INTRODUCTION

Compassion is not religious business, it is human business; it is not luxury, it is essential ... for human survival.
- Tenzin Gyatso, the 14th Dalai Lama of Tibet[1]

Prescription drugs are newsworthy, particularly when they are abused in violation of their intended medical purpose. Conservative radio commentator Rush Limbaugh grabbed many headlines when he admitted his own misuse of the painkilling opium derivatives known as opioids. Limbaugh is only 1 of many famous abusers of prescription drugs, although he is perhaps the most surprising example, because his proposed solution to the widespread abuse problem before his own arrest was to convict drug abusers and "send them up the river."[2] The nonfamous are similarly afflicted, according to a study from Columbia University in New York, which found that prescription drugs (including opioids, stimulants, and depressants) had attracted 15.1 million admitted abusers by 2003.[3] That figure is double the number from only a decade earlier, and it includes more people than the total population of Tokyo. Today, only marijuana, alcohol, and tobacco are more popular than prescription agents as drugs of abuse. Of all prescriptions, opioids attract the most new abusers.[4]

However, opioids, which are so dangerous in the hands of abusers, are beneficial or even lifesaving for millions of people who otherwise would live with intractable pain. Nearly everyone seeks medical treatment to control pain at some point. Some will be unlucky enough to experience chronic pain that does not respond to treatment; about 70 million people live with chronic pain in America today.[5] In a world with few alternatives, opioids remain the best treatment available for many chronic pain conditions and are the first choice of therapy for acute and postoperative pain.

Clinicians who prescribe opioids to treat chronic pain are often caught between their professional obligation to relieve suffering and their desire to avoid contributing to the nonmedical consumption of controlled substances. Many medical practitioners fear becoming a source of medications that can be diverted for sale on the black market. They also dread the possibility of regulatory scrutiny or even prosecution that results from their patients' misuse of medication.

Thus the medical community is faced with a conundrum: Opioids offer safe, effective treatment for many chronic pain conditions and pose little risk of addiction for most patients who take them to control pain. However, some patients treated with opioids do display behaviors consistent with addiction. The challenge is to curtail the abuse and diversion of prescription opioids while ensuring their availability for patients who benefit from their use. The first step in resolving those seemingly conflicting interests is to acknowledge that they exist. Patients who suffer pain are often treated with prescribed painkilling drugs that can be abused. Because a certain segment of the opioid-treated pain population exhibits an active substance-use disorder, steps should be taken to minimize the very real potential for the abuse of such medications. The obligations to battle pain and addiction are not mutually exclusive, they are mutually inextricable.

This complex dilemma is summarized in the following list of the rights and responsibilities of healthcare professionals who prescribe opioids to treat pain (Box).[6] Although the task of safeguarding against substance abuse appears (and is) daunting, patients are not at equal risk for opioid addiction or abuse. The key to managing a patient's opioid intake lies in screening for abuse potential and carefully monitoring the progress of treatment. Those skills are within the capability of every caring, committed healthcare professional, even given the time constraints of practicing medicine in today's clinical settings.

Primary care physicians, nurse practitioners and other first-contact clinicians are uniquely positioned to make a difference at the beginning of medical treatment. Research indicates that a patient with chronic pain is far more likely to seek treatment from a family doctor or other healthcare professional than from a pain management specialist. Likewise, an individual struggling with a substance-use disorder is more often treated by a primary care physician than by a physician certified in addiction medicine. Those realities create an opportunity for first-contact clinicians to maximize the chances for success when patients begin opioid therapy.

"The bottom line is that there will never be enough specialists to deal with the problem," said Scott Fishman, MD, during his time as president of the American Academy of Pain Medicine, "so we have to train primary care physicians at the front lines to be able to do this as part of the basic care that we give patients." [7]

The medical obligations of physicians include:

- Treating pain adequately in all patients.
- Screening new patients for potential drug abuse or addiction.
- Monitoring patients' progress and addressing any harmful effects as they participate in opioid therapy.

Clinicians may receive little support in those endeavors. Medical schools provide scant training in either managing pain or treating addiction; most curricula are focused instead on teaching future doctors to recognize and eradicate disease. In a survey of physicians conducted by the Columbia University National Center on Addiction and Substance Abuse in New York, only 40% of the respondents had received any medical school training to help them identify prescription drug abuse or addiction in patients. Almost half of respondents said that they have difficulty discussing prescription drug abuse with their patients.[3] Pain management, which is a subject similarly neglected in many medical school curricula, consisted of only a few hours' instruction for the less than half of physicians who received any training. Even though some recent graduates of medical school indicate that training has improved in recent years, many physicians are still failing to diagnose active substance abuse, and medical students frequently graduate without having taken a single course on the treatment of pain. Furthermore, medical textbooks that address opioid abuse and chronic pain often refer to the topics separately. The complex interplay between substance abuse, mental disease, and chronic pain is rarely grasped or explored. In this book, we acknowledge the danger posed by the misuse of prescription opioids — a danger often downplayed by pain-control advocates. At the same time, we affirm the right of all people to be treated for pain. The latter perspective is sometimes ignored by addiction-treatment specialists.

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We also assert with vigor that at no time should the guidelines presented here be taken as license to refuse to treat (or to undertreat) the pain of someone with a substance-use disorder. People who have problems managing drug intake experience acute, postsurgical, and chronic pain as often as do any other patients, and they are no less deserving of pain relief. The goal of providing good medical care is to improve the quality and duration of life for every patient. That goal is within reach; it simply requires a high level of professional concern and a strong commitment to monitoring patients' progress.

Policy and legal issues require attention from every prescriber of opioids. Because opioids can fall into the wrong hands, some policy makers want to solve the problem of substance abuse by banning certain agents from the U.S. market altogether. That solution is untenable, because some of the most frequently abused drugs are also the most effective against pain. Prohibition is not the answer to the problem of prescription drug abuse. Managing treatment with pharmaceutical analgesics is similar to managing an eating disorder. A person with problems managing food intake cannot solve the problem with abstinence, because eating is necessary for survival. Instead, that person's destructive impulses must be managed. Similarly, society cannot eliminate the use of opioids, even though they can harm

Rights and Responsibilities of Healthcare Professionals Who Prescribe Opioids to Treat Pain

- Pain is undertreated in part because healthcare professionals fear that patients may be harmed or that they themselves may incur regulatory, legal, or licensing penalties.
- The decision of whether to prescribe opioids is particularly difficult when a patient exhibits an addictive disorder or a risk factor for addiction.
- The decision to prescribe opioids must be made based on the healthcare professional's knowledge of the patient's medical and psychiatric conditions and response to treatment.
- The prescribing of opioids should not be deemed appropriate or inappropriate independent of such clinical knowledge.
- Healthcare professionals who prescribe opioids for pain may occasionally be misled by patients who wish to divert or misuse medications.
- Healthcare professionals who prescribe ongoing opioids have an obligation to understand the risks and management of addictive disease.
- Persistent failure to treat addiction is poor medical practice.
- Persistent failure to prescribe opioids effectively when their use is indicated is also poor medical practice.
- Physicians traditionally receive little or no education about pain management or the treatment of addiction.

Adapted from: American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine. Public policy statement on the rights and responsibilities of healthcare professionals in the use of opioids for the treatment of pain: A consensus document. Glenview, IL and Chevy Chase, MD; 2004.

some consumers. Like food, opioid analgesics are only as beneficial or as destructive as the motivations and compulsions of the user.

Opioids are not a cure-all, nor are they without significant risks for patients. However, opioids are used to control pain and improve function far more frequently than they serve as agents of destruction. The potential for prescription abuse is a challenge to be met and managed, not a reason to abandon pain management.

This book was written to help clinicians (including primary care physicians, nurse practitioners, psychiatrists, and others who treat pain) to sort out the clinical, regulatory, and ethical issues associated with the prescribing of opioid analgesics and to reduce the risk of medication misuse, abuse, and diversion. The recommendations presented here are based on the work of numerous experts in the fields of pain management and addiction. Although a book such as this can never be considered a complete treatise on those subjects, it can serve as a succinct and ready resource for clinicians. If knowledge is power, then the information published here is intended to instill the power and confidence needed for clinicians to safely treat their patients' pain and restore their dignity and lost quality of life. In that endeavor, knowledge is also compassion.

References

1. Tools for the study of Tibet: words for reflection. Global Source Education Web site. Available at: http://www.globalsourcenetwork.org/tibet_reflections.htm..Accessed April 8, 2007.
2. The Rush Limbaugh Show. Premiere Radio Networks. Oct. 5, 1995.
3. Under the Counter: The Diversion and Abuse of Controlled Prescription Drugs in the U.S. National Center on Addiction and Substance Abuse at Columbia University (CASA), New York, NY; 2005.
4. Substance Abuse and Mental Health Services Administration. (2006). Results from the 2005 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NSDUH Series H-30, DHHS Publication No. SMA 06-4194). Rockville, MD.
5. Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, Portenoy RK. Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. JAMA. 2003 May 14;289(18):2370-8.
6. American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine. Public policy statement on the rights and responsibilities of healthcare professionals in the use of opioids for the treatment of pain: A consensus document. Glenview, IL and Chevy Chase, MD; 2004.
7. Wallis C. The right (and wrong) way to treat pain. Time Magazine. 2005; February 20.

CHAPTER I

OPIOID ABUSE: PREVALENCE AND EPIDEMIOLOGY

I simply do not remember getting out of bed, being pulled over by the police, or being cited for three driving infractions. That's not how I want to live my life, and it's not how I want to represent the people of Rhode Island.
- Patrick Kennedy, US Congressman
On his way to the Mayo Clinic to seek help for addiction to prescription drugs.[1]

The abuse of prescription opioids is a real and increasing problem with steep costs to society and to individual patients. People abuse opioids for various reasons and not merely because they are addicted in a clinical sense. The failure to differentiate among common terms and definitions that pertain to substance-use disorders causes misunderstanding among physicians and patients. Clinicians should know that:

- Abuse and addiction are not synonymous.
- Abuse can usually be managed.
- Addiction can usually be predicted.

Fear of contributing to the abuse and illegal diversion for sale of these powerful medications is appropriate and should not be minimized. It is, however, possible to manage the risk while ensuring that opioids remain available for the many people who use them appropriately and benefit from them.

This chapter addresses the prevalence of opioid abuse in the United States and its relationship to chronic pain, and it provides an overview of the nomenclature common to the specialties of pain management and addiction. Armed with this knowledge, clinicians will be better positioned to recognize and address the various categories of problematic opioid use.

Prescription Abuse Is Increasing

Substance abuse is a leading cause of preventable illness and death in the United States.[2] The misuse of drugs ruins families, costs billions in lost productivity, strains the healthcare system, and ends lives.

Against this backdrop, prescription drugs are becoming the new substances of choice for many recreational drug users (Box I:1- Box I:2, Figure I:1). According to researchers at Columbia University, more Americans now abuse prescriptions than use cocaine, hallucinogens, inhalants, and heroin combined.[3] Opioid analgesics, tranquilizers, and stimulants are among the most frequently abused prescription drugs (Box I:3).

As the incidence of drug abuse skyrockets, more Americans every year are experimenting with the recreational use of prescription opioids for the first time. Many of those first-time users are young people.[4] Today, adolescents and people of college age appear caught in a cultural current in which prescription drug abuse is more accepted among peers than in the past (Box I:4). Older people are also at risk for substance abuse, particularly

Box 1.1

Prescription Drug Abuse in America: Columbia University Survey, 1992 - 2003

- The number of Americans who admitted to abusing prescription drugs nearly doubled (from 7.8 million to 15.1 million).
- The number of people abusing prescription drugs increased 7 times faster than the increase in the US population.
- Prescription drug abuse among teenagers more than tripled.
- Almost 1 in 10 people who ranged in age from 12 to 17 years abused at least 1 controlled prescription drug in 2003.
- Controlled prescription drugs were implicated in 29.9% of drug-related emergency-room deaths (opioids accounted for 18.9% of those deaths) in 2002.

Source: Under the Counter: The Diversion and Abuse of Controlled Prescription Drugs in the U.S. National Center on Addiction and Substance Abuse at Columbia University (CASA), New York, NY; 2005.

death from overdose. Middle age is the most vulnerable time for death from accidental drug poisoning, according to data from medical examiners in several states.[5]

The increase in substance abuse has heightened social costs and the number of drug-related fatalities. Hospital emergency departments are feeling the strain from such incidents: Reports of overdose from narcotic analgesics rose 20% from 2001 to 2002, according to the U.S. Drug Abuse Warning Network.[6]

Box 1.2

Current and New Nonmedical Users of Psychotherapeutic Prescriptions in the United States, 2005

An estimated 6.4 million people (2.6% of survey respondents age 12 years or older) used psychotherapeutic drugs nonmedically in the month before the survey.

- An estimated 4.7 million used pain relievers.
- 1.8 million used tranquilizers.
- 1.1 million used stimulants.
- 272,000 used sedatives.

"Nonmedical use of pain relievers" was the illicit drug category with the most new users (2.2 million) within the 12 months before the survey. The average age of new users was 21.2 years.

Source: Substance Abuse and Mental Health Services Administration. (2006). Results from the 2005 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NSDUH Series H-30, DHHS Publication No. SMA 06-4194). Rockville, MD.

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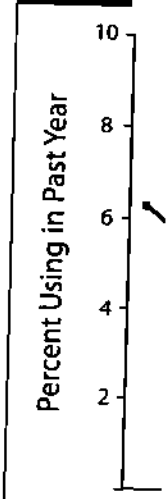

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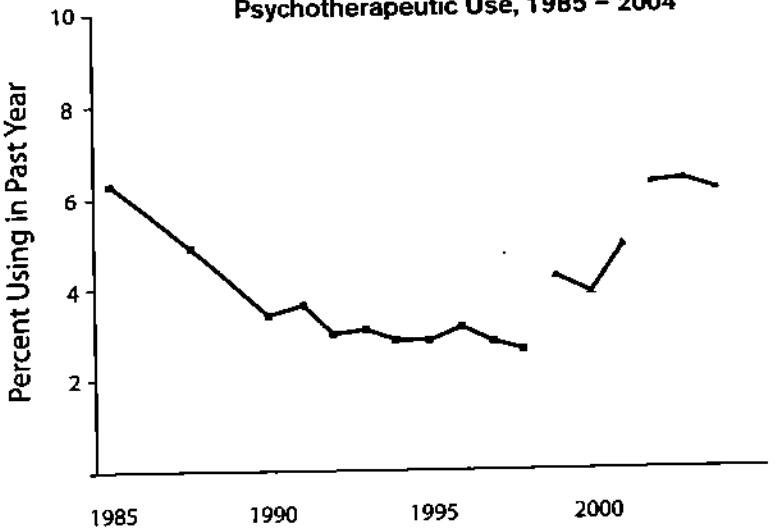

Note: Data points represent surveys conducted since 1985. The 1985-1998 data are from NHSDA (PAPI), the 1999-2001 data are from NHSDA (CAI), and the 2002-2004 data are from NSDUH (CAI). The three series of NSDUH/NHSDA data use different methodologies and are not comparable with the other series.

Substance Abuse and Mental Health Services Administration. (2005). Results from the 2004 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NSDUH Series H-28, DHHS Publication No. SMA 05-4062). Rockville, MD.

The number of unintentional deaths from prescription drugs is also growing larger nationwide. In North Carolina between 1997 and 2001, deaths from illegal drugs decreased while deaths involving prescribed opioids increased 300%.[7] Other states are posting similar or even greater increases.[5] A federal study on drug-related mortality showed that opiates, including prescription pain relievers and heroin, were involved in deaths more often than any other type of drug in 29 of 32 metropolitan areas and in 6 states.[8]

Why Prescription Drugs, and Why Now?

Several reasons may contribute to the rising popularity of prescription drugs for recreational purposes. Such drugs are relatively easy to obtain. A convenient supply found in the family medicine cabinet has replaced the necessity for street procurement and its accompanying stigma. The Internet has ushered in the "age of the electronic pusher" in which Web sites advertise and sell controlled substances to anyone with a credit card, often without regard to the purchaser's prescription status or age.

Some experts believe that drugs of abuse are fads that are popular for a generation and then cycle out of fashion. Evidence shows that this may indeed be happening with respect to prescription drugs. The U.S. National Drug Intelligence Center reports that although prescription drug abuse climbed sharply during the 1990s, it appeared to have peaked by 2002[6] and has since leveled off.

Box I:3

Most-Abused Prescription Drugs

- Opioids.
- Central nervous system depressants (used to treat anxiety and sleep disorders).
- Stimulants (used to treat attention-deficit hyperactivity disorder and narcolepsy).

Source: National Institute on Drug Abuse, National Institutes of Health, US Department of Health and Human Services. Abuse and Addiction, Research Report Series, *2005. NIH publication number 05-4881. Rockville, MD*

Certain drugs attain notoriety in the press, sometimes because of the involvement of law-enforcement agencies. Controlled-release oxycodone is one such opioid that has become a media sensation. When abusers circumvent the controlled-release formula of this or similar drugs by crushing tablets and then chewing, snorting, or injecting the powder, the result is the equivalent of 12 hours of medication delivered in a single "hit." Oxycodone abuse has spread in the United States and has generated publicity, particularly in rural areas and southern states.[9] Some attorneys have even begun trying to profit from media attention by running advertisements to recruit people treated with a prescribed drug who might want to seek restitution for the perceived fostering of addiction.

Any drug that is altered and consumed in defiance of medical direction has the potential to devastate lives. However, vilifying a brand-name drug that provides excellent analgesia for many compliant patients by applying nicknames such as "hillbilly heroin" confers to those treated the unfair stigma of implied drug abuse and encourages a certain societal complacency. If clinicians as a group conclude that prescription opioid abuse exists only in certain socioeconomic groups or in specific regions of the country, then they can remain uninvolved with issues of drug abuse. The resultant false sense of security obscures the truth: Any opioid can be abused in the hands of a determined and compulsive user.

A transdermal patch containing the potent opioid fentanyl is another narcotic pain reliever that has been associated with some deaths and is being closely watched by the U.S. Food and Drug Administration (FDA). The reasons for those deaths have not been established; however, fentanyl patches can be abused by extracting the medication intended for absorption through the skin and ingesting that form of the drug. Another delivery system of fentanyl also became a fad drug of abuse, although its popularity has not become a national problem. An analgesic lozenge that is absorbed through the oral mucous membranes to treat breakthrough pain and is dubbed the "perc-a-pop" by some recreational drug abusers appears to have special appeal to young people (Box I:5).

Regardless of the trends, no one (least of all ethical clinicians who treat pain) should underestimate the dangers posed by prescription drug abuse. However, it is important to distinguish between the illegal use of prescription opioids and the legal medical use of the same substances to treat pain. Media coverage and general public opinion often overlook a very important point: Most pain patients do not take analgesic medications to "get high." Every medication that can be abused is also a valuable tool for treating pain, often with few and manageable adverse effects.

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Box 1.4 **Prescription Drug Abuse in Young People**

- About 1 in 5 teenagers has tried prescription painkillers to get high, according to the Partnership for a Drug-Free America.
- In 2004, more US teens had abused a prescription painkiller than Ecstasy, cocaine, crack, or lysergic acid diethylamide.

The most popular prescription drugs abused by US teens were:

- Hydrocodone (Vicodin) about 1 in 5 youths (18%).
- Oxycodone (OxyContin) (10%).
- Drugs for attention-deficit hyperactivity disorder, such as methylphenidate (Ritalin) or amphetamine and dextroamphetamine (Adderall) (10%).
- Only 48% of teens said they saw "great risk" in experimenting with prescription medicines.
- "Ease of access" was cited as a major factor in trying prescription medications for recreational purposes.
- A medicine cabinet at home or at a friend's home was a likely source of prescription medications for recreational use.

"A new category of substance abuse is emerging in America. Increasingly, teenagers are getting high through the intentional abuse of medications. In other words, Generation Rx has arrived."

Roy J. Bostock, Chairman of The Partnership for a Drug-Free America

Source: Generation Rx: National Study Reveals New Category of Substance Abuse Emerging: Teens Abusing Rx and OTC Medications Intentionally to Get High. Partnership for a Drug-Free America Web site. http://www.drugfree.org/Portal/About/NewsReleases/Teens_Abusing_Rx_and_OTC_Medications. Accessed April 8, 2007.

Chronic Pain

Some pain does not resolve after the original injury or site of surgery has healed. Pain accounts for 80% of all doctor visits,[10] and the most unfortunate patients experience chronic intractable pain. Left unchecked, chronic nonmalignant pain can erode independence and mobility, damage career and family relationships, and cost at least $61.2 billion a year in lost productivity.[11] The cost in diminished quality of life is incalculable.

When is pain defined as chronic? Definitions vary, but in general, pain is considered chronic if it is persistent (it can be intermittent) and if the cause cannot be removed.

Chronic pain:

- Persists longer than 3 or 6 months (opinions vary) and may continue unabated for weeks, months, or years.
- Persists beyond the normal healing process.
- Occurs after injury or may have no apparent cause.
- May spread beyond the original site of injury.

- Appears to serve no biological purpose.
- Is of moderate-to-severe intensity.
- Limits physiologic function.
- Impacts psychologic and emotional function.
- Significantly interferes with daily activities.
- Reduces quality of life.
- Is refractory to treatment.

Box 1:5

Perc-a-Pop

Used to refer to fentanyl in lozenge form.
Nickname originated in Philadelphia, Pennsylvania.
Most buyers are teenagers in Philadelphia.
Sold on streets for about $20 per dose.
Easy to abuse, sweet, has high appeal for young people.
Abuse appears isolated; national abuse rates are growing but remain relatively low:
- 576 incidents of nonmedical use in 2000
- 1506 incidents of nonmedical use in 2002

Source: Scolforo M. Abuse of narcotic "perc-a-pops" reported in Philadelphia. Associated Press. April 28, 2004.

Prevalence of Chronic Pain in America

After considering the results of an international survey of almost 26,000 primary care patients, Rosenblum and colleagues suggested in 2003 that 70 million U.S. adults live with chronic pain.[12] According to a survey conducted for the American Pain Society, approximately 9% of the U.S. adult population experiences moderate-to- severe pain.[13] Chronic nonmalignant pain is difficult to treat because it is often refractory to conventional treatment. Long-term therapy with opioids can bring a degree of relief and a return of function to many chronic-pain patients.

Box 1:6

Opioids Often Prescribed to Treat Pain

- Codeine.
- Fentanyl.
- Hydrocodone.
- Hydromorphone.
- Levorphanol.
- Meperidine.
- Methadone.
- Morphine.
- Morphine sustained-release.
- Oxycodone.
- Oxycodone controlled-release.

Opioids are synthetic compounds that are similar in structure and action to the natural opiates derived from the poppy plant (Box I:6). Opioids bind to receptors in the brain and spinal cord as do endorphins (the body's natural analgesics). Thus opioids inhibit pain transmission by blocking the sensation of pain that is conveyed by nerve cells. Opioid treatment rarely produces complete relief from pain. However, a review of the literature revealed that patients with chronic nonmalignant pain experienced a significant improvement in function and quality of life as a result of long-term opioid therapy.[14] Chronic pain may even be

preventable if it is treated aggressively and early. For that reason, it is vital that common fears and misconceptions associated with the prescribing of opioids not be allowed to cloud treatment choices.

Chronic Pain Meets Fear of Opioids

The treatment of chronic nonmalignant pain presents a far more difficult clinical challenge than does therapy for acute or postoperative pain. The use of opioids is most controversial in patients with chronic nonmalignant pain, mainly because clinicians often fear that prescribing opioids could contribute to drug abuse or addiction. The fear that patients are faking some or all of their pain symptoms just to obtain narcotic pain medication causes some clinicians to stigmatize the use of opioids and to mislabel pain patients as addicts. This presents, perhaps, the greatest single barrier to the availability of pain relief. To a somewhat lesser degree, clinicians also fear regulatory or legal action connected with the prescribing of opioids and the induction of obtundation or oversedation in patients who are treated with opioids.

Cognitive tests performed in patients treated with opioids have shown that the agents produce little to no reduction in cognitive function.[15] Any sedation or impairment that does occur tends to develop in patients whose opioid therapy has just begun. Over time, those adverse effects of opioid treatment nearly always resolve.

Clinicians' common concern about "creating drug addicts" or otherwise increasing the societal problem with prescription drug abuse is understandable, but when such fears are allowed to drive decisions concerning pain management, patients suffer. Consider the following case:

> A patient was suffering severe pain because of complications after plastic surgery. The surgeon who performed her surgery refused to treat her pain with opioid analgesics because he feared losing his medical license. The patient was subsequently referred to a pain specialist who prescribed strong opioids that were required for only 2 weeks.

When physicians agree to perform surgery but then refuse to treat postoperative pain, their fear of prescribing opioids has become exaggerated. The refusal to adequately relieve postsurgical pain is unconscionable. Protection against legal penalties after prescribing opioids will be covered in greater detail in a later chapter. It should be noted, however, that opioids are controlled substances, and the government tracks their use closely. Careful documentation and familiarization with federal and state laws pertaining to opioids are the best tools clinicians can use to protect themselves and their practices.

Regardless of how experienced or careful the clinician, he or she will likely be fooled at some time by a patient seeking opioids for sale or for a nonmedical purpose. However, those individuals represent a minority, and far too many patients who require opioids to relieve severe pain are stigmatized as "drug seekers." Most patients seek relief from their pain and nothing more. Ways to avoid becoming the instrument of diverters will be outlined later in this book.

The Importance of Treating Pain

Out-of-control pain does not make the patient stronger from the suffering it induces; it

destroys health and well-being. Researchers have found that malignant tumor growth is slowed by the administration of painkillers.[16] Pain inhibits the body's immune system and impacts heart rate, blood pressure, and respiration. Pain that persists and becomes chronic rewires the body's nervous system to continue sending signals even after the original cause has healed or been removed. Subsequent damage to neural pathways can be permanent. Anxiety, depression, and insomnia make the pain doubly unbearable.

Fortunately, the last decade has brought greater emphasis on pain management and frequent calls for supportive pain-control guidelines and public policies. A spotlight focused on the issues in the summer of 2000, when the US Congress passed a bill designating a "Decade of Pain Control and Research." In January 2001, US hospitals were required to implement new standards from the Joint Commission on Accreditation of Healthcare Organizations to improve pain assessment and management. One of the standards requires healthcare professionals to consider pain as an entity separate from its cause. Pain became designated the "fifth vital sign" in addition to the other vital signs (body temperature, pulse, respiration, and blood pressure). Although these encouraging signs suggest that the serious detriment of pain is being recognized, the number of people who are undertreated for pain still far outstrips the segment of the population afflicted by drug abuse.[17]

In these pages, our focus is to acknowledge and address the drug-related behaviors that sometimes compromise pain treatment with opioids. For that reason, little space has been devoted to the appropriate clinical methods of pain management, such as initiating and changing doses or providing alternative pain therapies if opioid treatment becomes inadvisable for a given patient. Several good pain-management guides are available. A couple of recommendations for clinicians are *A Clinical Guide to Opioid Analgesia* by authors Fine and Portenoy, published by McGraw-Hill,[18] and *The Pain EDU.org Manual: A Clinical Companion* by Menefee and Katz published by Inflexxion, Inc.[19] Both are available online.

A History of Opium and Opioid Use

The history of opiates as instruments of pain relief has spanned millennia and produced many consequences, some good and some less than desirable. The use of opium harkens back at least to ancient Sumeria (c 3400 BC) and was known among the Egyptians in 1300 BC.[20] Although Hippocrates (c 460 BC) recognized the usefulness of opium as a painkilling narcotic, it was often consumed to produce euphoria for purely recreational purposes. The psychogenic effects proved very popular among 19th century writers such as John Keats and Elizabeth Barrett Browning.

The 19th century also brought 2 developments of immense medical significance: the isolation of morphine (the active ingredient in opium), which was termed "God's own medicine," and the invention of the hypodermic needle. However, as the 20th century dawned, opiates began to fall out of favor as addiction fears grew and the US government assumed legal control of the prescribing and dispensing of controlled substances.

The distrust of narcotics sometimes extended even to the practice of refusing sufficient medication to ease pain. The belief grew that pain, particularly if it is endured without complaint, fosters character. In the 1940s, the *British Medical Journal* quoted a respected practitioner who downplayed the importance of newly available anesthetics to ease childbirth pain.[21] He reasoned that mothers whose childbirth was not painful might cease to love their children.

In the United States, much needless suffering resulted from the "stiff upper lip" approach to medical care. Yet as the progress of scientific inquiry took hold, that attitude began to change. With the discovery of opiate receptors in the central nervous system, acceptance slowly was reignited for the administration of opioids sufficient to treat acute and postsurgical pain and the ongoing pain caused by cancer. Even so, the use of opioids to ease chronic nonmalignant pain continued to be frowned upon by the medical establishment and was sometimes even prosecuted by law.

A new era of greater pain control dawned in the late 1980s and gained in popularity throughout the 1990s. It was then that the widespread acceptance of opioids used to treat chronic nonmalignant pain grew in part as a result of numerous studies that reported the undertreatment of pain to be common and analgesia-induced addiction rare. As a hallmark of the increasing acceptance of analgesics used to control pain, a 1997 consensus document published by the American Academy of Pain Medicine and the American Pain Society advised all types of clinicians (not just specialists) to consider the use of opioids in selected patients for the management of chronic nonmalignant pain.[22] During that time, pain-control advocates, who were eager to heal the scourge of undertreated pain, may have underestimated the risk of abuse posed by opioid therapy. In recent years, those same advocates have begun to sound a cautionary note. One such expert is Russell K. Portenoy, MD, a pioneer and preeminent leader in pain management. In an Australian radio interview about the fight against chronic pain, Portenoy said he was embarrassed by his own minimization of the risk of drug abuse when he taught other clinicians how to use opioids to treat chronic pain 10 years earlier.[23] He said, "I did that because I thought that in patients with chronic pain, these risks could be minimized, and that compared with the problem of undertreated pain, the concern about abuse, addiction, and diversion was not that relevant. Fast-forward 10 years later, and we recognize that was a big error."[23]

This brief overview of the use of analgesic agents brings us to the present day, when the extent of the solution must parallel the size of the problem. As Portenoy said, "Doctors have to have two sets of skills to use these drugs safely and effectively, or they shouldn't use them." Those sets of skills are prescribing opioids and minimizing the risk of abuse.

Prevalence of Addiction in Chronic-Pain Patients

The prevalence of addiction in pain patients has almost certainly been underestimated in the recent past. In truth, the prevalence of drug abuse and addiction in patients treated with opioids for chronic pain has not been established because of the lack of prospective studies. Most research indicates that patients with chronic pain tend to abuse substances, including alcohol, at estimated rates of 10% to 18%, which are similar to or slightly higher than those in the general U.S. population.[24-25] About 1% of the general U.S. population demonstrates addiction to opioids.[26] At least 1 study has shown that 2% to 5% of chronic-pain patients manifest addiction (a rate more than twice that of the general population).[27]

However, the extent to which opioids prescribed for pain actively foster an addiction that did not already exist has sometimes been exaggerated, particularly in the popular imagination. According to the results of a survey of 1000 American adults in 2002, most (78%) believed that treating pain with strong medicines is very likely or somewhat likely to result in addiction.[28] Only 1 in 5 respondents thought the likelihood of addiction to be low. Although abuse, addiction, and diversion are serious issues in a minority of patients who ex-

hibit those problems, research clearly indicates that most patients treated with prescribed opioids for acute or chronic pain will not become addicted to their medication.

Patients with a history of substance abuse and poor social support who are not in a recovery program and who are receiving long-term opioid therapy are at high risk for abusing their medication, whether or not that abuse reflects true addiction.[29] However, even patients with a history of substance abuse are not destined to abuse prescribed opioids if they are adequately monitored and receive sufficient support. Whatever the true addiction rate in US chronic-pain patients, it is the risk of addiction or abuse in each individual patient that is of greatest concern to clinicians. Guidelines for assessing the potential for opioid abuse in individual patients are outlined in a later chapter.

When Pain Is the Problem

Chronic-pain patients who receive long-term opioid therapy often face deep resistance to their treatment from family members, friends, and employers who view those patients with suspicion. One such patient was in stable condition and her pain was well controlled by opioid medication for more than 20 years. Nevertheless, she was pleased when a newer pain-control method – a spinal implant that delivers medication – allowed her to reduce the number of tablets she took. When she shared this information, her sister took the opportunity to vent a long-held belief: "I always knew you were an addict." A lack of understanding about addiction leads to demeaning statements like this one. Incidents such as these are humiliating for pain patients and occur far too frequently.

Box 1:7

Characteristics of Chronic-Pain Patients Versus Addicted Patients

Chronic-Pain Patient

- Medication use is not out of control.
- Medication use improves quality of life.
- Wants to decrease medication if adverse effects develop.
- Is concerned about the physical problem that is being treated with the drug.
- Follows the agreement for the use of the opioid.
- Frequently has leftover medication.

Addicted Patient

- Medication use is out of control.
- Medication use causes a diminished quality of life.
- Medication use continues or increases despite adverse effects.
- Unaware of or in denial about any problems that develop as a result of drug treatment.
- Does not follow the agreement for the use of the opioid.
- Does not have leftover medication, loses prescriptions, always has a "story" about why additional drug treatment is necessary.

Much confusion abounds regarding what causes addiction (Box I:7). Some clinicians believe they have turned a patient into an addict if that patient displays symptoms of tolerance to an opioid medication. Far too many people believe that a family member is addicted because he or she "looks drunk." Because the nomenclature available to today's practicing clinicians does not always adequately reflect the reality observed in the patients they treat, the lexicon used most commonly to refer to opioid use should be reviewed.

Definitions Associated with Opioid Use and Abuse

Inadequate or misused terminology can limit the ability to speak with clarity and ac-

Box I:8

Definitions Associated with Opioid Use and Abuse

Abuse
The use of any substance for a nontherapeutic purpose or the use of medication for purposes other than those for which the agent is prescribed.

Addiction
A primary chronic neurobiologic disease influenced by genetic, psychosocial, and environmental factors. It is characterized by impaired control over drug use, compulsive drug use, and continued drug use despite harm and because of craving.

Tolerance
A physiologic state caused by the regular use of an opioid in which increased doses are needed to maintain the same effect. In patients with "analgesic tolerance," increased doses of the opioid are needed to maintain pain relief.

Physical Dependence
A physiologic state characterized by abstinence syndrome (withdrawal) if treatment with an opioid is stopped or decreased abruptly or an opioid antagonist is administered. It is an expected result of opioid therapy and does not by itself equal addiction.

Abstinence Syndrome (Withdrawal)
A syndrome characterized by symptoms that include sweating, tremor, vomiting, anxiety, insomnia, and muscle pain. Abstinence syndrome is caused by a reduction in the opioid dose or the administration of an opioid antagonist. It can be avoided by carefully tapering the opioid dosage and monitoring the patient.

Definitions adapted from the following sources:

American Academy of Pain Medicine, American Pain Society, and American Society of Addiction Medicine. Definitions related to the use of opioids for the treatment of pain: consensus document. Under review. Glenview, IL and Chevy Chase, MD; 2001.

Federation of State Medical Boards of the United States. Model policy for the use of controlled substances for the treatment of pain. Available at: http://www.fsmb.org/pdf/2004_grpol_Controlled_Substances.pdf. Accessed April 10, 2007.

curacy about substance-use disorders. To counteract such confusion, clinicians should give thorough consideration to what is meant by terms like "addiction," "abuse," "tolerance," and "physical dependence" (Box I:8). Such terms are frequently misunderstood in clinical circles, in casual conversations, in media accounts, by well-meaning friends and family members of patients, and by patients themselves.

The differences in meaning of terms that pertain to opioid use are important. A person who is physically dependent on a drug, for example, may experience symptoms of withdrawal if treatment with that drug is suddenly interrupted or terminated. Such symptoms do not in themselves indicate addiction. Similarly, a person who aggressively demands more medication may be suffering from undertreated pain and not from addiction. The following definitions are derived from several sources (primarily the 2001 consensus document titled *Definitions Related to the Use of Opioids for the Treatment of Pain*, which has been endorsed by the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine).[30]

Physical Dependence

This is one of the most frequently misunderstood and misapplied terms. "Physical dependence" is often misinterpreted as referring to addiction. Instead, it is a natural physiologic response to the persistent use of opioids. Physical dependence merely means that the body has adapted to the blood level of the opioid in the system and that the patient is likely to exhibit symptoms of abstinence syndrome, otherwise known as "withdrawal," if treatment with the drug is abruptly terminated or sharply decreased or if an opioid antagonist is administered.

Some of the confusion over the term "dependence" stems from definitions contained in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revised* (*DSM-IV-TR*).[31] The *DSM-IV-TR* defines substance dependence, including opioid dependence, as essentially synonymous with addiction; it fails to distinguish between the disease of chemical dependence and the natural physiologic response of physical dependence. The *DSM-IV-TR* even goes so far as to list tolerance and withdrawal symptoms among the "defining features" of addiction (substance dependence), thus further impeding the chances of differentiating a true disease process from a normal physiologic reaction.

It is essential to use correct terms to refer to medical and nonmedical opioid consumption. A person who is addicted to an opioid medication may also be physically dependent on that agent. However, an addicted person will not only exhibit abstinence syndrome if treatment with the opioid is stopped but will also display a lack of control over the use of the drug, compulsive use of the agent, craving for the drug, and continued use despite harm, all of which are hallmarks of addiction. Furthermore, the absence of physical dependence does not mean that a person is not addicted. Cocaine is an example of a strongly addicting substance that does not, when the drug is suddenly stopped, cause the type of withdrawal that opioids do. Thus cocaine is not a strong catalyst for physical dependence, but thousands of ruined lives attest to its addictive power.

Physical dependence can occur with drugs other than opioids. Treatment with certain anticonvulsants and antidepressants, for example, also cannot be stopped abruptly without inducing abstinence syndrome, yet those medications are not associated with addiction. Although abstinence syndrome does not develop when treatment with insulin is quickly with-

drawn, insulin is necessary for physical function and a good quality of life in some diabetic individuals. In that regard, some diabetic patients can be said to be dependent on insulin. In a similar manner, analgesics increase physical function and improve the quality of life for patients with chronic pain, even if opioid therapy is maintained long term and the opioid doses seem massive to laypeople.

When opioids become unnecessary because pain has resolved, dosages should be carefully and slowly tapered to avoid abstinence syndrome. Guidelines for discontinuing opioid therapy are provided in Chapter VI. The patient should be monitored closely for the development of clinical symptoms. Some patients are very sensitive to the withdrawal process and will require pharmacologic treatment. This tapering of medication is not equal to "detoxing" the patient, because the patient is not toxic if he or she is taking medication only to avoid withdrawal. Experts in pain management and the treatment of addiction prefer the term "transitioning."

To recap, physical dependence is:

- A normal physiologic state.
- An expected result of opioid use.
- Characterized by withdrawal (abstinence syndrome) if treatment with the opioid is suddenly terminated or decreased or if an opioid antagonist is given.
- Highly variable in its onset, depending on the individual patient.
- A phenomenon that sometimes coincides with addiction.
- Is not, by itself, an indication of addiction.

Tolerance

Like physical dependence, tolerance is a natural physiologic response to regular opioid use. Tolerance is defined as the need to increase an opioid dose to maintain the same effect or, if the dose is kept constant, a reduction in effect. The effects of opioids include those that are wanted, such as analgesia, and those that are unwanted, such as respiratory depression, sedation, nausea, constipation, and a reinforcing action on the brain's "reward center," which poses the danger of addiction. The rate at which tolerance to the various effects of opioids develops varies among patients.

Analgesic tolerance, or the need to increase the opioid dose to achieve the same level of pain relief, is not a sign of addiction, nor is it considered a factor that contributes to the risk of addiction. Not every individual experiences analgesic tolerance. Great variations exist in the individual response to opioids, just as pain perception varies greatly among individuals. Research shows that younger people develop tolerance more quickly (and thus need more frequent dose adjustments) than do older individuals.[32]

There is no arbitrary ceiling beyond which a dose of opioids is unsafe. Clinicians who treat chronic pain are able to administer large doses of opioids to opioid-tolerant patients; the same doses would be unsafe in opioid-naïve patients. Therefore, a physician cannot be said to be "overprescribing" opioids solely on the basis of the quantity and frequency of prescribing. Sometimes, more opioids are needed to treat pain because the patient's disease has worsened. Some patients may need more medication to treat pain caused by increased activity because their physical functioning has improved. Those types of dose titrations are not associated with tolerance.

In summary, tolerance:

- Is a natural state of neuroadaptation to drug-induced changes.
- May result in increased analgesic needs.
- Develops at different rates for different effects such as analgesia, sedation and nausea.
- Varies among individuals.
- Varies according to the type of pain.
- Develops more quickly in younger people than in older individuals.
- Is not addiction.

Tolerance begins to develop immediately after the first ingestion of an opioid. Only a few days of opioid therapy can lead to some degree of tolerance and physical dependence. Patients who receive short-term opioid treatment can experience mild flu-like symptoms when therapy with the drug is stopped. For most patients treated with opioids, these are manageable adverse effects of therapy. Patients with chronic nonmalignant pain who experience good analgesia with opioid therapy should not be deprived of pain relief because of those effects.

Abuse

The definitions or criteria for substance abuse include:

- Intentional overuse of the substance during periods of celebration, anxiety, or despair or as a result of self-medication or ignorance.
- A maladaptive pattern of substance use that leads to clinically significant impairment or distress.
- The use of any substance for a nontherapeutic purpose.
- The use of a medication outside the scope of usual medical practice.
- When the abuse of prescribed opioids is described, the best definition is probably that provided by the US Substance Abuse and Mental Health Services Administration: "any nonmedical use of a substance."

If abuse is defined as any use of a medication in defiance of medical direction, then abuse is a very widespread phenomenon indeed, and it encompasses a nearly infinite variety of behaviors and motivations. A few of the reasons why abuse occurs include:

- Experimentation.
- To escape stress or boredom.
- Peer norms.
- To manage anxiety or depression.
- To mitigate a comorbid mental disorder.
- To mask unhappiness stemming from life's problems, whether marital, financial, health, or other.
- To curb undertreated pain.
- Addiction.

The lifelong heroin addict is an abuser. So is the person who, when trying to conserve finances, consumes his wife's prescription opioids on only 1 occasion because he has a toothache.

Drug abuse is often confused with addiction, which is a medical condition that also involves the misuse of substances. There is a crucial distinction, however: Abuse that does not stem from addiction tends to decrease when adverse consequences (legal, social, or physical) begin to worsen the individual's life.

It is important to understand that:

- Abusers may or may not also be addicted.
- Abusers can often stop when harm occurs.

What exactly are the adverse consequences of medication abuse? The 2001 consensus statement[30] on opioid prescribing details some of them:

- Persistent sedation or intoxication resulting from overuse.
- Increasing functional impairment.
- Medical complications.
- Psychologic manifestations such as irritability, apathy, anxiety, or depression.
- Legal problems.
- Economic problems.
- Social problems.

Patients who misuse their medications may experience some of the above characteristics and still may not be addicted. Many possible reasons can drive prescription drug abuse, some of which will be explored later. Some cases of ongoing, egregious, or intractable abuse do indeed require the release of a patient from care — a process that must be accomplished according to legal and ethical guidelines. However, abuse is a common occurrence and can usually be managed by clinical interventions.

Addiction

Tolerance and physical dependence are expected physiologic effects of opioid therapy; addiction is not. Addiction is a chronic primary disease with a neurobiologic basis. Unlike abusers who can stop the abuse when harm occurs, addicted people so crave the substance they abuse that they are willing to sacrifice every aspect of their lives rather than do without that substance. Health, marriage, career, reputation, and financial status can crumble into ruin, but the addicted person cannot stop seeking the substance that is causing the destruction. A person with addictive disease is likely also to be physically dependent on the drug, and he or she is at high risk for the recurrence of addiction even after detoxification has been accomplished.

Addiction is characterized by the following behaviors, which are known as the "4C's:"

- Impaired control over drug use
- Compulsive use of the drug
- Continued use of the drug despite harm (physical, mental, and/or social)
- Craving for the drug

People with addictive disease may feel euphoric or "high" after taking an opioid. It is that euphoric experience or some other psychogenic reward that leads them to seek and reseek the substance to which they are addicted. It should be noted that patients without the disease of addiction are more likely than addicted patients to experience an unpleasant reaction to an opioid prescribed for pain. That said, the experience of a pleasurable feeling is sometimes simply an effect of taking opioid medications and does not, in itself, indicate that an individual has become addicted.

Drug-produced euphoria does not produce the disease of addiction. Most people exposed to a substance with addictive properties do not become addicted to that substance. Cocaine, for example, which is one of the world's most addictive drugs, induces true chemical dependence in only 16% of its users.[33] Opioid medications may trigger or retrigger addiction in individuals who exhibit a complex interplay of vulnerabilities, but medications do not cause addiction. If this were true, every patient who received a medication with addictive potential would become addicted to that drug.

It should also be noted that a patient with a history of addictive disease or a vulnerability that indicates the potential for addictive disease experiences pain, both chronic and acute, as frequently as does any other patient. Patients who are vulnerable to addiction deserve pain treatment, too, and they are at particular risk for having their pain ignored or minimized.

Abuse behaviors can indicate the presence of the disease of addiction, or they can indicate another underlying problem, such as undertreated pain or the presence of a mental disorder. More discussion on the many different possible triggers of medication abuse, some of which closely mimic addiction, will follow in Chapter III.

Conclusion

Prescription opioid abuse is a growing phenomenon that no ethical health practitioner can ignore. The correct use of language will help clinicians and patients to more precisely identify and address the various clinical conditions related to pain and the use of opioids. "Abuse" is not necessarily "addiction," nor should "addiction" be confused with other terms such as "tolerance" or "physical dependence," both of which are expected physiologic responses to opioid consumption.

References

1. Text of Patrick Kennedy's statement. The Associated Press. May 5, 2006.
2. Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. JAMA. 2003 Nov 12;290(18):2443-54.
3. Under the Counter: The Diversion and Abuse of Controlled Prescription Drugs in the U.S. National Center on Addiction and Substance Abuse at Columbia University (CASA), New York, NY; 2005.
4. Generation Rx: National Study Reveals New Category of Substance Abuse Emerging: Teens Abusing Rx and OTC Medications Intentionally to Get High. Partnership for a Drug-Free America Web site. Available at:

http://www.drugfree.org/Portal/About/NewsReleases/Teens_Abusing_Rx_and_OTC_Medications. Accessed April 8, 2007.

5. Centers for Disease Control and Prevention (CDC). Unintentional and undetermined poisoning deaths—11 states, 1990-2001. MMWR Morb Mortal Wkly Rep. 2004 Mar 26;53(11):233-8.
6. National Drug Intelligence Center. Pharmaceuticals: Drug Threat Assessment. US Department of Justice. Product No. 2004-L0487-001. November 2004.
7. North Carolina Department of Health and Human Services. Findings and recommendations of the task force to prevent deaths from unintentional drug overdoses in North Carolina, 2003. (Division of Public Health, Injury and Violence Prevention Branch). Raleigh, NC.
8. Substance Abuse and Mental Health Services Administration, Office of Applied Studies. Drug Abuse Warning Network, 2003: Area Profiles of Drug-Related Mortality. DAWN Series D-27, DHHS Publication No. (SMA) 05-4023. Rockville, MD, 2005.
9. Hays LR. A profile of OxyContin addiction. J Addict Dis 2004; 23(4):1-9.
10. The Arthritis Foundation Pain In America: Highlights from a Gallup Survey, 2000. Arthritis Foundation Web site. Available at: http://www.arthritis.org/conditions/speakingofpain/factsheet.asp. Accessed March 1, 2004.
11. Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. JAMA. 2003 Nov 12;290(18):2443-54.
12. Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, Portenoy RK. Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. JAMA. 2003 May 14;289(18):2370-8.
13. Roper Starch Worldwide, Inc. Chronic Pain In America: Roadblocks To Relief. Research conducted for the American Pain Society, the American Academy of Pain Medicine and Janssen Pharmaceutica, Jan. 1999. American Pain Society Web site. Available at: http://www.ampainsoc.org/whatsnew/conclude_road.htm. Accessed March 2, 2004.
14. Devulder J, Richarz U, Nataraja SH. Impact of long-term use of opioids on quality of life in patients with chronic, non-malignant pain. Curr Med Res Opin. 2005 Oct;21(10):1555-68.
15. Ersek M, Cherrier MM, Overman SS, Irving GA. The cognitive effects of opioids. Pain Manag Nurs. 2004;Jun;5(2):75-93.
16. Jiang Y, Weinberg J, Wilkinson DA, Emerman JT. Effects of steroid hormones and opioid peptides on the growth of androgen-responsive Shionogi carcinoma (SC115) cells in primary culture. Cancer Res 1993 Sep 15;53(18):4224-9.
17. Douglas E. Clinicians underestimate pain, resulting in undertreatment. Anesthesiology News. 2005 April;31(4).
18. Fine PG, Portenoy RK. *A Clinical Guide to Opioid Analgesia*. Minneapolis, MN: McGraw-Hill; 2004.
19. Menefee L, Katz N. *The Pain EDU.org Manual: A Clinical Companion*. Newton, MA: Inflexxion, Inc., 2003.

20. Booth M. Opium: A History. 1st US ed.. New York, NY: Thomas Dunne Books; 1998.
21. Without pain. Time Magazine. 1948; June 28.
22. American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain: A consensus statement. Glenview, IL; 1997.
23. A world of pain. ABC Radio National – Background Briefing. Produced by Helen Thomas. Dec. 5, 2004.
24. Savage SR. Assessment for addiction in pain-treatment settings. Clin J Pain. 2002 Jul-Aug;18(4 Suppl):S28-38.
25. Weaver M, Schnoll S. Abuse liability in opioid therapy for pain treatment in patients with an addiction history. Clin J Pain. 2002 Jul-Aug;18(4 Suppl):S61-9.
26. Robinson RC, Gatchel RJ, Polatin P, Deschner M, Noe C, Gajraj N. Screening for problematic prescription opioid use. Clin J Pain. 2001 Sep;17(3):220-8.
27. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. Pain Med. 2005 Nov-Dec;6(6):432-42.
28. American Chronic Pain Association. Pain Awareness Is Important to Nurses. Pain Awareness Survey, June 2002. Partners for Understanding Pain [tool kit], September 2003. Rocklin, CA: American Chronic Pain Association; 2003.
29. Dunbar SA, Katz NP. Chronic opioid therapy for nonmalignant pain in patients with a history of substance abuse: report of 20 cases. J Pain Symptom Manage. 1996 Mar;11(3):163-71.
30. American Academy of Pain Medicine, American Pain Society, and American Society of Addiction Medicine. Definitions related to the use of opioids for the treatment of pain: consensus document. Under review. Glenview, IL and Chevy Chase, MD; 2001.
31. American Psychiatric Association, ed. Diagnostic and Statistical Manual of Mental Disorders. 4th ed, text revised (DSM-IV). Washington, DC: American Psychiatric Association; 2000.
32. Buntin-Mushock C, Phillip L, Moriyama K, Palmer PP. Age-dependent opioid escalation in chronic pain patients. Anesth Analg. 2005 Jun;100(6):1740-5.
30. American Academy of Pain Medicine, American Pain Society, and American Society of Addiction Medicine. Definitions related to the use of opioids for the treatment of pain: consensus document. Under review. Glenview, IL and Chevy Chase, MD; 2001.
33. O'Brien CP, Gardner EL. Critical assessment of how to study addiction and its treatment: human and non-human animal models. Pharmacol Ther. 2005 Oct;108(1):18-58.

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