose opiate medication for the treatment of the severe chronic intractable pain as long as the prescribing is in conformance with the provisions of the California Intractable Pain Treatment Act, Section 2241.5 of the Business and Professions Code.
- A physician treating a patient who suffers from severe chronic intractable pain may prescribe a dosage deemed medically necessary to relieve severe chronic intractable pain as long as the prescribing is in conformance with the provisions of the California Intractable Pain Treatment Act, Section 2241.5 of the Business and Professions Code.
- The patient’s physician may refuse to prescribe opiate medication for a patient who requests the treatment for severe chronic intractable pain. However, that physician shall inform the patient that there are physicians who specialize in the treatment of severe chronic intractable pain with methods that include the use of opiates.

California Law, California Division of Health & Safety Code.\textsuperscript{1997}

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**Excerpts from the Federation of State Medical Boards Model Guidelines for the Use of Controlled Substances for the Treatment of Pain**

- The medical management of pain should be based upon current knowledge and research and includes the use of both pharmacologic and nonpharmacologic modalities. Pain should be assessed and treated promptly and the quantity and frequency of doses should be adjusted according to the intensity and duration of the pain. Physicians should recognize that tolerance and physical dependence are normal consequences of sustained use of opioid analgesics and are not synonymous with addiction.
- Physicians should not fear disciplinary action from the Board or other state regulatory or enforcement agency for prescribing, dispensing, or administering controlled substances, including opioid analgesics, for a legitimate medical purpose and in the usual course of professional practice. The Board will consider prescribing, ordering, administering, or dispensing controlled substances for pain to be for a legitimate medical purpose if based on accepted scientific knowledge of the treatment of pain or if based on sound clinical grounds. All such prescribing must be based on clear documentation of unrelieved pain and in compliance with applicable state or federal law.
- The Board has adopted the following guidelines when evaluating the use of controlled substances for pain control: Evaluation of the patient; Treatment plan; Informed consent and agreement for treatment; Periodic review; Consultation; Medical record; Compliance with controlled substances laws and regulations.

Federation of State Medical Boards of the United States, Inc.\textsuperscript{51}
**Sample Medication-Use Agreement**

I, __________________________, understand that I have pain that has not been adequately controlled with other medications and that my function is limited by my pain. I understand that the intent of the medication is to increase my ability to do more, though the medication is unlikely to eliminate the pain. I will take the medication only as prescribed. I will not take any sedatives, alcohol, or other pain medications without the prior approval of my doctor.

I understand that the medication will be prescribed only by Dr. __________________________ and only according to the agreed-upon schedule. Prescriptions will be provided only during regularly scheduled appointments. Refills will never be provided by telephone. I will not seek or accept any medications for pain other than those prescribed by my doctor. “Medications for pain” includes prescriptions from other doctors, medications borrowed or accepted from family or friends, and any illicit or street drugs. Medication refills will be provided as written prescriptions only. No refills will be given prior to the next scheduled appointment date. If I do not keep my appointment, I will not receive a refill. Two (2) appointment cancellations with less than 1 working day’s notice or two (2) no-show appointments may constitute grounds for immediate termination of this agreement.

I understand that my doctor is under no obligation to provide these medications to me, and that she or he reserves the right to discontinue these medications at any time. At my doctor’s discretion, I agree to cooperate with random drug testing which may be requested at any time. If I refuse, I understand the medication will be stopped. I understand that lost or stolen medications will not be refilled under any circumstances. It is my responsibility to protect and secure any medications. This includes keeping the medication out of reach of children. A copy of a police report will be required for any lost or stolen narcotics or narcotic prescriptions. I understand that my doctor may require specialist evaluation of my treatment, and I agree to keep appointments when my physician refers me. My doctor will send a report of my care and a copy of this agreement when a referral is made.

In addition to the above agreements, I accept the right of my doctor’s medical staff to terminate this agreement for any of the following reasons:

1. I seek or obtain any pain medication from a source other than my doctor.
2. I give, sell, or in any way distribute prescribed medications to any other person(s).
3. I in any way attempt to forge or alter a prescription.
4. My medical condition declines to the point at which, in the judgment of my doctor, continued therapy with this medication presents a danger to my well-being or safety.
5. There is evidence that I am no longer receiving a reasonable therapeutic benefit from the medication, or my doctor determines that I am no longer a good candidate to continue the medication.

I agree to fill my prescriptions only at the pharmacy I list below. If I change pharmacies, I will contact my doctor’s office and provide them with the name, address, and phone number of the new pharmacy. Under no circumstances will I obtain medications from more than 1 pharmacy at a time. In order to verify appropriate medication use, my doctor’s office will provide my chosen pharmacy with a copy of this agreement. I understand that any alteration in my medication prescriptions will require a new written agreement.

| Pharmacy name | __________________________ |
| Pharmacy address | __________________________ |
| Pharmacy telephone | __________________________ |

Medication name, dose, and directions _____________________________
Number of pills prescribed ______ Frequency of appointments ________ days

I understand that by signing this agreement, I must abide by the rules reviewed above and that failure to abide by these agreements will result in the termination of medication prescriptions and possibly the termination of services from my doctor and his or her practice.

| Patient signature | __________ | Date | __________ |
| Physician signature | __________ | Date | __________ |

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review, consultation, medical records, and compliance with controlled substances laws and regulations. Documentation of care is critical both to assist in the assessment and management of these patients and to protect the clinician against possible questioning by legal authorities.

The initial evaluation should include a complete medical history and physical examination. A thorough description of the patient’s pain should be obtained, including current and past pain treatments, any history of substance abuse, and documentation of medical indications for the use of a controlled substance. The physician should then devise a treatment plan that includes the specific treatments currently offered and the parameters that will be used to determine treatment success, set short- and long-term treatment goals (eg, level of pain relief, functional improvement), and describe additional diagnostic evaluations or treatments.

Informed consent is an essential part of the documentation. Some physicians prefer to document the verbal exchange of information, while others specify the terms of treatment in a written contract between patient and physician that is signed before long-term opioid treatment begins. Either way, it is important that patients be advised of the potential benefits and risks of opioid treatment. Model medication-use agreements have been issued by the American Academy of Family Physicians and the American Academy of Pain Medicine that can be tailored to suit the individual needs of the physician. While they may not be necessary for every patient, these agreements are recommended for patients with a history of substance abuse or those taking higher doses of opioids. A medication-use agreement can stipulate that the patient is obligated to obtain medications only from that physician and from a designated pharmacy; not to exchange, lend, or sell any of the medication; not to alter prescriptions; and to understand that lost or stolen medications will not be replaced. It may also be useful to advise patients of possible random urine testing, and that they should notify the physician immediately if their pain medication is insufficient, rather than run out of medication at an inopportune time. Medication-use agreements serve the dual purpose of documenting and ensuring that conduct and treatment expectations are clearly delineated to facilitate patient accountability. They have the added benefit of reducing miscommunication between patient and physician.

A prescription log (Figure 2) can also be helpful. The log can be expanded to incorporate notes on pain intensity and adverse events. The information can remain available to anyone examining the chart.
The FSMB guidelines also recommend periodic reviews of the care provided for each patient to determine how well the treatment plan is proceeding and whether the treatment goals have been achieved or need to be changed. Currently, there is no specified timeframe for periodic review, although a minimum of once every 6 months is reasonable. To achieve the treatment objectives, physicians are urged to refer patients for additional evaluation as needed, and to comply with the applicable federal and state regulations, including licensure.

Random urine drug testing (UDT) is usually not a necessary component of care, but it may be helpful in caring for patients who are initiating opioids, who may be at risk for addiction or drug diversion, or who exhibit aberrant behavior. UDT provides confirmation that patients are taking the medications prescribed and are not taking other controlled or illegal substances that the physician is unaware of. Rapid immunoassays screen for multiple compounds in the urine; however, they can result in false-positive and false-negative results in many situations.

Therefore, confirmatory testing should always be requested when looking for specific drugs, using gas chromatography/mass spectrometry (GC/MS) or high-performance liquid chromatography (HPLC) technology. Before discussing unexpected results with patients, clinicians should always talk with the laboratory technician to confirm the proper interpretation of the results.

The Future of Analgesia for Chronic Pain

There is a great need for healthcare professionals to do a better job treating pain. Regulatory agencies have recognized the need for more effective pain management and have published guidelines meant to help physicians feel more comfortable prescribing potent medications. Professional societies are also providing educational initiatives to help the medical community improve pain management. With more research, new, safer, and more effective treatments for chronic pain will undoubtedly become available in the future. Yet, even now, there is much reason for optimism. Better outcomes can be achieved when clinicians and healthcare organizations, using currently available therapeutic tools, make the evaluation and treatment of chronic pain a top priority.

REFERENCES


Figure 2. Sample of Controlled Drug Prescription Log

<table>
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<tr>
<th>Name/MR#</th>
<th>Diagnosis</th>
<th>Medication</th>
<th>Date Begun</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refills</td>
<td>------------</td>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>Date</td>
<td># pills</td>
<td>refills</td>
<td>dose and directions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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