

Opioid Abuse and Addiction

Opioids are one of the most frequently abused drugs.^{1,2} The number of people abusing prescription drugs, including opioids, more than doubled, from 7.8 million in 1992 to 15.1 million in 2003.³ In a 2006 survey of drug use in the United States, it was estimated that 5.2 million persons abused pain relievers, a 32% increase from the 4.7 million reported in 2005.² Opioid abuse imposes substantial costs on society and payers, as well as the users themselves.⁴ In 2002, prescription opioids accounted for 18.9% of the drugs implicated in multiple-drug-related deaths.³ Direct healthcare costs for opioid abusers have been shown to be 8 times higher than for nonabusers (\$15,884 vs \$1830, $p < 0.01$).⁴ These costs are driven primarily by the high utilization rates of medical services and prescription drugs and the high prevalence rates of costly comorbidities.

IN MY OPINION

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The increase in opioid abuse is particularly alarming among teens, with an estimated increase of 542% from 1992 to 2003.³ In 2003, an estimated 2.3 million teens (aged 12-17 years) abused prescription drugs, of which about 1.9 million abused opioids.³ The Partnership for a Drug-Free America estimated that 1 in 5 teenagers have used prescription pain killers to "get high."¹ The short-acting opioid hydrocodone was the most popular drug abused by teens (18%), followed by oxycodone (10%). A surveillance of Internet message boards dedicated to drug abuse observed that of 3 targeted opioids, the number of postings significantly differed for oxy-

codone, hydrocodone, and morphine sulfate extended-release tablets (1813, 940, and 27 postings, respectively; $p < 0.001$).⁵

The startling rise in opioid abuse necessitates more action on the part of health care providers to reverse this trend, particularly among teenagers. Health care providers need to better understand the mechanisms of abuse among patients and the risk of abuse associated with individual agents.

USE AND ABUSE OF PRESCRIPTION OPIOIDS

In addition to relieving pain, opioids can have iatrogenic effects that may increase the risk of abuse—cravings, withdrawal symptoms, and euphoria. The etiology of abuse may include deception or illicit methods to obtain opioids.⁶ In many cases, fear of uncontrolled pain may cause the patient to increase the dose without consulting the prescribing physician and may lead to eventual abuse and/or addiction behaviors.⁶

Generally, risk of addiction or abuse is higher for patients with a history of substance abuse than for those without such a history.⁷ Patients with a history of underlying mental illness, including depression, may be at high risk for abuse of opioids and also may benefit from appropriate psychological evaluation and treatment prior to the initiation of opioid therapy.^{3,8}

Chronic Pain and Risk of Opioid Abuse

Use of opioids in the chronic pain patient population is particularly common and is a known risk factor for abuse and addiction.⁹ Chronic-pain patients frequently utilize both short- and long-acting opioid agents with mild or potent analgesic effects.⁶

A limited number of studies have investigated the abuse of opioids in chronic pain populations. Moreover, chronic pain is prevalent among those

Table 1. Tolerance, Physical Dependence, and Addiction^{6,10}

Tolerance	Develops when a constant opioid dosage produces a decreasing effect Tolerance develops to the analgesic effects and to the opioid-induced side effects (except constipation)
Physical dependence	Describes the predictable pharmacologic effect that occurs after abrupt discontinuation of opioid therapy Manifested by development of withdrawal symptoms The withdrawal symptoms that occur are often confused with addiction Can occur in patients taking opioids for ≥ 2 weeks Withdrawal can be avoided by tapering doses by 10–20% per day
Addiction (psychological dependence)	Not related to the property of the drug Characterized by continued craving for an opioid and the need to use the opioid for effects other than pain relief Patients with addiction often exhibit aberrant drug-seeking behaviors and make obtaining the drug the primary focus of their life

with a history of substance abuse.⁹ Addiction has been shown to range from 3.2% to 18.9% in chronic pain populations.¹⁰

TOLERANCE, PHYSICAL DEPENDENCE, AND ADDICTION

Drug use can be seen as a continuum, which can progress from casual use to addiction (Figure 1).¹¹ As the pattern of drug use approaches addiction, the desire for the drug assumes increasing control of the individual's behavior. It is important for practitioners to distinguish the differences between tolerance, physical dependence, and addiction (Table 1).^{6,10}

Mitigating Opioid Abuse

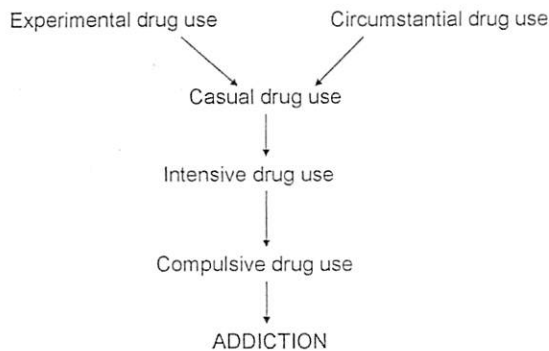
Because opioids are very effective for managing pain, banning these substances is an untenable approach. Health care providers need to be aware of the potential signs for drug diversion and abuse. To help minimize the potential for abuse, health care providers should screen patients for the potential of drug abuse and carefully monitor the progress of their treatment.^{12,13} Health care providers should understand and monitor for drug diversion mechanisms, which include: employees stealing from inventory, prescription forgery, robberies of pharmacies and drug distributors, "doctor shoppers," health care providers (physicians, den-

tists, pharmacists), friends and family, illegal Internet pharmacies, and illegal trafficking from foreign countries.^{3, 12}


The development of new advances in drug technologies and new tamper-resistant formulations of opioids to treat acute and chronic pain while reducing the risk of abuse would fulfill a significant unmet need, as these products could potentially play a central role in optimizing the risk-benefit ratio of opioid analgesics.¹⁴ A New Drug Application for a new formulation of morphine, which has a naltrexone core, was submitted to the Food and Drug Administration on February 28, 2008.¹⁵ This formulation is designed to provide effective pain relief with long-acting morphine when used as directed. However, if the product is chewed, crushed, or dissolved, the sequestered naltrexone mitigates the euphoria associated with morphine and deters the misuse of the drug.

Also in Phase 3 clinical development, is a version of long-acting oxycodone that is being studied in patients with severe chronic pain.^{5,16} This formulation releases a fraction of oxycodone upon freezing, crushing, or submerging in high-proof alcohol compared with Oxycontin. Other abuse-deterrent opioid products are in earlier phases of clinical development. A proof of concept clinical trial has recently been completed for an abuse deterrent, sustained release, oral oxycodone formulation that is designed to be more resistant to tampering and abuse than traditional formulations of the drug.²

Figure 1. Continuum of drug use: progression from casual drug use to addiction.¹¹



SUMMARY

"The obligations to battle pain and addiction are not mutually exclusive, they are mutually inextricable."¹² Abuse of opioids is a serious and increasing problem, particularly among teenagers. Physicians need to be aware of the factors associated with opioids and take steps to mitigate the risk of abuse by individual patients. This includes proper screening and monitoring and the use of emerging agents that will effectively control pain and may be associated with a lower risk of abuse. 

References

1. The Partnership for a Drug-free America. Generation Rx: national study reveals new category of substance abuse emerging: teens abusing Rx and OTC medications intentionally to get high. Available at: http://www.drugfree.org/Portal/About/NewsReleases/Teens_Abusing_Rx_and_OTC_Medications. Accessed November 20, 2007.
2. Substance Abuse and Mental Health Services Administration. Results from the 2006 National Survey on Drug Use and Health: National Findings. Rockville, MD: (Office of Applied Studies, NSDUH Series H-30, DHHS Publication No. SMA 06-4194). Available at: <http://oas.samhsa.gov/nsduh/2k6nsduh/2k6Results.pdf>. Accessed June 5, 2008.
3. The National Center on Addiction and Substance Abuse at Columbia University. Under the counter: the diversion and abuse of controlled prescription drugs in the U.S. 2005. Available at: http://www.casacolumbia.org/absolutenm/articlefiles/380-under_the_counter_-_diversion.pdf. Accessed November 20, 2007.
4. White AG, Birnbaum HG, Mareva MN, et al. Direct costs of opioid abuse in an insured population in the United States. *J Manag Care Pharm.* 2005;11(6):469-479.
5. Butler SF, Venuti SW, Benoit C, Beaulaurier RL, Houle B, et al. Internet surveillance: content analysis and monitoring of product-specific internet prescription opioid abuse-related postings. *Clin J Pain.* 2007;23(7):619-628.
6. US Pharmacist. Opioid pharmacology and considerations in pain management. Available at: <http://www.uspharmacist.com/print.asp?page=ce/105473/default.htm>. Accessed November 20, 2007.
7. Ives TJ, Chelminski PR, Hammett-Stabler CA, et al. Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. *BMC Health Serv Res.* 2006;6:46.
8. Edlund MJ, Steffick D, Hudson T, Harris KM, Sullivan M. Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. *Pain.* 2007;129(3):355-362.
9. Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, et al. Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. *JAMA.* 2003;289(18):2370-2378.
10. Fishbain DA, Rosomoff HL, Rosomoff RS. Drug abuse, dependence, and addiction in chronic pain patients. *Clin J Pain.* 1992;8(2):77-85.
11. Bozarth MA. Drug addiction as a Psychobiological process. Available at: <http://wings.buffalo.edu/aru/ARUreport04.html>. Accessed December 18, 2007.
12. Webster LR, Dove B. *Avoiding opioid abuse while managing pain.* North Branch, MN: Sunrise River Press, 2007.
13. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain.* 2005;113(1-2):9-19.
14. Katz NP, Adams EH, Chilcoat H, et al. Challenges in the development of prescription opioid abuse-deterrent formulations. *Clin J Pain.* 2007;23(8):648-660.
15. Alpharma submits new drug application for EMBEDA. Available at: <http://www.alpharma.com/pages/getpage.aspx?id=4C60605D-ACC5-4A41-85A8-1CC948BC4039>. Accessed March 12, 2008.
16. Friedmann N, de Kater AW, Butera PG, et al. Remoxy, a novel drug candidate, deters oxycodone abuse in humans [abstract]. Paper presented at 3rd International Congress World Institute of Pain, September 21-25, 2004; Barcelona, Spain.

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