Treating Chronic Pain: New Knowledge, More Choices

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Introduction
In routine medical practice, treatment for primary pain fails to achieve adequate relief in at least 40% of patients even though effective treatments are currently available. Many clinicians were trained years ago, when little was known about pain. The rapid expansion of knowledge about pain mechanisms challenges health care practitioners to keep their knowledge base current. Myths, misconceptions, and the resulting fears often bridge gaps in this knowledge. Lack of knowledge limits treatment choices and may hinder desired patient outcomes by allowing pain hypersensitivity and progressive dysfunction to develop (Table 1).

This article—the third in a series about management of chronic pain—offers practical treatment advice based on the newest science. Readers who seek more detail are referred to several recent reviews that provide more complete descriptions of cellular mechanisms.

Multimodal Treatment: Importance for Managing Pain
The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional response associated with actual or potential tissue damage or described in terms of such damage.” Perception of pain is a dynamic interaction between sensory, emotional, and behavioral factors (Table 2). Figure 1 describes normal pain processing and the pathologic changes that accompany development of chronic pain. Pain processing includes six major components: transduction, inflammation, conduction, transmission, modulation, and perception.

Transduction
Acute pain processing (nociception) begins when imminent or real injury from a thermal, chemical, or mechanical source stimulates peripheral endings of sensory neurons (nociceptors). Nociceptors translate (transduce) the physical stimulus into an electrical signal which, if strong enough, triggers an action potential. The effect is analogous to lighting a fuse: Not every stimulus is strong enough to “light the fuse;” but, once “lit,” the signal progresses along the length of its course unless the signal is interrupted.

Local Inflammation
Trauma also triggers damaged cells to release inflammatory substances that increase sensitivity to pain: The resulting flood of prostaglandins, substance P,
bradykinin, serotonin, and histamine causes the area
of injury to become red, swollen, and painful and leads
to hyperalgesia, a lowered pain threshold. Increased
numbers of action potentials and spontaneous dis-
charges occur in response to stimuli. Not only do pain-
ful stimuli become more painful than usual, but previ-
ously nonpainful stimuli can become quite painful
(allodynia). Increased skin sensitivity from sunburn is
a good example of both allodynia and hyperalgesia.

Conduction
The pain signals are then conducted along nerve
fibers via the passage of action potentials along neurons.
Sodium ions enter during depolarization, then potas-
sium ions leave to restore baseline negative charge. The
type of fiber carrying the signal affects the quality of the
pain. A-delta fibers carry sharp, well-localized pain,
whereas C fibers carry poorly localized burn and ache
from around the area of injury. However, because they
are nonmyelinated, C fibers are more easily damaged.
In shingles and in painful diabetic neuropathy, C fibers
bear the brunt of injury. Not surprisingly, the quality of
pain in these conditions is often a burning allodynia.

Transmission
Wherever one nerve conduction pathway ends and
another begins, neurotransmitters—including glutamate,
substance P, norepinephrine, dopamine, and serotonin—
transmit the signal across the synaptic gap separating them. Transmission occurs at three junctions: first, between nociceptor and dorsal horn of the spinal cord; second, between the spinal cord and the thalamus and brainstem; and third, from the thalamus into the cerebral cortex. Figure 2 compares sensitive and nonsensitive patient responses to pain as shown in MRI scans.\(^5\) Data on individual differences were published in Coghill RC, et al.\(^6\)

**Modulation**

Modulation—adjustment of pain intensity—is performed by an extensive antinociceptive (antipain) system. Opioid medications work because opioid receptors already exist to bind endogenous opioid substances, such as endorphins and enkephalins. The pain of acute injury often fades within minutes. The injury has not yet healed, but the antinociceptive system reduces pain intensity, allowing return to function.

One way to conceptualize this pain inhibition is the Gate Theory, first introduced by Melzack and Wall.\(^7\) Nerves are analogous to telephone cables: Both carry many types of calls or signals, but the total number of these carried at any moment is limited. Checks and balances built into the system help triage those signals. For example, if you hit your thumb with a hammer, rubbing the injury decreases pain because rubbing generates inhibitory signals that “close the gate” to the pain.

An intense level of pain for a short time produces stress-analgesia, a short-term protective mechanism whereby the limbic system inhibits pain signals within the spinal cord. (On the battlefield, for example, a soldier may not feel a wound until after fighting stops.) However, the spinal cord is excited by prolonged stimulation of the limbic system by either stress or pain, and this prolonged stimulation can produce hypersensitivity to pain. Patients with chronic pain have reduced pain thresholds and therefore feel pain more intensely.

Pain is diminished by factors which “close the gate” and is intensified by factors that “open the gate.” Medications, emotions, behaviors, and thoughts both open and close the gate by affecting transmission and modulation.

**Perception of Pain**

When pain signals ultimately enter the brain through the thalamus—the brain’s “master switchboard”—these signals are then routed to regions of the brain involved with sensation, autonomic nervous system, motor response, emotion, stress, and behavior. The complex interactions of all these areas define the patient’s perception of pain.

Research shows that patients who describe themselves as more sensitive to pain actually have a heightened response (shown on functional MRI scans) in the three areas of the brain responsible for pain perception: the thalamus, limbic system, and periaqueductal gray area.\(^8\) Distraction—long known to help some patients decrease the level of pain—decreases pain-related brain activity as seen on functional MRI scans.\(^9\) A distracted person literally processes less pain. When focusing on pain, a

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**Table 2: Factors influencing pain**

<table>
<thead>
<tr>
<th>Factors that CLOSE the gate decrease pain</th>
<th>Factors that OPEN the gate increase pain</th>
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<tbody>
<tr>
<td><strong>Physical</strong></td>
<td><strong>Physical</strong></td>
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<tr>
<td>• Comfortable furniture that fits (beds, chairs, car seats)</td>
<td>• Inactivity/deconditioning</td>
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<tr>
<td>• Heat/cold</td>
<td>• Poor or nonrestorative sleep</td>
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<td>• Pacing activities</td>
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<td>• Adequate rest</td>
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<td>• Massage</td>
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<tr>
<td><strong>Chemical</strong></td>
<td><strong>Chemical</strong></td>
</tr>
<tr>
<td>• Medications</td>
<td>• Drug and alcohol dependence</td>
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<tr>
<td>• Diet: eg, Mg++, Ca++, vitamin B complex</td>
<td>• Nicotine</td>
</tr>
<tr>
<td><strong>Behavioral</strong></td>
<td><strong>Behavioral</strong></td>
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<tr>
<td>• Relaxation</td>
<td>• Trying to do too much too quickly</td>
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<tr>
<td>• Direct, rewarding communication</td>
<td>• Difficult relationships</td>
</tr>
<tr>
<td>• Humor</td>
<td>• Social isolation</td>
</tr>
<tr>
<td>• Pleasurable activities</td>
<td>• Stress</td>
</tr>
<tr>
<td>• Relaxation/meditation/prayer</td>
<td>• Persistent worry</td>
</tr>
<tr>
<td><strong>Thoughts and emotions</strong></td>
<td><strong>Thoughts and emotions</strong></td>
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<tr>
<td>• Optimism/positive outlook</td>
<td>• Negative outlook/catastrophizing</td>
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<tr>
<td>• Setting realistic goals</td>
<td>• Hopelessness/worry</td>
</tr>
<tr>
<td>• Affirming of self</td>
<td>• Suppressing emotions</td>
</tr>
<tr>
<td><strong>Structural</strong></td>
<td><strong>Structural</strong></td>
</tr>
<tr>
<td>• Surgery (sometimes)</td>
<td>• Anger</td>
</tr>
<tr>
<td></td>
<td>• Depression/anxiety</td>
</tr>
<tr>
<td></td>
<td>• Focusing on pain</td>
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[Figure 2. Functional MRI scans show brain response in pain-sensitive (left) and nonsensitive (right) patients. (Reproduced by permission of the author from: Coghill RC. Brain mechanisms of pain: Overview. Section on: Neural correlates of inter-individual differences in the subjective experience of pain [homepage on the Internet]. [cited 2005 Oct 4] Available from: http://www1.wfubmc.edu/Nba/Faculty/Labs/ coghill/IndividualDifferences.htm.)]
Clinical contributions

Figure 3. Diagram shows “vicious cycle” of pain.

- Loss of strength makes reinjury more likely and can lead to muscle atrophy.
- Loss of flexibility makes reinjury more likely and can lead to loss of elasticity.
- Odd positions taken to avoid tension make the muscles more taut to protect the body, which can impair the patient’s ability to participate in rehabilitation.
- Odd positions taken to avoid tension spreading pain to other parts of the body.

Fear and anxiety, depression, disturbed sleep, and central nervous system changes lead to other physical impairments in a “vicious cycle,” which, if left unbroken, can worsen pain (Figure 3). Multimodal treatment is therefore vital to pain care (Table 3). Helping patients learn to better manage the pain inhibits pain transmission and improves pain management.10 Exercise and psychological treatment are effective for treating chronic pain because these treatments may help retrain the nervous system to reestablish more normal neural connections.11 Especially important is for clinicians to recognize and treat depression and anxiety, which affect 20% to 50% of patients with chronic pain.12 These conditions affect patients’ ability to participate in their own self care and recovery as well as altering the balance of neurotransmitters involved in modulating pain.

Pathologic Mechanisms of Chronic Pain

AMPA and NMDA receptors are important to our understanding of how acute pain becomes chronic pain.

In acute pain, glutamate (an important neurotransmitter that acts on many different types of pain-related receptors) attaches to the AMPA receptors, which are present on the sodium and potassium channels of the dorsal horn neurons. If enough neurotransmitter effect occurs, another action potential is generated. The signal is propagated along the second leg of its journey toward the thalamus and then from the thalamus to the cortex.

In contrast, NMDA receptors at the cleft between one neuron and the next are apparently strongly involved with development of chronic pain. Prolonged stimulation of an AMPA receptor changes the resting polarization state of the membrane and, as a result, the magnesium ions that plug the neighboring NMDA receptors are removed. This process primes the NMDA receptors for glutamate activation, thus triggering a cascade of events leading to central nervous system hypersensitization (“central windup”).13,14 Activation of NMDA alters the balance of neurotransmitters; induces synthesis of gene proteins; triggers changes in receptor binding and the firing threshold of nerves; promotes creation of new synaptic contacts; and can even result in cell death. NMDA activation and central windup have several important implications for chronic pain:

- Threshold receptivity of surrounding nerves is lowered, thereby producing hyperalgesia.
- Nonpain nerves begin to fire and carry pain messages, thereby causing allodynia.
- The threshold of opioid mu receptors is increased, thereby causing
  - Decrease in effectiveness of endogenous and exogenous opioids
  - Greater need for antinociceptive input, which

Table 3. Multimodal approach to treating chronic pain

<table>
<thead>
<tr>
<th>Blocking the pain mechanism</th>
<th>Potential multimodal treatments</th>
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| Prevent peripheral nociception | • Prevent pain; treat early and aggressively  
• Start low and go slow  
• Facing; positioning  
• Ice  
• Membrane stabilizers: eg, gabapentin  
• Mg**, Ca**, vitamin B complex  
• NSAIDs  
• Block COX-2 induction in inflammation |
| Prevent gene transcriptional changes | • TCA, opiates, Ca/Na channel blockers, anticonvulsants  
• Inhibit COX-2 induction  
• NMDA antagonists:  
  - methadone, dextromethorphan, ketamine |
| Membrane stabilizers/decrease membrane excitability | • Local anesthetics  
• Ca/Na channel blockers, anticonvulsants  
• TENS/DCS; acupuncture |
| Increase neuropeptidergic modulation at multiple sites | • Acupuncture, manual therapies  
• TENS, DCS  
• Hypnosis; Distraction  
• Education, reduction of anxiety/depression  
• Opiates; TCAs  
• Have fun  
• Placebo |
| Disrupt transmission of peripheral impulse to cord, thalamus, and cortex | • Ablation; Neuromodulatory, radiofrequency, cryoablation, neurosurgery  
• Implanted devices |
is necessary for stopping pain conduction

- Tolerance to opioid substances.
- Threshold sensitivity to catecholamines is lowered, thereby facilitating transmission of pain signals.
- Pain fields spread to adjacent neurons in the spinal cord and nondermatomal representation results. At first, uninjured areas of the body close to the injury begin to hurt; then as additional nerves are recruited, areas increasingly further away become affected.
- All pain is felt as more severe.

In the short term, these changes allow healing by forcing protection of the injured area. “Windup” usually resolves as the injury heals; in some patients, however, these changes persist. The more severe the pain and the longer it persists, the more likely that the change will become permanent. We do not yet know the exact combination of pain severity, duration, etiology, and genetic predisposition that leads to chronic pain, but one important conclusion is clear: Inadequate pain control increases the likelihood that pain will become chronic.

Neurogenic inflammation is an additional mechanism that produces peripheral nervous system sensitization to pain. Increased prostanoid production at the injury site may cause widespread induction of COX-2 as well as activation of macrophage-like cells within the spinal cord. These cells release cytokines and chemokines, which act on neurons and glia to alter gene transcription. This alteration produces allodynia and hyperalgesia, which manifest as spontaneous pain.

Pain that is poorly controlled or prolonged can also inhibit the antinociceptive system. Fibromyalgia, a condition that has been erroneously considered factitious, is now thought to be a debilitating disease caused by antinociceptive dysfunction. In fibromyalgia patients, positron-emission tomography (PET) and functional MRI scans show changes in pain processing.

Pain Management: Target the Type of Pain When Possible

Given that painful medical conditions may be inflammatory or neuropathic (Figure 4), the type (cause) of a patient’s pain should be a factor dictating treatment choice. Long-term use of opioid drugs is not the best approach for treating all pain syndromes. Pain from inflammation responds better to antiinflammatory drugs. Widespread central induction of COX-2 contributes to generalized aching, loss of appetite, and changes in mood and sleep cycles that often accompany any illness with an inflammatory component. Thus, nonsteroidal antiinflammatory drugs (NSAIDs) and COX-2 inhibitors have high utility in many common pain states. However, patients receiving long-term therapy with these drugs are put at potential risk of complications (eg, gastrointestinal bleeding) by the ubiquity of COX receptors in multiple organ systems. Several COX-2 inhibitors were recently withdrawn from the market because of concerns about possible cardiovascular complications. These drugs offer little to no benefit to patients whose pain results from abnormal excitability of sodium channels, as in painful diabetic neuropathy.

Neuropathic pain—pain caused by nervous system pathology, such as peripheral nerve injury or spinal cord injury—often responds better to adjuvant medication, such as anticonvulsant or antidepressant drugs. Without restoring nerve function, adjuvant medication can reduce the burning quality of pain in many patients by directly affecting function of sodium channels as well as other mechanisms of nerve transmission and conduction. By limiting excitation and enhancing inhibition, these classes of drugs can modulate hypersensitivity-related changes of the nervous system.

Opioid drugs effectively treat nociceptive pain that has no coexisting nervous system pathology. In general, however, opioid drugs are much less effective for treating neuropathic pain, because windup decreases opioid efficacy by a variety of mechanisms, including decreasing the number of mu receptors. This generalization does not apply to all patients; in some patients, neuropathic pain does respond to opioids, although the effective dose may be higher than expected.

Many patients have coexisting nociceptive and neuropathic pain that may require a combination of medi-
Pharmacological Management of Chronic Pain

Is the patient experiencing neuropathic pain?

TCAs contraindicated?
- elderly
- cardiac history
- urinary retention

NO

YES

Initiate TCAs, eg,
- nortriptyline
- desipramine
Use below with caution (esp >65 years)
- amitriptyline
- doxepin
- imipramine
- trimipramine

TCA adequate?

NO

YES

Choose one of the following:

Consider adding opioid analgesics to NSAIDs or use opioid alone.1
 Review opioid therapy plan with patient.

Opioid analgesics plus TCAs effective?

NO

YES

Opioid analgesics adequate?

NO

YES

Anticonvulsants adequate?

NO

YES

Topical agents adequate?

NO

YES

Add/substitute with opioid analgesics.

YES

Periodic follow-up at 3 - to 6-month intervals or more frequently based on patient circumstances.

Mild to moderate pain (1– 6 on NRS)2

YES

Initiate NSAIDs

NSAIDs failed, not tolerated, contraindicated?

NO

YES

Consider adding opioid analgesics to NSAIDs or use opioid alone.2
 Review opioid therapy plan with patient.


1 If acute pain patient is at high risk for developing chronic pain, treat aggressively using similar algorithm.
2 More significant functional impairment (eg, 7-10 on functional impairment scale) may indicate more aggressive treatment.

Note: Use antiarrhythmics only with referral to pain medicine specialist.
Invasive pain management interventions, eg, therapeutic nerve blocks, are not addressed by these guidelines.
Please confer with your pain management specialist.

cations, including opioid drugs. For instance, opioid agents are often effective for treating postherpetic neuralgia. Although most patients with fibromyalgia do not need opioid drugs, some affected patients have pain that is so severe and disabling that opioid drugs are necessary for improved function. In a typical primary care practice of 2500 patients, approximately 1% of these members have severe disabling pain with fibromyalgia as one of the interacting causes. If even 5% of these patients need opioid drugs to improve function, then every primary care practitioner has one or two patients with fibromyalgia who may benefit from opioid therapy. The patient’s medical history, description of pain quality, and clinical responses should guide multimodal treatment choices (Figures 5–18 and 6–11).

When to Suspect Neuropathic Pain and Nervous System Hypersensitivity

Suspect neuropathic pain when the pain is described as burning, shooting, lancinating, “pins and needles,” or a strange sensation (e.g., crawling insects). Many patients with neuropathic pain have allodynia. In patients with neuropathic pain, physical examination may show no obvious cause of the pain. Examples include painful diabetic neuropathy, postherpetic neuralgia, and complex regional pain syndrome (CRPS), previously known as reflex sympathetic dystrophy (RSD).

Early CRPS is often considered one of the few conditions warranting urgent consultation with a Pain Medicine Specialist. Signs of possible CRPS in an extremity include:
- Allodynia and/or hyperesthesia seen at physical examination
- Abnormal skin color (often ruddy or bluish)
- Temperature 1°C higher or lower in the affected extremity than in the opposite limb
- Edema
- Pseudomotor activity (increased sweating or dry skin).

Firstline treatment for neuropathic pain is secondary amine tricyclic antidepressants (e.g., nortriptyline, desipramine). In adults older than 65 years, tertiary amines (e.g., amitriptyline, doxepin) should be used with caution because of their strong sedative, anticholinergic, and orthostatic hypotensive effects in this population. Caution and increased monitoring are recommended when using tricyclic antidepressants in patients who have severe heart disease, symptomatic prostatic hypertrophy, neurogenic bladder, dementia, or narrow-angle glaucoma.

Some patients with chronic pain achieve effective analgesia by using considerably lower doses of antidepressants than necessary to treat depression; in nearly half of this population, however, an antidepressant dose may be necessary to achieve pain relief. Benefit may be seen within two weeks or may be delayed for several weeks. Starting at a low dose and slowly increasing the dose by
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Titration is important to minimize side effects, which hinder compliance with a regimen that needs time to become effective.

For patients who do not respond to or tolerate tricyclic antidepressant agents, recommended alternatives include:

- Adding an opioid analgesic to current tricyclic antidepressant therapy
- Starting anticonvulsant therapy, eg, with carbamazepine (for trigeminal neuralgia), phenytoin, or gabapentin.

Although no more effective than tricyclic antidepressant agents or other anticonvulsant drugs, treatment with gabapentin (Neurontin) is an option for older adults and for patients taking medication for comorbid conditions. Although gabapentin too can cause sedation and confusion, this drug may be safer in this group of patients because it has fewer drug-drug interactions. The high cost of gabapentin, however, can be a hardship both to patients and to practitioners.

When suspected neuropathic pain is not responding, early referral to a Pain Medicine Specialist is recommended. The longer pain remains severe, the worse it can become and the more resistant to treatment.

Long-Acting Opioid Drugs May Be Preferable for Some Patients with Chronic Pain

Opioid drugs—the class of drugs with the longest history of use for pain management—are also the drugs most often avoided because of fears of side effects, social stigma, and potential regulatory oversight. The recognition that chronic pain is associated with measurable pathologic change has helped to prompt a shift in philosophy toward considering opioid treatment for chronic, nonmalignant pain. However, a key criterion should be to consider use of these drugs only if they improve patient function. The patient must take an active role in self-management, including following recommendations for activity, exercise, lifestyle, and use of medication.

Long-term use of opioid drugs is not innocuous. Indeed, administration of high-dose opioid drugs can, in rare cases, produce nervous system hypersensitivity itself, probably through the activation of the NMDA receptor. Theoretically, this hypersensitization would be more likely with use of short-acting opioid agents because of the frequent rise and fall of serum levels.

Key organizations that strongly support use of opioid drugs to treat chronic pain have published consensus statements to guide prescription of these drugs. These statements emphasize the importance of a standardized approach in which the drug regimen is initiated only after the physician has assessed the relative risks and benefits of long-term opioid therapy. Long-term opioid therapy should be considered only when:

- Nonopioid drug treatment and nonpharmacologic management is inadequate; and
- The pain substantially impairs the patient’s quality of life and activities of daily living.

Short-acting opioid drugs are extremely useful for short-duration pain or flares. Many patients who have mild chronic pain are very satisfied with use of short-acting agents (eg, 2-4 tablets a day). These agents can also have a limited role in treating “breakthrough pain” in patients with more severe chronic pain.

The problem with short-acting opioid drugs for management of moderate to severe chronic pain is that their rapid rise and fall in blood levels creates short-lived analgesia (Figure 7). This situation:

- Puts patients at risk for acetaminophen toxicity from taking a combination product containing acetaminophen
- Facilitates development of opioid tolerance, which increases the likelihood of escalating medication needs
- Can disrupt sleep (when analgesia is lost)
- Makes patients focus on their medication instead of on their function or progress
- Provides palpable euphoria at peak levels, raising risk of activating addiction in patient prone to substance abuse.

General consensus maintains that use of long-acting opioid drugs should be considered when chronic pain is no longer well managed by short-acting opioid drugs (ie, usually when use reaches 6-8/day on a regular basis). Doses of long-acting opioid drugs should be given at fixed intervals and not on an as-needed basis.

Doses of long-acting opioid drugs should be given at fixed intervals and not on an as-needed basis.
Unfortunately, patients and some clinicians may erroneously fear that the use of long-acting opioid drugs—especially methadone—may either lead to or be interpreted as evidence of drug addiction. Long-acting opioid drugs have some key advantages (Figure 8):24

- Use of these drugs attenuates the rise and fall of drug levels in the blood and correlates with smoother overall pain control.
- Miniwithdrawals and minirebounds do not occur as they sometimes do with short-acting opioid drugs.
- Theoretically, drug tolerance should evolve more slowly than with short-acting opioid drugs.
- Long-acting opioid drugs are not compounded with acetaminophen; the risk of liver and renal toxicity is thus avoided.
- Dosing is more convenient, and compliance may therefore improve.
- By improving pain control and by lengthening the duration of relief, sleep is improved to allow 6-8 (or more) uninterrupted hours of sleep.
- Long-acting opioid drugs should be less likely to trigger addictive behavior and generally have lower potential for drug diversion.

Clinically significant genetic variation exists in mu receptors and possibly in other opioid receptors.25,26 Therefore, failure of one opioid analgesic agent cannot predict patient response to another opioid agent. If the initial opioid analgesic agent is ineffective in controlling pain or if side effects are unacceptable, a different opioid drug should be prescribed.

Opioid drugs are classified into six general families: 1) codeine and morphine; 2) oxycodone, oxycodone/APAP products, and long-acting oxycodone; 3) hydrocodone/APAP products, which are related to hydromorphone (Dilaudid); 4) fentanyl; 5) methadone; and 6) meperidine, which should never be used for chronic pain or for any pain requiring more than a single dose.27 When switching from one opioid family to another, or to a different route of administration, decrease the equianalgesic dose by 30% due to incomplete cross-tolerance. Then, titrate up to clinical response.

Methadone is increasingly used in pain management programs. This drug provides good analgesia with minimal euphoria. Methadone also is an NMDA inhibitor; therefore, its use may help to rebalance nervous system input. However, methadone has unpredictable pharmacokinetics and accumulates with repeated dosing, often requiring a decrease in dose size and frequency. Consultation with a pain medicine expert is highly recommended when initiating treatment with methadone.24 After the patient’s pain has stabilized, however, methadone analgesia can be managed in a primary care environment.

**Recalcitrant Pain**

Reassess your patients periodically for adequate pain control and side effects. Patients often do not take any medication consistently and correctly over time. As the cost of medications becomes a more critical factor for our members, we have noticed a cost-based trend toward not filling prescriptions. If pain is continuing, check to see whether patients are taking their medications correctly and are following the care plan. Pain that persists despite optimal medical management should be referred to your Pain Medicine Program for consultation and for recommendations. Moderate- to high-risk patients who do not respond to aggressive treatment should be referred early to try to minimize development of central hypersensitization.

Creative, mechanism-specific, multimodal treatment can help your patients with chronic pain to regain their lives. Pain reduction and maximized function should be the treatment goals. Active participation of the patient in his or her own self care is vital for improving pain management. Care plans must address reconditioning as well as improving function, sleep, and mood as well as reducing nociception and enhancing neuromodulation. For more discussion of these topics, see the first two articles in this series, *ie*, *Pain Management Doesn’t Have to be a Pain*28 and *Chronic Pain is a Chronic Condition, Not Just a Symptom.*29 Additional information regarding these and other issues related to chronic pain can be found in the CMI Chronic Pain Guidelines at: http://cl.kp.org/pkc/national/cmi/programs/chronicpain/management.html.

In the words of Albert Schweitzer: “We must all die. But that I can save him from days of torture, that is what I feel ...
as my great and ever new privilege. Pain is a more terrible lord of mankind than even death himself.”

References

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