AN OVERVIEW OF PAIN MANAGEMENT

June L. Dahl, Ph.D., *Professor of Pharmacology, University of Wisconsin Medical School*

ABSTRACT

In spite of major advances in pain management practices, the undertreatment of pain remains a major public health problem in the United States. A basic knowledge of pain assessment and management is critical to removing the barriers that are responsible for poor pain control. Pain assessment is the essential first step in the management of any type of pain as it guides the development of a rational approach to treatment. Pharmacologic therapies are often essential to successful pain management. Three major classes of pain medications are available: non-opioids, opioids, and adjuvant analgesics for special pain problems. This paper provides an overview of the various drugs in each of these classes as well as recommendations to guide their use. The goal of therapy is to reduce pain and improve function. A comprehensive approach to pain management should be based on the use of multimodal therapy, rational combinations of pharmacologic and non-pharmacologic treatments.

INTRODUCTION

"Pain is the oldest medical problem and the universal affliction of humankind."[1] Because it is understood to be a signal of disease, "it is the most common symptom that brings a patient to a physician's attention."[2] Therein lies its benefit: it serves as a warning sign that something is wrong in our body. Two hundred years ago, surgeons valued pain as a symptom, as a sign of a patient's vitality and felt it was critical to healing.[1] We now recognize quite the opposite is true and unrelieved acute postoperative pain is a leading cause of delayed discharge and readmission to the hospital and effective treatment of acute pain may prevent the development of chronic pain problems.[3,4] Pain that persists beyond the usual period of healing after injury or after a disease has subsided, may cause significant physical, psychological and social disability.[5,6,7] The cost of uncontrolled chronic pain is enormous both to individuals and to society as it leads to decline in quality of life and ability to function. Data from the American Productivity Audit estimate that lost productive time from common pain conditions such as headache, back pain, arthritis and other musculoskeletal problems costs an estimated $61.2 billion dollars a year.[8]

Thus, there is much evidence that the undertreatment of pain is a major public health problem in this country. Recognition of this fact led to the development of initiatives to address the multiple barriers responsible for the undertreatment of pain.[9] Patient advocacy groups[10,11] and professional organizations[12,13] focused on improving the management of pain have been formed, and numerous clinical practice guidelines have been published.[14,15,16,17,18,19] In 2001, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) adopted standards requiring accredited facilities to institute policies and procedures to assure that pain is assessed and managed appropriately.[20,21] That same year, the Centers for Medicare and Medicaid Services initiated a pain management quality improvement program for the nation's long-term care facilities because of evidence that pain is inadequately treated in those care settings.[22,23] In 1998, the Federation of State Medical Boards (FSMB) issued *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain* to alleviate physician uncertainty about opioid use and "to encourage better pain management."[24] In 2004, the FSMB updated the *Model Guidelines* and changed the title from *Model Guidelines* to *Model Policy* to better reflect the practical use of the document."[25] The FSMB *Model Policy* emphasizes that treating pain with controlled substances is an integral part of the practice of medicine, that good outcomes will weigh heavily in evaluating physician conduct, and "state medical boards should consider inappropriate treatment, including undertreatment of pain, as a departure from an acceptable standard of care." Medical board members and staff need to

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have a basic understanding of pain and its management and apply this knowledge as they review complaints that come before them in order "to improve the quality of life for those patients who suffer from pain and to reduce the morbidity and costs associated with untreated or inappropriately treated pain."[25]

THE NATURE AND TYPES OF PAIN

The International Association for the Study of Pain has defined pain "as an unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such damage."[26] The pain experience "involves not only the transduction of noxious stimuli, but also cognitive and emotional processing by the brain."[27] It is noteworthy that pain is defined as an experience, not a sensation and it does not require actual organic damage. There is no device or blood test to measure pain. The patient's self-report is the "gold standard" or to paraphrase a prominent nurse educator: pain is what the patient says it is, existing when the patient says it does.[28]

Pain can be classified as acute or chronic on the basis of its temporal characteristics: Acute pain is associated with strains, sprains, fractures, surgery, diagnostic procedures, or trauma and gradually diminishes as healing occurs. Chronic pain may be associated with cancer, burns, rheumatoid and osteoarthritis, and peripheral neuropathies. There is a variety of other pain conditions such as fibromyalgia, myfascial pain syndrome, phantom limb pain, low back pain, complex regional pain syndrome, and headaches. The terms chronic pain and persistent pain are often used interchangeably. Many prefer the term persistent pain as it "may foster a more positive attitude" since chronic pain is a pejorative term that "is associated with negative images and stereotypes."[16]

Pain can also be classified based on its pathophysiology: Nociceptive pain is related to stimulation of specialized receptors (nociceptors) by processes that cause tissue injury. Nociceptive pain may be somatic or visceral, arising from stimulation of somatic or visceral afferent nerves. Somatic pain is often described as dull or aching and is well localized whereas visceral pain is described as cramping and gnawing and tends to be poorly organized and is often referred to distant dermatomal sites. Neuropathic pain is the term applied to pain syndromes resulting from pathophysiologic changes in the peripheral or central nervous system. It may be described as burning or shock-like. There may be allodynia (pain due to a non-noxious stimulus) or hyperalgesia (an exaggerated response to a mildly noxious stimulus). Nociceptive pain usually responds to treatment with traditional analgesics, i.e., the non-opioids and opioids. Neuropathic pain may require treatment with local anesthetics or drugs developed for the treatment of depression or seizures, but there are no treatments that completely, predictably, and specifically control this type of pain.[29]

PAIN ASSESSMENT

Pain assessment is the essential first step in pain management. Without a thorough baseline assessment, it is not possible to develop a rational approach to treatment. Subsequent frequent reassessments are essential to evaluating the effectiveness of a treatment strategy. A medical history and physical exam are critical. A thorough pain history should be obtained including information about intensity, location, quality, temporal characteristics, aggravating and alleviating factors, impact of the pain, the meaning of the pain, individual goals and expectations, and associated medical and psychological conditions.

Intensity is one of the most important parameters to be determined. A variety of assessment scales are available. These include:

1. The numeric 0 to 10 scale (0 is no pain, and 10 is the worst pain imaginable);
2. the verbal descriptor scale: mild, moderate or severe; and
3. faces scales first developed for young children. Now there are variants that may be useful for the elderly: these scales have six to eight different facial expressions that depict a range of emotions.

In assessing quality, the patient's own words should be used if possible. The quality of the pain can provide important clues as to the type and nature of the pain and is critical in differentiating between nociceptive and neuropathic pain. Persons may have more than one site and type of pain. It is important to determine not only what makes the pain better or worse, but how the pain interferes with daily life or with work. Patients should be asked what pharmacologic and non-pharmacologic therapies have helped and about the use of herbal remedies. They should be asked if they have specific fears about pain medicines, particularly opioids, as such fears may diminish adherence to a treatment regimen.

MANAGEMENT OF PAIN

Many different strategies are employed in pain manage-

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ment. Medications are critical elements of a comprehensive treatment plan for both acute and cancer pain.[18] For many patients with chronic non-cancer pain, a combination of pharmacologic treatment with educational, behavioral and physical/rehabilitative therapies provides the most successful approach. Invasive methods involving interventional and surgical procedures may also play a role. The goals of treatment are to relieve pain and to improve function. Complete resolution of chronic pain is rarely achieved in spite of comprehensive multidisciplinary pain management. Recent studies suggest that a 30 percent reduction in pain intensity represents a clinically significant improvement and, with that reduction, function improves so as to give patients an acceptable quality of life.[30]

Depression and anxiety are common in chronic pain patients and may preexist or complicate pain management strategies; their effective treatment may reduce, though not necessarily eliminate, the need for analgesic drugs. Insomnia may also be a complicating problem. Although relief of pain frequently leads to improved sleep, insomnia may need specific attention. Any remediable contributing factors such as excessive caffeine consumption or the use of other stimulant drugs should be corrected; treatment with benzodiazepine or non-benzodiazepine hynotics may be needed.

PHARMACOLOGIC MANAGEMENT

Pharmacologic therapies are essential to successful management of pain. As indicated in Table 1, pain medicines may be classified as non-opioids, opioids and adjuvant analgesics. The major characteristics of each of these three classes of medications will be reviewed with specific emphasis on the opioid analgesics as their use is often a source of confusion and concern. Non-opioids are effective for the treatment of mild to moderate pain, opioids have efficacy against moderate to severe pain (both nociceptive and neuropathic), and the adjuvant analgesics are useful for special pain problems such as neuropathic pain. Recommendations to guide pharmacologic management are given in Table 2.

Table 1.

Classes of Pain Medicines		
Non-opioids	NSAIDs* Acetaminophen	Mild to moderate pain
Opioids	Morphine is the prototype	Moderate to severe pain
Adjuvant Analgesics	A diversity of agents including tricyclic antidepressants, anticonvulsants, local anesthetics and others	Special pain problems, e.g., neuropathic pain

* Nonsteroidal antiinflammatory drugs

Non-Opioid Analgesics (NSAIDs and Acetaminophen)

A variety of drugs from several chemical classes are available. These include non-selective cyclooxygenase (COX) inhibitors such as aspirin, ibuprofen, naproxen, sulindac,

Table 2.

Recommendations to Guide Analgesic Drug Use
• Define the goals of therapy before ordering/prescribing. What constitutes a desirable outcome: less pain, better function or both?
• Base the initial choice of analgesic on the severity and type of pain. Severity: mild, moderate or severe Type: nociceptive or neuropathic
• Give adequate doses. Titrate to the dose that relieves pain without producing dose-limiting side effects.
• Give drugs an adequate therapeutic trial. When treating neuropathic pain, realize the benefits may take weeks or longer to appear.
• Don't prescribe two drugs in the same class at the same time. Instead, strive for complementarity by using drugs with different mechanisms of action. Examples: an opioid and a non-opioid for acute pain; an opioid and an NSAID for chronic arthritic pain.
• Be alert for possible interactions with other drugs, (e.g., additive sedative effects).
• Add non-drug therapies to maximize pain relief while decreasing side effects.
• Look for drug-related fears or misconceptions, as they may lead to poor adherence to a therapeutic regimen.
• Know how to manage side effects whether the drugs are being used acutely or chronically.
• Remember that while the development of addiction is rare during a course of pain treatment with opioids, it can occur. It is important to monitor patients on chronic opioid therapy for behaviors suggestive of addiction.
• Consider disease-modifying treatments, e.g., bisphosphonates for patients with pain related to osteoporosis.
• Taper and discontinue drugs that don't meet treatment goals.

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diclonfenac and the more newly released selective COX-2 inhibitors (the coxibs) NSAIDs are useful for the treatment of pain and inflammation; there is no evidence one drug has greater efficacy than another be it a non-selective or selective COX inhibitor, but there is significant individual variation in response. Each NSAID has a characteristic analgesic dosage ceiling above which an increase in dose provides no additional analgesia, but does increase the risk of serious adverse reactions.

The NSAIDs are used in the treatment of both acute and chronic pain. There is no evidence they have efficacy against neuropathic pain. NSAIDs reduce the level of inflammatory mediators generated at the site of tissue injury. They have demonstrated efficacy when used as the sole analgesics after minor surgical procedures and may play an important role as part of a multimodal approach to the treatment of perioperative pain.[31] They have a significant opioid-sparing effect which results in a decrease in the severity of opioid side effects. COX-2 selective NSAIDs do not affect platelets and therefore can be administered without the increased risk of perioperative bleeding associated with the non-selective NSAIDs.[32]

Non-selective NSAIDs cause a number of adverse effects, some of which can be life-threatening (Table 3). Long-term use increases the risk of significant side effects, and their use should be carefully monitored, especially in the elderly. The selective COX-2 inhibitors were designed to avoid the gastrointestinal complications common to the non-selective drugs. However, the apparent reduction in GI toxicity is not observed if patients are also taking low-dose aspirin for its cardioprotective effects.[33] Enthusiasm for these drugs has been further tempered by evidence of their cardiovascular toxicity, i.e., an increased incidence of heart attack and stroke associated with their use.[34,35] Two of the three coxibs marketed for clinical use have been withdrawn from the market and the remaining coxib, celecoxib, has a "black box" warning. The future of COX-2 selective inhibitors is uncertain since their association with cardiovascular risk still is inconclusive.

Acetaminophen (APAP) is equivalent to aspirin as an analgesic and antipyretic, but is not an anti-inflammatory. In therapeutic doses, it is relatively non-toxic, but it is hepatoxic in large doses or when given to persons with a history of alcoholism or liver disease. Experts advise that the daily dose be limited to two to three grams despite the fact the labeling specifies an upper limit of four grams per day. It is important to use caution with combination analgesics (e.g., hydrocodone/APAP or oxycodone/APAP) as they contain variable amounts of acetaminophen.

Opioid Analgesics

Opioid analgesics[36] are widely used in the treatment of acute postoperative and trauma pain and are the mainstay of the management of moderate to severe pain associated with cancer.[17,18] Although their role in the management of chronic pain not related to cancer is controversial, there is mounting evidence for their benefit in select patient populations.[37] For many patients with chronic pain, long-term opioid therapy may provide the only means of achieving a functional lifestyle. Studies have also documented their effectiveness for neuropathic pain.[38]

Opioids have many advantages: They are very effective analgesics, most of them have no analgesic ceiling and they do not produce end-organ damage even with long-term use.

Table 3.

Adverse Effects of NSAIDs		
Adverse Effect	**Non-Selective COX Inhibitors**	**Selective COX-2 Inhibitors**
Gastritis/peptic ulcer/GI bleed	Yes*	May be less†
Alterations in renal function	Yes	Yes
Decreased platelet aggregation	Yes, easy bleeding or bruising	No
Hypersensitivity reactions	Yes‡	Unknown
Hepatotoxicity	Possible	Not reported
Cardiovascular Effects	Yes, due to effects on the kidney, bp, fluid retention	Cardiovascular toxicity

* May be no symptoms before a bleed occurs. NSAID-associated gastropathy has been estimated to cause upwards of 3,000 deaths and 20,000 hospitalizations each year in persons with rheumatoid arthritis alone.

† Risk same as with non-selective NSAIDs if patient taking low-dose aspirin

‡ Acute urticaria, bronchospasm, severe rhinitis, or shock. Not an allergic reaction.

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The guidelines from the American Geriatrics Society conclude "that in the final analysis, the chronic use of opioids for persistent pain or some other analgesic strategies may have fewer life-threatening risks than does the long-term daily use of high-dose nonselective NSAIDs."[16] A recent review did express concerns about the effects of prolonged therapy on hormonal and immune systems.[39] At the same time, the authors recognized that pain itself may impair immune function.[40]

The family of opioid analgesics includes codeine, hydrocodone, oxycodone, morphine, hydromorphone, methadone, levorphanol, meperidine, propoxyphene, fentanyl and tramadol. They produce their effects by binding to specific receptors in the CNS. Those receptors are found in highest concentrations in regions of the CNS involved in the perception of pain and in our emotional response to pain. Receptors are also present in the GI tract and on peripheral nerves where they are "up-regulated" during inflammatory pain states.

Opioid analgesics can be administered by a variety of routes: orally, rectally, intravenously, subcutaneously, intraspinally, transdermally, transmucosally and by aerosol. Of the drugs listed above, only methadone and levorphanol have long durations of action. However, controlled release forms of short-acting drugs such as morphine, oxycodone and fentanyl are available; and a controlled release of hydromorphone has been approved by the FDA.[41] The transdermal delivery system for fentanyl can provide up to 72 hours of analgesia. The other controlled release formulations were developed for oral administration and can provide analgesia from eight to 12 hours or longer.[42] Although these long-acting opioids are similar in efficacy, some patients may respond better to one drug than to another or may experience fewer adverse effects from one drug as compared to another.[43] Long-acting opioids have greater utility than short-acting opioids for managing chronic pain, although short-acting drugs may be used during initial titration to an effective dose or as rescue medications for episodes of breakthrough pain.

Certain opioids have limitations that are important clinically. For example, codeine has dose-limiting side effects; furthermore, it is a pro-drug and 10 percent of Caucasians lack the enzyme that metabolizes it to morphine and are unlikely to get pain relief from the drug; hydrocodone is only available in combinations with a non-opioids which limits the dose that can be administered; meperidine has a short duration of action and is converted to a long-lived metabolite which is a CNS stimulant that can produce seizures; its use should be reserved for short procedures; and, propoxyphene has efficacy similar to that of aspirin or acetaminophen. The guideline from the American Geriatrics Society points out because propoxyphene can cause ataxia or dizziness and has a toxic metabolite, its use may add unnecessary morbidity or mortality in older persons.[16] Mixed agonist-antagonist opioids such as butorphanol and nalbuphine can produce analgesia when used alone, but will reverse or antagonize the effects of pure agonists when given with those drugs. Although they have a lower addiction liability and are less likely than pure agonists to produce respiratory depression, they have an analgesic ceiling and can produce psychotomimetic effects. Buprenophine is classified as a partial agonist. It too has an analgesic ceiling and at high doses can act as an antagonist. It is approved for use as an analgesic and for office-based treatment of opioid addiction.[44] Tramadol binds weakly to opioid receptors, but also potentiates the activity of serotonin and norepinephrine. It has an analgesic ceiling, variable efficacy and side effects and can cause seizures, so it should be used with caution in persons with a history of seizure disorder or in those taking other drugs that lower the seizure threshold. Methadone is an effective analgesic and is growing in popularity for the treatment of chronic pain because it is the least expensive opioid. It has complex pharmacokinetics so clinicians must be very careful when initiating therapy with this drug and/or when increasing its dose. Although it is an excellent analgesic, it often misunderstood by patients and physicians because of its use in addiction treatment.

Opioid analgesics can produce a variety of side effects that are predictable and manageable in experienced hands. The most common of these are constipation, nausea and vomiting, sedation and mental clouding, itching and urticaria. Patients may experience more severe side effects with one drug than with another at an equianalgesic dose. Respiratory depression is a feared and misunderstood potential side effect of opioids. It is always preceded by sedation and can be treated with the opioid antagonist, naloxone. Serious side effects such as delirium or respiratory depression can occur if the dose is increased too quickly, especially in an opioid-naïve individual. Tolerance develops to many opioid side effects within a few days. However, tolerance does not develop to the constipating effects. At the very high doses that are sometimes required to provide relief of pain in persons with advanced cancer, myoclonic jerks and hallucinations may occur.

The severity of side effects can play an important role in the success or failure of pain management with opioids. An

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understanding of the incidence, severity, and mechanisms of side effects can help the clinician develop an optimal side effect treatment plan. Opioid rotation, which involves switching from one opioid to another, may optimize analgesia and minimize side effects because as stated previously, there is great individual variation in response to the different drugs.

One of the major concerns associated with long-term use of opioids relates to possible adverse effects on psychomotor and cognitive function. Reports from a variety of studies have provided conflicting results, and none has involved persons on very long-term therapy, i.e., patients who have been treated for several years. Cognition can be significantly impaired within the first two weeks of initiating opioid therapy so driving and operating heavy equipment should be curtailed. However, patients soon adapt to these effects. A report involving twelve months of treatment with oral morphine showed no disruption of cognitive functioning in patients with chronic non-cancer pain and instead showed a moderate improvement of some aspects of cognitive functioning, as a consequence of the pain relief and concomitant improvement of well-being and mood.[45] However, there were a significant number of dropouts either because of lack of efficacy or unacceptable side effects, notably constipation. Another study which looked at patients treated for 90-180 days with oxycodone/acetaminophen or transdermal fentanyl showed no significant impairment of cognitive ability or psychomotor function.[46]

Chronic use of opioid analgesics also brings fears of tolerance, physical dependence and addiction. Twenty years ago, many physicians were so afraid of addicting their patients they were uncomfortable about prescribing opioids even to dying patients. There was the perception that anyone who was treated for even a short period of time with opioids would become addicted. There was also confusion about the meaning of the term and it was often confused with tolerance and physical dependence. Because of the confusion about the meaning of the terms, the Liaison Committee on Pain and Addiction, a collaborative effort of the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine, developed a consensus document with clear and concise definitions of the terms. These are given in Table 4.[47] One of the guidance points from the FSMB *Model Policy* relates to the need to recognize tolerance and physical dependence are normal consequences of sustained opioid use and, as is clear from the definitions in Table 4, not the same as addiction. The policy further states to equate physical dependence with addiction is to stigmatize patients and to risk underutilization of the opioids they may need for effective pain control. Studies involving patients with pain related to cancer have shown that analgesic tolerance is not an inevitable consequence of chronic opioid therapy. Clinicians should be alert to the possibility of tolerance development, but must realize many patients remain on a stable dose of drug for a long time. Furthermore, there is incomplete cross-tolerance among the opioids, so if patients do become tolerant to one drug, they may not be tolerant to another.

There is evidence that the non-medical use of opioids is increasing.[48] However, there is no evidence physicians who are prescribing these drugs for legitimate pain patients are a major source of the drugs on the street.[49] Nevertheless, the abuse of these drugs does pose a threat to individuals and society, and physicians have a responsibility to minimize the potential for diversion and abuse.[25] Careful assessment of patients can identify individuals who are at risk for abuse. Studies have shown in patients taking opioids for chronic non-cancer pain, variables such as reported family history of substance abuse, past problems with drugs or alcohol, and a history of legal problems can be useful in predicting problems with opioid use. Other items closely correlated are a higher required dose of opioids for pain, dependence on cigarettes, psychiatric treatment history, multiple car accidents and reporting fewer adverse symptoms.[50,51] Gourlay, Heit and Almahrezi recommend Universal Precautions in Pain Medicine, consisting of 10 steps to guide patient assessment, management and referral.[52] Of course, addiction can occur and is obviously a substantial risk in patients with a

Table 4.

Definitions related to use of opioids for treatment of pain*
1. Addiction: a primary, chronic, neurobiologic disease with genetic, psychosocial and environmental factors influencing its development and manifestations. It is characterized by behaviors including one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.
2. Physical Dependence: 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.
3. 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.

* Reference 33

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history of substance abuse. Opioids are not contraindicated in these patients, but their use must be much more carefully monitored.[53]

There is much evidence that medical decisions about opioid use are influenced by fears of regulatory scrutiny.[54,55,56] There have been major collaborative efforts by federal and state agencies and members of the pain community to improve the regulatory climate and thus encourage better pain management.[57] In September 2001, the Drug Enforcement Administration (DEA) joined with 21 health organizations to issue a state calling for balance: preventing abuse of prescription pain medications while ensuring they remain available for patients who need them for pain control.[58] Last August, the DEA worked with pain experts to publish a document containing questions commonly asked by clinicians and law enforcement and reinforced statements previously made by the DEA. In October the document was removed from the DEA website and then on Nov. 16, 2004 the DEA published an Interim Policy Statement (IPS) in the *Federal Register* that contradicted their previous positions.[59] The IPS has been a cause of great concern among clinicians who prescribe opioids for pain control. In January 2005, the DEA asked for comment on the IPS; thousands of comments have been received. It is hoped that the DEA will join once again with health organizations to reaffirm the statement on balance because it gives assurance to health care professionals that DEA understands their fears of regulatory scrutiny and the critical role that opioids play in providing pain control for many patients.

Adjuvant Analgesics

Adjuvant Analgesics are used to treat concurrent symptoms and provide relief of specific pain problems. These drugs commonly have FDA-labeling for indications other than pain. They include a diversity of agents with very different mechanisms of action.

Drugs for Neuropathic Pain

Neuropathic pain is particularly difficult to treat and if a response is obtained, it may be modest at best. The drugs identified as first-line treatment for neuropathic pain are listed in Table 5.[60] They are not listed in order of preference, but in alphabetical order because there are no studies to guide decisions about which will be more or less effective than another for a given patient. Often the approach to treatment is a matter of trial and error, but cost, age of the patient and co-morbidities will influence decisions.[61] In fact, a combination of therapies may be necessary. Second-line treatments include other anticonvulsants [both first- and second-generation drugs such as carbamazepine and lamotrigine], non-tricyclic (TCA) antidepressants can be recommended to patients who have not responded to a TCA.[35] There is some evidence for benefit from treatment with bupropion and venlafaxine. With the exception of paroxetine, the SSRIs have not been shown to have efficacy. However, relief of depression may improve patient's pain. A new antidepressant, duloxetine, which inhibits the reuptake of both serotonin and norepinephrine was recently approved for treatment of depression and diabetic neuropathy pain.

Topical Agents

Topical therapies are helpful for continuous pain/dysesthesias caused by peripheral nerve injury. Topical lidocaine is one of the first line drugs listed in Table 5. Capsaicin prepa-

Table 5.

First-line Medications for Neuropathic Pain*		
Medication	**Dosing**	**Side Effects**
Gabapentin (Neurontin)†	Start with 100-300 hs, can titrate to 3600 mg/d or more	Somnolence and dizziness, GI symptoms
5 percent Lidocaine patch (Lidoderm)	Max. three patches for 12 hrs	Mild skin reactions
Opioid analgesics (morphine)	Start with a short-acting drug, if that is effective, switch to a long-acting agent	Constipation, sedation, nausea and vomiting, itching, abuse (rare)
Tramadol (Ultram)	Titrate slowly, max 400 mg/d	Dizziness, nausea, constipation, somnolence seizures±
Tricyclic antidepressants (Nortriptyline, desipramine)	Start low dose (25mg hs), titrate slowly to max of 150 mg/d if tolerated	Cardiac conduction defects, anticholinergic side effects

* Reference 34

† Pregabalin, an analog of gabapentin, has very recently been released to treat postherpetic neuralgia and diabetic neuropathy pain

± Seizures in those who have a history of seizure disorders

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rations have potential value, but can cause local burning, which may be severe. They must be applied several times daily for approximately six weeks for full effectiveness. Counterirritant ointments or liniments, many containing menthol, may be helpful for musculoskeletal pain. Compounded ointments containing NSAIDs are also claimed to be effective. Topical ketoprofen has just been approved by the FDA.

Other Adjuvants

Corticosteroids may be useful for treatment of severe inflammatory pain. They can be administered systemically or locally. Systemic administration is limited by serious potential side effects so it is essential to use the lowest effective dose for the shortest possible time period. Baclofen has been used in the treatment of lancinating, paroxysmal neuropathic pain. It also may help to reduce painful spasticity. It has many side effects: nausea, dizziness, confusion, drowsiness and hepatotoxicity. Tizanidine is also an antispasticity agent that may be useful in controlling neuropathic pain. It may also be helpful in fibromyalgia, but evidence is anecdotal. Side effects are similar to those of baclofen.

"Muscle relaxants" are a heterogeneous class of drugs that reduce muscle pain and often induce sedation. Cyclobenzaprine (Flexeril) has been widely prescribed.[62] These drugs may be helpful for short-term use, as in pain flares or acute injury. Long-term use is not recommended. Carisoprodol (Soma), a muscle relaxant metabolized to a potent non-barbiturate sedative-hypnotic (meprobamate), is not recommended.

NON-PHARMACOLOGIC THERAPIES

Multimodal management of pain involves the use of many therapeutic modalities including education, psychological interventions, and physical and rehabilitation therapies in addition to appropriate analgesic drug use. An overview of these therapies is provided in Table 6. It is important to have active patient involvement to build self-reliance and a sense of control over the pain.

Education

Patient and caregiver education is essential to setting realistic pain-relief goals. All educational activities should be sensitive to culture, ethnicity and the values and beliefs of the individuals. Education should include information about pain, its assessment, methods for pain relief, the goals of therapy and also address common patient fears, barriers, myths and misperceptions. Patient education programs do significantly improve overall pain management.[16]

Psychological Factors

Psychological factors play an important role in the experience of persistent pain. The use of interventions that change behavior, thoughts or feelings help patients experience less distress, enjoy more satisfying productive lives.[64] Psychological approaches include individual cognitive behavioral psychotherapy, hypnotic analgesia, vocational counseling, group and family cognitive behavioral psychotherapy and biofeedback.

Physical and Rehabilitation Therapies

Physical and rehabilitation therapies. Physical rehabilitation is a common treatment for pain and is often one component of a multidisciplinary strategy. Graded exercise programs seek to maximize functional range of movement and

Table 6.

Non-Pharmacologic Therapies for Chronic Pain*	
Patient and caregiver education	• should be sensitive to culture, ethnicity, values and beliefs • essential to setting realistic pain-relief goals • include information about pain, its assessment, pain treatments, address common fears, barriers, myths and misperceptions
Behavioral and Cognitive-Behavioral Therapy	• Individual cognitive behavioral psychotherapy • Hypnotic analgesia • Vocational counseling • Group and family cognitive behavioral psychotherapy • Biofeedback
Physical and Rehabilitative Therapies	• Graded exercise programs • Heat, cold, massage • TENS
Complementary and Alternative Medicine	• Chiropractic • Acupuncture • Herbs and nutritional supplements
Other Physical and Invasive Modalities	• Serial nerve blocks controversial • Epidural steroid injections – evidence not definitive • Surgical interventions when all other treatments have failed

* Adapted from the American Medical Association, *Part 3: Management of Persistent Nonmalignant Pain*, 2003

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correct poor posture. Belief systems that physical activity will cause pain leads to physical deconditioning which can complicate the chronic pain syndrome. Additional physical therapeutic modalities (self-administered heat and cold, massage[65] and the use of liniments and other topical agents) may be useful. Transcutaneous electrical nerve stimulation (TENS), the application of electrical stimulation to the skin for pain control, is noninvasive, inexpensive, safe and easy to use.[66] The clinical literature on TENS is controversial. While the majority of studies support the use of TENS, a number refute its effectiveness and point out TENS has a significant placebo effect.

Complementary and Alternative Medicine

Chiropractic and acupuncture therapies can be very beneficial. Chondroitin sulfate, glucosamine, and various herbs have been popular with patients who have musculoskeletal pain.

Other Physical and Invasive Modalities

Treatment with serial nerve blocks remains controversial. Epidural steroid injections may be effective for low back pain, but the evidence is not definitive. Surgical interventions should not be considered until all other possible treatments have failed.

CONCLUSION

Many different strategies are employed in pain management. Pain assessment is the essential first step as it guides the development of a rational approach to treatment. Medications are critical elements of a comprehensive plan for managing both acute and chronic pain. The goals are to relieve pain and to improve function — goals best achieved by the use of multimodal therapy involving the use of combinations of drugs that work by different mechanisms as well as rational combinations of drug and non-drug therapies. Clinicians need to have an understanding of the three major classes of analgesics (the non-opioids, opioids and adjuvants), in order to provide optimal treatment. Non-opioid and adjuvant analgesics such as antidepressants and anticonvulsants are essential components of treatment, but it is the opioids that present the greatest challenges to physicians and to those who regulate medical practice because they have the potential to be abused. Opioid analgesics are essential for the management of postoperative and trauma pain. They are the mainstay of the management of moderate to severe pain due to cancer, and may also be essential for relief of certain chronic pain problems. It is essential to understand the many advantages of these drugs for pain control and to recognize that the severity of side effects plays an important role in the success or failure of managing pain with these drugs. Clinicians must understand the distinction between addiction, physical dependence, and tolerance; otherwise they risk stigmatizing patients who are treated with these drugs and underutilizing these medications for pain control. Because the abuse of these drugs poses a threat to individuals and society, physicians have the responsibility to minimize the potential for their diversion and abuse. At the same time, they must not let their concerns about these issues interfere with the rational, appropriate use of these drugs in treatment, as that would result in abrogation of their responsibility to relieve pain and suffering.

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