Pain Management

Daniel P. Alford, MD, MPH
Carol A. Waldmann, MD

Chronic pain is an extremely common and particularly challenging problem in the homeless population. Co-morbid psychiatric, behavioral, and addictive disorders are prevalent and complicate the management of pain in this population. Homeless individuals are less able to safeguard their medications and more vulnerable to theft and accompanying assault from others. Mutual mistrust between homeless persons and medical providers is widespread. Finally, acute and chronic pain is common among homeless persons due to the frequency of trauma and injuries in this group. Health professionals who care for homeless persons should develop expertise and comfort with the treatment of pain.

Pathogenic mechanisms of pain can be either nociceptive or neuropathic. Nociceptive pain is due to potential or actual tissue damage. Nociceptive pain is protective and elicits a coordinated reflex and behavioral response to keep injuries to a minimum. On the other hand, neuropathic pain is abnormal, persistent, and maladaptive pain with no obvious biological advantage.

Pain is often divided into three categories: acute pain, cancer pain, and chronic non-malignant pain. In the pain treatment community and the medical field as a whole, a general consensus has evolved on the treatment of acute and cancer pain. The US Department of Health and Human Services has disseminated Clinical Practice Guidelines for the management of acute and cancer pain. In addition, the World Health Organization (WHO) has developed an analgesic ladder for the management of cancer pain. While these guidelines are not universally followed, it is accepted that addiction should not interfere with the adequate treatment of pain in the acute or cancer setting.

The treatment of chronic pain is somewhat more complex for a variety of reasons. Chronic pain is subjective, often with no obvious organic lesion on examination or imaging studies. Myriad conditions can result in "chronic pain", and no single treatment modality fits all of them. By definition, chronic pain continues beyond the usual recovery period for an injury or illness, and therefore often without an ongoing nocioceptive injury. Considerable controversy exists regarding the effectiveness of long-term opioid medication for the treatment of chronic pain.

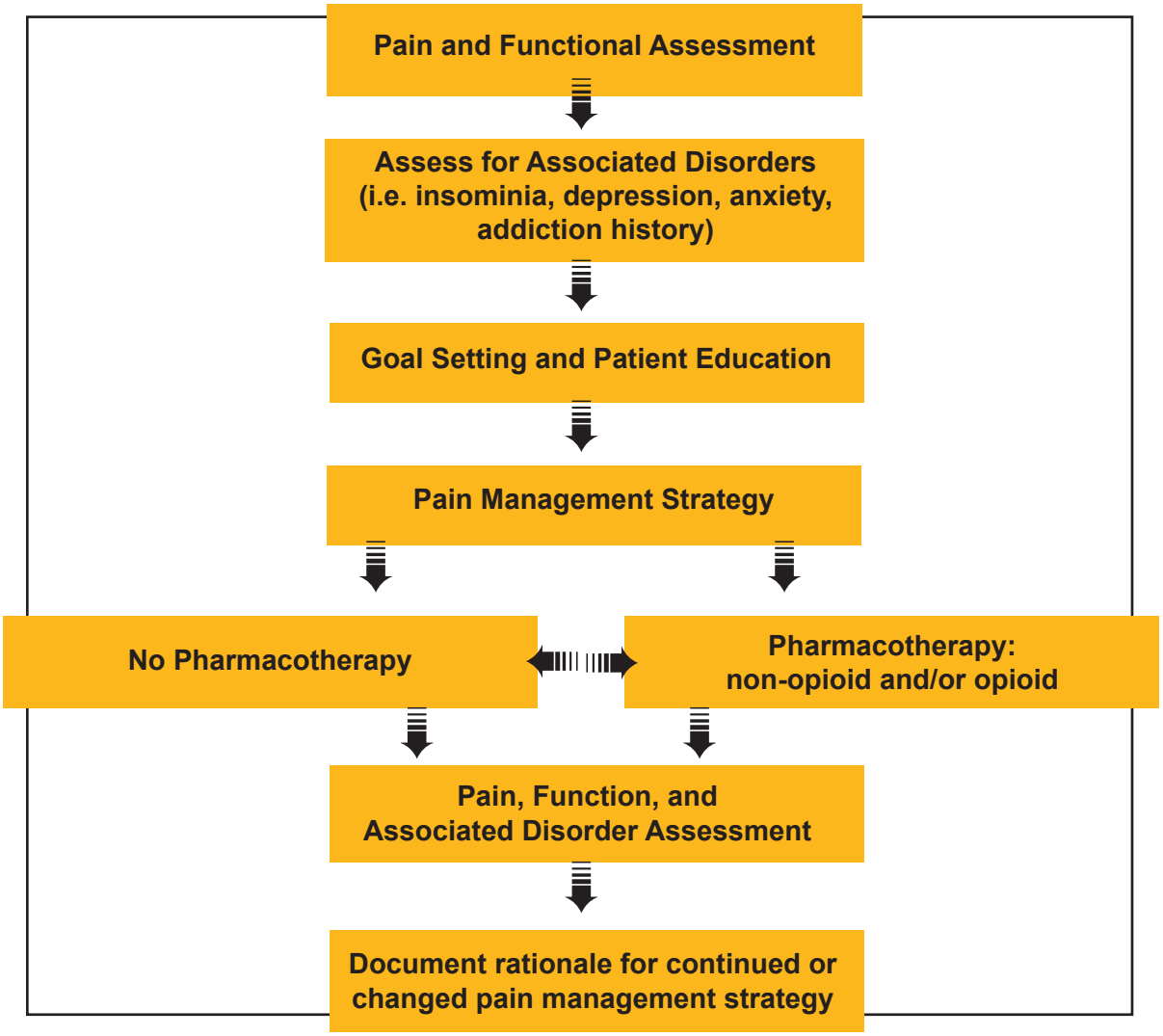
Cancer Pain. This 50 year old man has squamous cell carcinoma of the head and neck. During the two years from diagnosis to death, he underwent two major surgeries, chemotherapy, and radiation therapy. Photo by James O'Connell MD

Epidemiology

Acute Pain

All people experience some acute pain during

APPROACH TO CHRONIC PAIN



their lifetime. Acute pain is triggered by tissue damage, and the type of pain that generally accompanies injury, surgery, or illness. Muscle pain affects 53% of Americans. Lower back pain is the most common form of acute pain and the fifth most common reason for all physician visits. Low back pain is responsible for direct health care expenditures of more than $20 billion annually.

Cancer Pain

Most cancer pain is the result of tissue damage caused directly by the cancer or by complications, such as infections or blood clots. Approximately 30-40% of people diagnosed with any form of cancer experience moderate to severe pain. Cancer patients are more likely to downplay the severity of pain to their doctors because they fear it means worsening of the cancer or because they fear being seen as a burden or a "complainer".

Chronic Pain

The American Chronic Pain Association (ACPA) estimates one in three Americans (50 million people) suffer from some type of chronic pain. The cost to the American public is approximately $100 billion each year in health care, compensation, and litigation. Common causes include lower back problems, arthritis, reflex sympathetic dystrophy syndrome, repetitive motion injuries, shingles, headaches, and fibromyalgia. Diabetic neuropathy, phantom limb sensation, and other neurologic conditions can also cause chronic pain. Chronic pain is associated with physical, emotional, psychological, and social (including financial) disability. Over half of patients with chronic pain experience symptoms of depression or anxiety.

A subset of chronic pain patients have a syndrome that results in marked restrictions in

daily activities and severe alterations in behavior and affect. These patients tend to rely excessively on medications and medical services and undergo multiple non-productive tests, treatments, and surgeries.

Approach to Chronic Pain

The approach to patients with chronic pain begins with a complete pain and functional assessment, followed by goal setting and a treatment plan. Both pain and functional status should be assessed and documented on initial and subsequent evaluations. Therapy should be evaluated based on pain relief and functional improvement. A variety of pain scales can be used, including numeric and visual analog intensity scales. One quick approach is to ask: "On a scale of 0 (no pain) to 10 (most severe pain), what is the level of pain at the present time? What is the level of the best and worst pain experienced in the past 24 hours?" Functional assessments should inquire how pain interferes with daily activities. Setting goals is a critical part of managing chronic pain. Health care providers and patients should discuss realistic expectations regarding pain control and functional improvement prior to initiating therapies. Improvement of both quality of life and functionality are as important as pain relief. In order to reach that goal, treatment of chronic pain must address all aspects of the pain syndrome, including issues of self-esteem, depression, anxiety, sleep, strength and mobility, financial and social support issues, and the experience of pain itself. Finally, the avoidance of the adverse effects of medication, including addiction, is another important goal.

Management of Chronic Pain

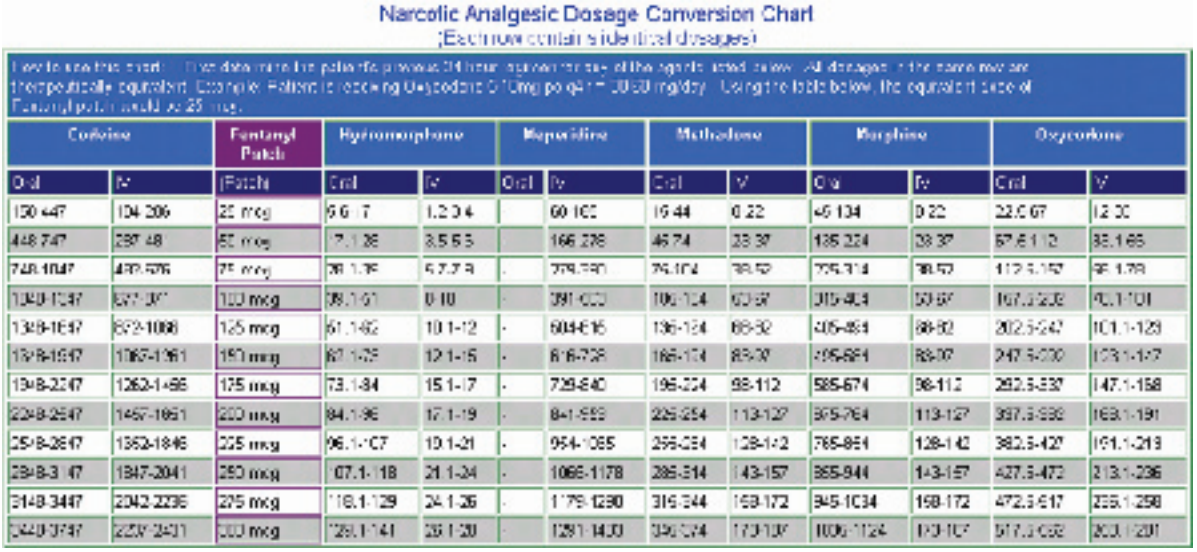
Management of chronic pain is most successful when a multidisciplinary treatment plan is employed that utilizes both pharmacologic and non-pharmacologic approaches. Functional rehabilitation may require physical, occupational, psychological, and stress management therapy. Cognitive behavioral therapy has been noted to be particularly useful in treating chronic pain. Treatment of co-morbid conditions such as obesity, addiction, mood disorders, and cardiopulmonary conditions should be aggressive.

While treatment of acute and cancer pain has improved significantly in the last several years, barriers still exist to the adequate treatment of chronic pain. The physiological mechanism of chronic pain is complex, and we do not fully understand why some episodes of acute pain in some people result in chronic pain while others do not. Evidence suggests the under-treatment of acute pain may play a role in long term changes in the brain that affect the ongoing perception of pain. Inflammation, injury, and disease can all cause neurological changes (neuronal plasticity) that result in increased or persistent pain.

New discoveries have been made in our understanding of the physiology of pain. Some common features of chronic pain include hyperalgesia (lowered pain threshold), allodynia (perception of pain caused by non-painful stimuli, such as touch or vibration), and the spread of pain to areas other than those involved with the initial tissue damage. In animal models, central nervous system plasticity can be clearly demonstrated by permanent changes in the brain after a temporary injury of a peripheral nerve. Hyperalgesia is a result of increased sensitivity of neurons or amplification of the pain signal in the dorsal horn, the section of the spinal cord that conveys pain. Allodynia results from the redistribution of neurons so that receptors that usually respond to touch stimulation (mechanoreceptors) now communicate with pain sensing areas of the dorsal horn.

Chronic pain does not have a single cause and has diverse manifestations and characteristics. The treatment of chronic pain must therefore be individualized. For example, low back pain is improved by intensive (>100 hrs) bio-psychosocial rehabilitation that includes physical therapy. On the other hand, corticosteroid injection improves the painful shoulder significantly more than physiotherapy. Unfortunately, access to intensive multidisciplinary pain treatment is not available to many people. Concurrent addiction, psychiatric illness, and unstable living situations such as homelessness may preclude chronic pain patients from the pain clinics that do exist. Homeless patients also often have fewer family and social supports. The limited access to appropriate specialty clinics and the lack of adequate social supports complicate the care of chronic pain for homeless individuals and place a heavy burden on their primary care clinicians. Evidence indicates that primary supports play an important role in the improvement of functional status of patients with chronic pain. Patients without the support of family or friends are likely to benefit from a close trusting relationship with caregivers.

Narcotic Conversion Chart. This chart provides equianalgesic dosage conversion guidelines for the common opiates. Courtesy of GlobalRPh.com



Narcotic Analgesic Dosage Conversion Chart

(Each row contains identical dosages)

To help use this chart, first determine the patient's previous 24 hour equivalent dose of the agents listed below. All dosages in the same row are therapeutically equivalent. Example: Patient is receiving Oxycodone CR 60mg po q8h = 180 mg/day. Using the table below, the equivalent dose of Fentanyl patch would be 25 mcg.

Codeine		Fentanyl Patch	Hydromorphone		Meperidine		Methadone		Morphine		Oxycodone	
Oral	IV	(Patch)	Oral	IV	Oral	IV	Oral	IV	Oral	IV	Oral	IV
130-447	104-286	25 mcg	6.6-17	1.2-3.4		60-160	16-44	0.22	45-134	0.22	22.5-67	12.30
448-747	287-48	50 mcg	17.1-26	3.5-6.5		166-276	45-74	23-37	135-224	23-37	67.5-112	33.1-55
748-1047	479-676	75 mcg	26.1-35	6.7-9.1		276-390	75-104	38-52	225-314	38-52	112.5-157	55.1-77
1048-1347	677-867	100 mcg	36.1-47	9-12		391-503	106-134	53-67	315-404	53-67	157.5-202	78.1-101
1348-1647	868-1058	125 mcg	47.1-62	12.1-15		504-616	136-164	68-82	405-494	68-82	202.5-247	101.1-123
1648-1947	1059-1251	150 mcg	62.1-75	15.1-18		616-728	165-194	83-97	495-584	83-97	247.5-292	123.1-147
1948-2247	1252-1468	175 mcg	73.1-84	18.1-21		729-840	195-224	98-112	585-674	98-112	292.5-337	147.1-168
2248-2547	1469-1661	200 mcg	84.1-96	21.1-24		841-953	225-254	113-127	675-764	113-127	337.5-382	169.1-191
2548-2847	1662-1846	225 mcg	96.1-107	24.1-27		954-1065	255-284	128-142	765-854	128-142	382.5-427	191.1-213
2848-3147	1847-2041	250 mcg	107.1-118	27.1-30		1066-1178	285-314	143-157	855-944	143-157	427.5-472	213.1-236
3148-3447	2042-2236	275 mcg	118.1-129	30.1-33		1179-1290	315-344	158-172	945-1034	158-172	472.5-517	235.1-258
3448-3747	2237-2431	300 mcg	129.1-141	33.1-36		1291-1403	345-374	173-187	1035-1124	173-187	517.5-562	258.1-281

Pharmacotherapy for Chronic Pain

Not all chronic pain is the same, and different medication choices are made for different types of pain. Analgesics used for the treatment of chronic pain will be discussed in this section. The treatment of neuropathic pain will be discussed separately. Many conditions, such as migraine headache, have treatments specific to that diagnosis.

Non-Steroidal Anti-inflamatory Drugs (NSAIDs) inhibit the cyclooxygenase 2 (COX 2) enzyme. First generation NSAIDs are nonselective inhibitors of cyclooxygenase enzymes and also block cycloxoyenase 1 (COX-1), which is thought to play a role in the protection of the gastric lining. The nonselective NSAIDs include aspirin (Ecotrin™, ASA™, Bayer™, Anacin™), ibuprofen (Motrin™, Advil™), naproxen (Naprosyn™, Aleve™), ketoprofen (Orudis™), and many more. Taken in low doses, these NSAIDs offer mild to moderate analgesia. In larger doses, these NSAIDs have an anti-inflammatory effect. This is particularly beneficial when inflammation contributes to pain, such as musculoskeletal conditions including arthritis. NSAIDs taken on a long-term basis may have dangerous side effects, including gastrointestinal bleeding and renal failure. The newer COX-2 selective NSAIDs, celecoxib (Celebrex™) and rofecoxib (Vioxx™), are known as COX-2 inhibitors. With similar analgesic and anti-inflammatory effects as the nonselective NSAIDs, these COX-2 inhibitors may also marginally reduce some of the gastric side effects caused by other NSAIDs. COX-2 inhibitors have no effect on platelet aggregation but have the same nephrotoxic potential as nonselective NSAIDs. COX-2 inhibitors are very expensive, and the use of these medications should be reserved for persons with peptic ulcer disease or at risk for GI bleeding, such as individuals on chronic anticoagulation and the elderly. In general, lack of clinical response to one NSAID does not reliably predict response or lack of response to other NSAIDs.

Acetaminophen (Tylenol™) is a mild to moderate analgesic that can be used on a long-term basis and is as effective as NSAIDs. When used in doses higher than the recommended daily dose (greater than 4000mg/day) severe liver damage can result. In fact, patients with known liver disease should not take daily doses that exceed 3000mg/day. Acetaminophen does not reduce inflammation.

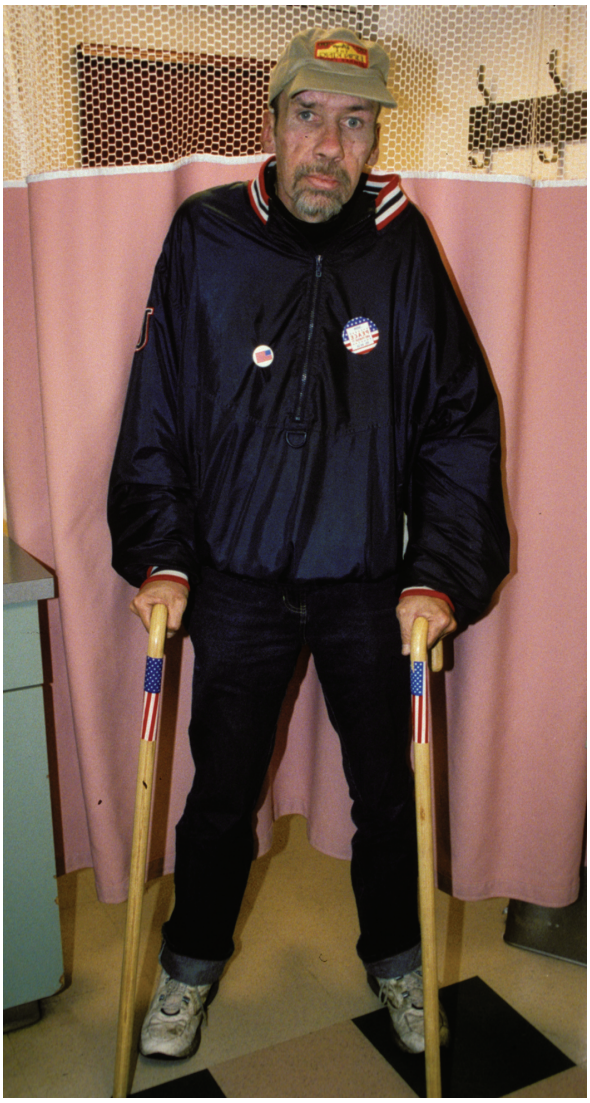
Tramadol (Ultram™) is a synthetic opioid analogue of codeine that has low affinity for the opioid receptors in the brain. The most active metabolite has an affinity for these receptors that is 6000 times lower than morphine. This analgesic effect is complemented by a separate effect, the blockade of painful impulses at the spinal level via inhibition of serotonin and norepinephrine re-uptake. This enhancement of the inhibitory pathway is similar to the action of tricyclic antidepressants such as amitriptyline (Elavil™). This may be particularly beneficial in the treatment of neuropathic pain. The addiction potential of tramadol remains controversial. Early studies showed a very low addiction potential, but some later studies have challenged those findings. All agree that the addiction potential with tramadol is lower than with the other more potent opioids.

Opioids remain highly controversial in the treatment of chronic pain. The most common opioids used are morphine, oxycodone, hydrocodone, fentanyl, and methadone. Opioids primarily bind

to mu receptors in the brain, spinal cord, and in the periphery, and decrease the transmission of painful stimuli and diminish the perception of pain by the brain. In the latter, the pain is not removed but experienced as less aversive. The effects of opioids include analgesia, euphoria, constipation, and respiratory depression. Used at appropriate doses, the physiologic side effects are minimal and can be easily controlled. As opposed to NSAIDs and acetaminophen, opioids have no analgesic ceiling. Analgesic doses are only limited by respiratory and central nervous system depression.

In general, opioid analgesics should be started at low dose and titrated slowly using the following broad guidelines: titrate to efficacy (pain relief and functional improvement) and minimize side effects; titrate initially with short-acting preparations and convert to long-acting preparations. The fentanyl (Duragesic™) patch is a convenient long-acting preparation. The patch is applied every 72 hours and will take approximately 8 hours after the first application to achieve peak serum levels. The lowest dose patch is 25 mcg, which is equivalent to 90 mg of morphine or 9-10 Percocet™ or Percodan™ per day. Unfortunately, patients who are stable on lower doses of short-acting opioids will not be able to tolerate the smallest fentanyl patch. A major concern with the use of long-term opioids is the potential for addiction and diversion. See our separate section on the treatment of chronic pain with opioids.

Adjuvant analgesics are used to treat pain, even though analgesia is not the primary indication for the use of these medications. Antidepressants and anticonvulsants are good examples. Antidepressants, including tricyclic antidepressants (TCAs) such as amitriptyline (Elavil™) and imipramine (Tofranil™), have been used successfully in some patients to treat both peripheral and central neuropathic pain. They are believed to potentiate the body's own pain relieving systems by affecting neurotransmitters such as norepinephrine. Studies evaluating selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Prozac™) and paroxetine (Paxil™), have shown them to have inconsistent effectiveness in treating neuropathic pain compared to placebo. A meta-analysis found SSRI's to be less effective than TCA's, but with 50% fewer side effects. Pain relief usually requires lower doses than those used for treating depression. Therefore doses should balance pain relief and side effects. Such a balance is usually reached at a dosage of 75-150 mg of amitriptyline (Elavil™).



Compression Fractures of the Spine. This man with osteoporosis suffers from severe pain as a result of compression fractures in his back. Lung cancer was later diagnosed, with metastases to the T9 and T10 vertebral bodies. Photo by James O'Connell MD

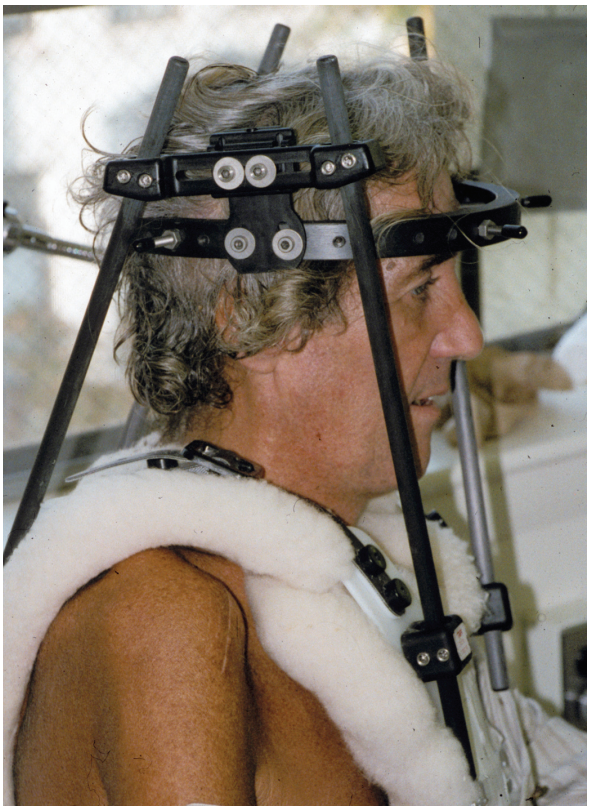
Anticonvulsants such as carbamazapine (Tegretol™) and phenytoin (Dilantin™) have been commonly used at anti-epileptic doses with some success. Gabapentin (Neurontin™) is a second generation anticonvulsant that has shown great promise in the treatment of painful neuropathies. Studies have shown the efficacy of gabapentin (Neurontin™) to be equal to that of amitriptyline (Elavil™) but with fewer side effects. Anticonvulsants seem most effective with neuropathic pain described as lancinating or electric shock-like. The mechanism of action is unclear but presumed secondary to suppression of the spread of aberrant discharges through neuronal sodium channels.

Topical analgesic agents include lidocaine and capsaicin. Lidocaine is a local anesthetic agent available as a patch (Lidoderm™) as well as an injection for mononeuropathies. An oral antiarrhythmic lidocaine analogue, mexiletine (Mexitil™), has been used at doses of 200-400 mg three times a day with mixed results. Capsaicin (Zostrix™), an

active ingredient in hot chili peppers, has been used with some success in patients with hyperalgesia and allodynia. This cream must be applied 3-4 times a day to be effective and often causes a burning sensation followed by anesthesia. Pain relief is usually modest and can take several weeks to take effect. A topical anesthetic like lidocaine gel can be used prior to application for the first several days to avoid the initial burning sensation.

Treatment of Chronic Pain with Opioids

Opioids are indicated for moderate to severe pain that has a significant impact on functionality and quality of life or when non-opioid pharmacotherapy has failed. Opioid therapy for chronic pain remains highly controversial. No controlled trials have evaluated the effectiveness of long-term opioids for the treatment of chronic pain. Some clinical evidence suggests that opioids are less effective with neuropathic types of chronic pain, a finding consistent with the known decrease in opioid receptors in the spinal cord dorsal horn after peripheral nerve damage. Other studies have found that patients with painful neuropathies may be relatively insensitive to opioids, but larger doses of opioids provide relief in double-blind, placebo-controlled trials. Many medications are useful in the treatment of chronic pain, but specific concerns have arisen around the use of opioids.



Neck Fracture. This man sustained a fracture of several vertebrae in the cervical spine when he collided with a bus while riding his bicycle. Photo by James O'Connell MD

The use of opioids raises concerns about tolerance, addiction, misuse, respiratory depression and other side effects, risk of diversion for non-medical uses, and regulatory issues. For these reasons, opioids are often underutilized, and their use is associated with tension and controversy. These concerns must be addressed in order to achieve the best treatment of chronic pain syndrome.

In 1997 the American Academy of Pain Medicine and the American Pain Society issued a joint statement on the treatment of chronic pain with opioids. This document, available on the website of either of these organizations, addresses many of the key concerns in detail and outlines suggested principles of practice for the use of opioids. These principles, an extension of the principles of good medical practice, should include a thorough evaluation of the patient, the development of a treatment plan, the determination whether specialty consultation is needed, the periodic review of treatment efficacy, and good documentation. The joint statement challenges many commonly held assumptions about opioid use and abuse:

- the *de novo* development of addiction when opioids are used for pain is low;
- respiratory depression induced by opioids is usually short lived, occurs in the treatment naïve, and is antagonized by pain;
- tolerance to analgesia has not proven to be a prevalent limitation to long-term opioid use;
- the risk of diversion can be reduced by paying attention to patterns of prescribing requests.

State laws and policies are evolving to recognize explicitly that the use of opioids in the treatment of chronic pain is appropriate in many cases.

Addiction, physical dependence, and tolerance are three discrete entities that are often confused. Treating clinicians and persons living with chronic pain should understand the definitions of these terms and their differences. In 2001 the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine wrote a consensus statement that recognized the following definitions of these terms and recommended their use.

Physical dependence is a state of adaptation 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 is a state of adaptation in which

exposure to a drug induces changes that result in a diminution of one or more of the drugs effects over time.

Addiction is a primary, chronic, neurobiological disease with genetic, psychosocial and environmental factors influencing its manifestations. Addiction 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. Providers should not confuse addiction with pseudo-addiction. Pseudo-addiction is a behavior, seen in patients who have severe unrelieved pain, that mimics aspects of addiction. These patients are intensely focused on obtaining more opioids in order to achieve acceptable pain relief rather than trying to obtain more drugs. This behavior should resolve when adequate pain relief is provided.

Treatment Contracts

Much of the tension between health providers and patients arises when no explicit agreement has been reached on a treatment plan. Uncertainty about receiving adequate pain relief provokes much anxiety in patients with significant pain. Similarly, health providers can become very uncomfortable without clear behavioral expectations about the use of the prescribed medication. Controlled Substance Medication Consent and Agreement Forms delineate the possible side effects of opioids and are very useful for both patient and clinician. Treatment contracts codify the expected use of medication by the patient and the expected response to prescribing requests by the health provider. Examples of these forms can be found on the AAPM website.

Special Considerations for Homeless Populations

Many issues surrounding chronic pain are exaggerated in the homeless population. Homeless persons lack a full range of social supports. They often must be outside for most of the day and are unable to follow advice about physical activity and protection from weather. Adequate rest and sleep are often difficult for homeless persons. While *de novo* addiction after the use of opioid medication for pain is rare, substance abuse and addiction are common in the homeless population. Homeless people have less control of their possessions, rarely have access to a location where medications can be locked and stored, and are thus vulnerable to assault and theft. Such challenges must be acknowledged, and plans to avoid such complications should be a shared responsibility between patient and caregiver. Brainstorming with patients about strategies to avoid complications before troubles arise can help to form an alliance rather than an antagonistic relationship between the health provider and the patient. From the onset of treatment each patient should understand the prescribing limits that the provider will follow. Discussing these general rules beforehand assures that they are not "taken personally" or viewed as evidence of prejudicial treatment by the patient. Caregivers should empathize with their patients and recognize that homeless persons have minimal supports and will need considerable support from their primary care clinicians.

Opioid Treatment and Methadone Maintenance

People with addiction may require the use of opioids when they experience acute pain or cancer pain. Other chronic pain syndromes may also require the use of opioids. In such situations, explicit treatment agreements between patient and prescribing clinician are imperative. Multidisciplinary treatment, including substance abuse treatment, is critically important. The risk of addiction can be ameliorated slightly with the use of long-acting opioids, such as sustained release morphine (MS Contin™) and oxycodone (Oxycontin™) preparations, methadone (Dolophine™, Methadose™), or fentanyl patches (Duragesic™). This reduces the repeated pain/reward cycle that is characteristic of the rapidly acting, short duration medications such as oxycodone (Percocet™, Percodan™), hydrocodone (Vicodan™), and meperidine (Demerol™).

Studies confirm that patients with a history of opioid dependency are more pain sensitive than controls. Daily methadone maintenance treatment may confer some analgesia at peak plasma levels (2-3 hours after the dose), but these patients remain more pain sensitive (hyperalgesic) compared to controls. In addition, the daily methadone dose may cause cross-tolerance to the effects of administered opioid analgesics. Because methadone maintenance doses do not provide analgesia and may cause tolerance to opioids, the management of pain in these patients will often require higher doses and more frequent dosing intervals. Patients on methadone maintenance should continue with their regular daily dose in addition to the opioid being prescribed for pain management. Avoid using mixed agonist/antagonist opioid analgesics such as pentazocine (Talwin™) in methadone-maintained patients, as they may precipitate opioid withdrawal.

Summary

Chronic pain is common in the homeless population, and homeless persons experience significant barriers and obstacles to treatment for chronic pain. Trauma, mental illness, and addiction are common problems that contribute both to the incidence of chronic pain and the complications in caring for homeless persons with chronic pain. Barriers to care include poor understanding of chronic pain in the general medical community, inadequate access to multidisciplinary pain clinics, minimal social supports, inadequate shelter, and difficulty in storing medications. Chronic pain affects all aspects of life, including physical and mental health. The causes of chronic pain are complex and include brain plasticity and pain perception that is effected by mood, anxiety, and duration of painful stimuli. Each patient requires an individualized treatment plan. Many general strategies can be used to increase the success of treatment in most cases. Communication and empathy are critical in caring for homeless persons in pain. Clear expectations help reduce anxiety and tension between caregivers and patients. A caring and involved clinician can help reduce suffering, even when some physical pain persists. ■

Pain Management Medication List

Generic	Brand	Cost
aspirin	Anacin, ASA, Bayer, Ecotrin	$
ibuprofen	Advil, Motrin	$
naproxen	Aleve, Naprosyn	$$$
ketoprofen	Orudis	$
celecoxib	Celebrex	$$$
rofecoxib	Vioxx	$$$
acetaminophen	Tylenol	$
tramadol	Ultram	$$$
morphine sustained release	MS Contin	$$$$$
oxycodone sustained release	OxyContin	$$$
oxycodone	Percocet, Percodan	$$$
methadone	Dolophine, Methadose	$
hydrocodone	Vicodin	$
meperidine	Demerol	$$$
fentanyl patch	Duragesic	$$$$$
amitriptyline	Elavil	$
imipramine	Tofranil	$
carbamazepine	Tegretol	$
phenytoin	Dilantin	$
gabapentin	Neurontin	$$$$
lidocaine patch	Lidoderm, Xylocaine	$$$$
mexiletine	Mexitil	$$$
capsaicin	Zostrix	$
pentazocine	Talwin	$$$

References

American Pain Society. The Use of Opioids for the Treatment of Chronic Pain: A consensus statement from American Academy of Pain Medicine and American Pain Society. 1996.

Ashburn MA, Staats PS. Pain: management of chronic pain. *Lancet* 1999;353(9167):1865-1869.

Ballantyne JC, Mao J. Opioid therapy for chronic pain. *New England Journal of Medicine* 2003;349(20):1943-1953.

Besson JM. Pain: The neurobiology of pain. *Lancet* 1999;353(9164):1610-1615.

Gallagher RM. Treatment planning in pain medicine: integrating medical, physical, and behavioral therapies. *Medical Clinics of North America* 1999;83(3):823-849.

Katz WA. Approach to the management of nonmalignant pain. *American Journal of Medicine* 1996;101(1A):54S-63S.

Lipsky PE. Introduction. The role of COX-2-specific inhibitors in clinical practice. *American Journal of Medicine* 2001;110(Supplement 3A):1S-2S.

Marcus D. Treatment of nonmalignant chronic pain. *American Family Physician* 2000;61:1331-1346.

McQuay H. Pain: Opioids in pain management. *Lancet* 1999;353(9171):2229-2232.

Portenoy RK. Opioid therapy for chronic nonmalignant pain: clinician's perspective. *Journal of Law, Medicine and Ethics* 1996;24(4):296-309.

Savage SR. Opioid use in the management of chronic pain. *Medical Clinics of North America* 1999;83(3):761-786.

Stimmel B. Pain, analgesia, and addiction: an approach to the pharmacologic management of pain. *The Clinical Journal of Pain* 1985;1(1):14-22.

Woolf CJ, Mannion RJ. Pain: Neuropathic pain: aetiology, symptoms, mechanisms, and management. *Lancet* 1999;353(9168):1959-1964.

Drugs for pain. *The Medical Letter on Drugs and Therapeutics* 2000;1085:73-78.