
Chronic Pain Management With Opioids in Patients With Past or Current Substance Abuse Problems

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Among patients who present to medical providers with chronic pain complaints, there is an elevated prevalence of illicit substance use and prescription misuse. For those with legitimate pain, this predicament potentiates the risk of being medically underserved or undertreated. Complicating factors include a lack of specificity and sensitivity to the issue of defining substance abuse or misuse in the health care setting. Irrespective of whether patients have histories of addiction, problematic behavior manifests during the course of chronic

pain therapy, making a conceptualization of the nature and function of this behavior difficult. The objective of this article is to highlight known confounds in the assessment of “normal” pain-related vs. substance abuse behavior. Our aim is to offer important points to consider, a set of systematic guidelines to follow, and an armamentarium of essential tools to facilitate contingency management planning in the context of treating chronic pain with controlled substances.

KEY WORDS: Chronic pain management, substance abuse, pseudoaddiction, opioid therapy, controlled substances.

INTRODUCTION: THE EPIDEMIC OF UNDERTREATED PAIN

Nearly one third of the US population has experimented with illicit drugs, and substance use disorders are estimated to have a base rate of 6% to 15%.¹⁻³ In the year 2000, more than 4 million Americans used prescription medication for nonmedical purposes. Due to the high prevalence of illicit substance use and heightened national concerns about prescription misuse, the manner in which clinicians approach chronic pain treatment is often compromised.⁴ The effect of this compromise is most salient for patients who have current or past histories of substance abuse and progressive life-threatening or life-compromising disease. These individuals frequently present with numerous physical and psychosocial issues that bear import on medical treatment generally and pain and symptom management specifically. Many physicians and midlevel practitioners do not specialize in issues of addiction and may encounter substantial difficulty in their effort to treat these patients effectively and compassionately. The fact that there exists a lack of specificity and sensitivity to the issue of defining substance

abuse or misuse in the chronic pain medical setting results in an unclear treatment approach. Irrespective of whether patients have bona fide histories of addiction, problematic behavior can become manifest during the course of chronic pain therapy, making a conceptualization of the nature and function of this behavior difficult for the practicing clinician.

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It is toward providing a more sophisticated understanding of these issues that this article will focus. One of the factors that has the most detrimental effect on pain management in this country is the undertreatment of pain due to opiophobia.⁴ *Opiophobia* defined refers to the fear experienced by prescribing clinicians of the processes and consequences of prescribing opioid analgesics.⁵⁻⁷ It is believed that opiophobia may stem from multiple concerns including apprehension about “opening the door” to abuse, incurring regulatory and legal sanction, inducing respiratory depression in vulnerable patients, and ultimately establishing a diagnosable addiction problem.⁸

While it is estimated that approximately 3% to 16% of patients with chronic pain are (psychologically) addicted to opioids, this statistic may not reflect the true base rate of addiction in this population due to the considerable diversity in patient samples and the many discrepancies or inconsistencies in the definition of addiction.⁹⁻¹¹ However, empirical data do suggest an elevated prevalence of general substance use disorders in the chronic pain population in the range of 0% to 40%, a statistic higher than previously reported.¹²⁻¹⁵ Consequently, there is greater potential for the inadequate treatment of pain if a patient has a history of substance abuse.¹⁶

In light of these issues, and in spite of the establishment of exemplary national guidelines for the treatment of cancer pain that one would think should foster confidence and specificity in pain treatment, both malignant and nonmalignant pain continue to be undertreated in the medical setting. Regarding cancer-related pain, it is estimated that 40% to 50% of patients with metastatic disease and 90% of patients with terminal illness experience unrelieved pain.¹⁷⁻¹⁹ In an effort to promote a clinically useful understanding of the potential role of vulnerability to abuse or misuse in the treatment of chronic pain with controlled substances, this article will examine relevant conceptual and clinical aspects of aberrant prescription medication use and illicit (herein referenced as the use of either drugs or alcohol) substance abuse or addiction. Furthermore, our objective is to clarify some issues that will assist clinicians in better differentiating the function of relevant clinical behaviors with the aim of improving the identi-

fication and treatment of acts of noncompliance ranging from the innocuous to the illegal.

THE CHALLENGE OF DEFINING ABUSE AND ADDICTION IN THE MEDICAL SETTING

Chronic opioid therapy has gained progressive acceptance among medical clinicians as an appropriate and effective method of pain management, not only for the treatment of malignant pain but also for nonmalignant pain.²⁰⁻²⁴ Despite growing acceptance, the use of chronic opioid therapy remains a controversial topic due to the possibility that some patients may be at an increased risk for developing opioid abuse or activating a premorbid or latent addiction associated with the use of other substances.¹¹ Therefore, while prescribing or dispensing chronic opioids, it is essential that particular attention is paid to the assessment of a patient's clinical outcomes such as degree of pain relief, level of psychosocial and physical functioning, extent of medication side effects, and the presence of potentially problematic substance use behavior.^{25,26}

The challenges encountered in attempting to identify a substance use disorder or related problem among medical patients arise because the definitions of abuse and misuse have been, perhaps, erroneously extracted from observations of the population of individuals without medical illness and inappropriately applied to the population of individuals with medical illness. Clarification of terminology and concepts, as well as population-specific investigation, is therefore crucial to facilitating the accurate diagnosis and management of abuse or misuse of substances in the medical setting.^{27,28}

Definition of Terms

Because there is a great deal of semantic and theoretical confusion regarding the terms and constructs of interest, in the following exposition, they are operationally defined in Table 1.

Pseudoaddiction

As previously mentioned, a host of studies provide compelling evidence that pain is undertreated among the medically ill.¹⁷⁻¹⁹ In addition, clinical experience suggests that the inadequate management of chronic pain and related symptoms may serve to motivate or maintain aberrant substance use behavior. Pseudoaddiction is one term used to delineate the manifestation of distress and medication-seeking behavior of in-

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Table 1
Differentiation of Relevant Terms⁶⁰

Term	Definition	Utility
Substance abuse/addiction	A primary, chronic, neurobiological condition with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by the emergence of psychological abuse and/or dependence (<i>DSM-IV</i> criteria) and includes 1 or more of the following: craving, impaired control, compulsive use, overuse, and continued use despite harm. Behaviors of addiction lead to life interference and distress and are characterized by a loss of emotional and/or behavioral control.	Very useful construct that involves the important tenet of "use despite harm." Chronic pain management must comprise clear treatment planning and extensive monitoring and follow-up.
Substance misuse; aberrant, problematic, compulsive, or impulsive use of substances	The intentional use of a medication characterized by overuse or use to achieve a desired psychic effect (eg, change in affect or mood) in the absence of physiological dependence. Those who exhibit aberrant medication-taking behavior by using prescriptions other than as prescribed, in response to negatively valenced emotion, or to improve chronic boredom, often have comorbid personality disorders.	Potentially useful construct whereby use may involve experimentation or criminal diversion. Behavior must be monitored closely, and patients may require psychiatric referral and follow-up concomitant with pain management.
Pseudoaddiction	A term used to describe problematic substance use behaviors that may be comparable to the behavior of addiction but that are motivated by unrelieved pain. Patients who are undertreated may "clock-watch," become focused on obtaining medication, and otherwise seem to engage in inappropriate "medication-seeking" behavior. Behavior such as illicit substance use and deception can even occur in a patient's effort to obtain relief. Pseudoaddiction can be distinguished from true addiction when the problematic behavior resolves because pain is perceived satisfactorily or adequately treated.	Potentially useful construct whereby the diagnosis is made after effective medication therapy is delivered.
Physiological tolerance	A state of physical adaptation to a medication involving a reduction in the desired effect of a stable dosage or to the need to increase the dosage to garner an equivalent effect to that previously achieved. Tachyphylaxis is the term used when this process happens quickly.	Not useful for determining substance use disorders because all patients may experience this physical state.
Physiological dependence	A state of physical adaptation to a medication composed of the emergence of withdrawal symptoms when a medication is tapered without adequate titration (ie, on abrupt cessation, rapid dose reduction, decreased blood level, and/or administration of an antagonist). Physical dependence is not a clinical problem when patients are tapered appropriately.	Not useful for detecting substance use disorders or addiction because all patients may experience this physiological state.
Opiates versus opioids	Chemicals derived from natural versus synthetic sources, respectively	—

dividuals with unrelieved pain.²⁹ Pseudoaddictive behavior may be comparable in form to the behavior of true addiction. However, the hallmark feature of this syndrome, and the characteristic that makes it quite distinct, is the cessation of aberrant behavior on achieving adequate pain relief.^{27,30}

The clinical differential between addiction and pseudoaddiction presents numerous challenges to the practitioner in the assessment of individuals with known substance abuse and comorbid medical illness. Clinical reports indicate that aberrant behaviors evoked by unrelieved pain may be so adverse that pa-

tients with past substance abuse return to using illicit substances as a method of coping with the stress of intolerable levels of pain. Other patients who engage in less blatant patterns of behavior, however, are the ones who present the greatest challenge to practitioners and raise the strongest concerns about the presence of true addiction. It is important to note again that while it may be apparent that behavior associated with illicit substance abuse and prescription misuse are equally aberrant, the intent or function of these behaviors may be difficult to discern in the context of unrelieved pain symptoms.^{27,30}

Differentiating Aberrant Substance Use Behavior: True Addiction Versus Pseudoaddiction

While assessing the degree of aberrancy of given substance use behaviors, it is also necessary to remain cognizant of the fact that these behaviors exist along a continuum of severity, from less aberrant (such as aggressive requests for medication) to more aberrant (such as injecting oral medication). Furthermore, they may vary in function (behavior motivated by a desire to achieve a change in a mood state such as euphoria versus to reach a state of relief from refractory pain) as well as form (behaviors that are overt or apparent versus those that are covert or surreptitious). Classification of these questionable behaviors as representative, or not, of the social or cultural norm presupposes a degree of certainty regarding the parameters of what defines normative behavior. In the area of prescription medication utilization, there are no empirical data defining these parameters. Illustrating this point, if a large proportion of patients were to be observed engaging in a specific behavior, the behavior could be illness specific and therefore normative of the particular population from which observations are drawn. Consequently, it is critical that judgments concerning aberrancy should be examined and considered contextually, that is, on the basis of their corresponding population reference points.^{27,30}

A study performed at Memorial Sloan-Kettering Cancer Center revealed that 26% of cancer patients admitted to borrowing anxiolytics from a family member at some time during the course of treatment.³¹ The high incidence of this prescription-borrowing behavior raises concerns about the predictive validity of a characteristically aberrant behavior as an index of the presence of substance abuse. Clearly, there is a need for empirical study to clarify the nature of prescription medication utilization among qualitatively different patient populations to guide the accurate conceptualization of the severity, function, and form of behaviors that are likely to manifest during chronic pain treatment.^{27,30}

The behaviors associated with abuse of illicit substances versus prescription medication are more clearly established in the addiction literature. Therefore, it is a much easier task for the clinician to apply these indices of addiction toward the understanding of patients with comorbid medical illness receiving concurrent pain therapy. Variables associated with the problematic use of substances are noted in Table 2 and

are founded on years of retrospective and prospective, experimental and quasi-experimental research. Of note, the relative reliability and validity of these variables are more established for some (age, socioeconomic status, gender, familial history) than others (race/ethnicity, marital status, educational level). Nonetheless, our efforts to manage coexisting illicit (or other) substance use problems are further guided by a variety of known behavioral and physical predictors of substance abuse, including those listed in Table 3. Clinicians working in the area of chronic pain management are advised to be sensitive to the presence of both psychological and physical complaints (eg, social anxiety, depression, sexual dysfunction) as well as to physical findings suggestive of the presence of current alcohol and drug use (eg, tremor, tachycardia, odor).

Disease-Related Variables: Additional Factors to Consider

Alterations in physical and psychosocial functioning caused by medical illness and related treatment may parallel those produced by long-term substance abuse behaviors and serve to further confound the establishment of a common practice of defining addiction in the medical care setting. In this regard, it may be particularly complicated to assess one of the most critical variables in the diagnosis of addiction, that is, "use despite harm." For example, it is often difficult to discern problematic substance use behavior among patients who develop social withdrawal or cognitive change after brain irradiation for metastases. In this instance, even if impaired cognition is clearly related to adverse prescription medication use, this effect might only represent an attempt to reach a narrow therapeutic window of pain relief rather than to attain a desired psychic effect.^{27,30} In addition, in situations in which disease and pain have severely limited psychological, social, and vocational or physical functioning, it can be difficult to ascribe harm secondary to particular substance use behaviors in the context of pervasive dysfunction. Further demonstrating this point, the presence of a symptom such as mild mental clouding may be insignificant when compared to other outcomes such as noncompliance with prescribed therapy and engagement in those behaviors that compromise relationships with friends and family members, physicians, and other allied health care professionals and are secondary to chronic substance abuse.^{27,30} To accurately conceptualize the nature of substance-related behavior among medical patients, detailed information is

Table 2
Correlates and Suspected Risk Factors for Addiction to Illicit or Other Substances (ie, Drugs and Alcohol)^{61,62}

Gender	More common among men than women; differences in prevalence and incidence are attributed to a number of variables including societal standards, cultural norms, body size, metabolism, presence of comorbid psychopathology, history of trauma, other life events, and so forth.
Age	Higher among younger people (adolescents and young adults), lower among older adults; prevalence may be reduced with age because of increase in remission or decrease in survival rates; reduced tolerance with age or willingness to disclose; period, age, or cohort effects
Race-ethnicity	Prevalence and incidence rates of substance use by racial-ethnic group are very complex; findings are not yet conclusive here
Family history	Substance use disorders and problems cluster in families; study is under way as to the role of genetic transmission versus environmental factors
Employment status	Unemployed versus employed people exhibit higher rates of problematic substance use; prevalence also differs by type of occupation, with higher rates noted among blue-collar jobs or those lower in socioeconomic status
Marital status	Higher rates of substance use problems are evident among people who cohabit but have never been married or those in unstable marriages; in addition, cohabitating women may exhibit an elevated risk as do partners of those who evidence problematic use
Educational level	Failure to meet educational goals is associated with elevated risk for substance use problems

Note: The association between these factors may be bidirectional and reflect a correlational, not necessarily causal, relationship.

Table 3
Behavioral Predictors of Addiction to Illicit or Other Substances^{61,63}

Presenting Complaints That Are Red Flags for Alcohol and Other Substance Use Problems	Physical Findings Suggestive of Alcohol and Other Substance Use Problems
Frequent absences from work or school	Mild tremor
History of frequent trauma/accidental injuries	Odor of alcohol on breath or marijuana on clothing
Depression or anxiety	Nasal or conjunctival irritation (suggestive of cocaine insufflation or exposure to marijuana smoke, respectively)
Labile hypertension	Labile blood pressure (suggestive of alcohol withdrawal)
Gastrointestinal symptoms	Enlarged, tender liver
Sexual dysfunction	Tachycardia and/or cardiac arrhythmia
Sleep problems	"After shave/mouthwash" syndrome (to mask the odor of alcohol)

required concerning the role or function of substances in a patient's life across multiple domains in personal functioning (ie, social, physical, recreational, emotional, cognitive, etc).

Refinements in the Conceptualization of Substance Abuse and Misuse in the Medical Setting

Various definitions of substance abuse that embody the phenomenon of physical dependence or tolerance as defined in the *DSM-IV*³² (Table 1) are not wholly applicable to patients who receive potentially abusable medication for legitimate medical purposes. In this

case, development of the physiological states of dependence or tolerance is well within the norm of clinical expectations. Nonetheless, a differential diagnosis should be explored if questionable behaviors occur during chronic pain treatment. True addiction is only one of several possible explanations for the development of these physiological states and is most likely evident only when other behaviors (such as multiple unsanctioned dose escalation or the receipt of opioids from multiple prescribers) are present. Examples of specific behaviors predictive of prescription medication abuse or misuse are listed in Table 4.

Again, keep in mind that the differential diagnosis of pseudoaddiction must be considered if patients report

Table 4
Behavioral Predictors of Addiction to Prescription Medication^{21,32,64,65}

Behaviors More Predictive	Behaviors Less Predictive
Use of prescription medication in an inappropriate manner (eg, cutting time-release preparations; injecting oral formulations, chewing, or otherwise misusing transdermal fentanyl; stealing or "borrowing" medication from another person; multiple unilateral dose escalations despite warnings from clinicians)	Aggressive complaining
Obtaining medication from a nonmedical source	Drug hoarding when symptoms are milder
Repeatedly requesting dose increases or early refills despite the presence of adequate analgesia	Requesting specific drugs
Illicit or inappropriate prescription use behavior (eg, selling or forgery, multiple episodes of prescription "loss," or prescription-seeking behavior without the permission or knowledge of current clinician or following warnings to desist)	Acquisition of drugs from other medical sources
Continual resistance to changes in therapy despite clear evidence of adverse physical or psychological effects from the drug	Unsanctioned dose escalation once or twice in frequency
Concurrent alcohol or illicit drug abuse/positive urine or blood drug screens (ie, cocaine, opioids, amphetamines, barbiturates, PCP, marijuana, or alcohol, etc)	Unapproved use of the drug to treat another symptom
Objective evidence of substance-related deterioration in the ability to function at work, in the family, or socially (eg, repeated episodes of gross impairment or dishevelment)	Occasional impairment in personal functioning
Meeting <i>DSM-IV</i> criteria for substance abuse or dependence	Reporting psychic effects not intended by the clinician

distress secondary to unrelieved symptoms. For example, behavior such as aggressive complaints about the need for higher doses or occasional unilateral medication dose escalations may be an indication that a patient's pain is undermedicated. Uncontrolled substance use may also indicate the existence of another psychiatric disorder, the accurate detection of which may have beneficial therapeutic implications. For example, patients with borderline personality disorder may be categorized as exhibiting aberrant substance use behavior when they use prescription medication to communicate to others (knowingly or unknowingly) something about the level of their emotional distress or to alleviate chronic boredom. Similarly, patients who use opioids to self-medicate symptoms of anxiety, depression, insomnia, or problems with adjustment may be classified as aberrant substance users. It is important to note, however, that problematic behavior associated with prescription medication use infrequently represents criminal intent, as evidenced by reports of pain with the intention of selling or diverting.

CONCERN FOR THE ABUSE OF PRESCRIPTION ANALGESICS IN THE REGULATORY SETTING

Within the past decade, the introduction of new drug delivery systems has resulted in important ad-

vances in pain treatment. Implantable pumps, transdermal patches, and controlled release formulations, for example, have dramatically improved the lives of millions of pain patients. According to the Drug Enforcement Agency (DEA), between 1990 and 1997, the number of C-II substances approved for medical use increased from 300 to more than 400, with about 75% of new drugs classified as analgesics.³³ Unfortunately, the DEA also reports that diversion, theft, trafficking, and abuse of opioid analgesics have been rising along with their increased medical use.

By definition, all controlled substances have some potential for abuse. Most prescription pain medications, particularly C-II and C-III narcotic drugs, have a high potential for abuse. As a result, these drugs are in great demand on the street where they may sell for 10 times or more their retail cost. This sizable price differential between the retail cost and the street value attracts criminals and drug abusers who may pose as doctor shoppers, forge prescriptions, commit pharmacy theft, or engage in other unlawful activities to obtain drugs for their own use or for resale on the street.³⁴

Within the past several years, the development of more powerful sustained-release opioid analgesics has led to an increase in another, somewhat unique, form of drug-related criminal activity that has become known as the "patient-dealer." Unlike the doctor shopper who skillfully but fraudulently feigns illness, the patient-

dealer has a verifiable condition or pain syndrome that warrants treatment with potent analgesics. In a sense, the patient-dealer presents a double threat. First, because they tend to present with obvious conditions, patient-dealers arouse little or no suspicion in trusting practitioners when they ask for additional medication for increased pain complaints. For example, most chronic pain patients, particularly those with malignant pain, will experience "analgesic tolerance"—an expected and normal side effect of long-term opioid therapy. Because of this, or due to a progression in an underlying disease state, practitioners expect that they will have to increase dosing levels for such patients over time. Thus, when the patient-dealer makes a similar request, the practitioner is likely to honor it without question. But unlike the law-abiding patient who needs the additional medicine, the patient-dealer intends to redistribute the unneeded drugs to others.

A second threat posed by patient-dealers is their ability to visit multiple doctors to obtain excess medication for resale on the street. Without very much trouble, a patient-dealer with an apparent or verifiable serious condition warranting pain medication can seek treatment from several different practitioners at once, with each practitioner oblivious to the fact that his or her patient is receiving similar care from other practitioners. One successful patient-dealer, a terminally ill cancer patient in Maine, was indicted in 2001 for unlawfully distributing opioid analgesics obtained by establishing treatment relationships with multiple practitioners. While the exact number of practitioners this patient-dealer visited on a regular basis was not stated in the public record (because, presumably, they were not at fault), the indictment revealed that the defendant was earning an average of \$8000 per week selling OxyContin, a sustained-release form of oxycodone that, according to media accounts at the time, was selling for \$1 per milligram on the street.³⁵

Unlike the doctor shopper who is a fraud and has no illness or pain but is expert at feigning symptoms to deceive practitioners into providing drugs for resale on the street, the patient-dealer in all cases has an actual and verifiable condition requiring treatment. By secretly visiting additional practitioners, or untruthfully reporting an escalation of pain for the purpose of receiving additional medication, the patient-dealer is able to acquire sizable amounts of controlled substances. Given the unique and peculiar nature of this enterprise, regulatory and law enforcement communities are unable to estimate its scope, much less prevent its occurrence. While there are due diligence procedures recommended for detecting or deterring the doctor shopper, at present there are no similar proce-

dures to detect or deter the patient-dealer. States with prescription-monitoring programs appear, at least anecdotally, to have reduced levels of doctor shoppers and patient-dealers. However, these programs are still defeated by professional criminals who use fraudulent identification and pay cash for their services and drugs.

Of additional concern for today's pain management practitioner are past or present substance abusers who, as a group, tend to have higher accident rates and other abuse-related trauma injuries leading to chronic pain conditions.³⁶ These patients can be successfully treated for pain if they work closely with practitioners in a treatment alliance or structured relationship that takes into account their special status. Several years ago, in an effort to allay practitioners' fears when using controlled substances for treating chronic pain, the US Federation of State Medical Boards (FSMB) issued guidelines specifically aimed at helping doctors safely manage the high-risk pain patient.³⁷ The FSMB guidelines describe the high-risk pain patient as someone with chronic pain who is a past or present substance abuser.³⁷ As would be expected, treating such patients requires additional precautions and vigilance. The FSMB recommends using written treatment agreements to establish a therapeutic alliance between the high-risk patient and the practitioner. According to the FSMB, the agreement should set forth explicit performance expectations and requirements to ensure the patient's compliance with the treatment plan. The FSMB asserts that written treatment agreements will not be applicable in all cases but particularly for those involving high-risk patients as a means toward reducing drug diversion. Moreover, the use of a written treatment agreement may protect a practitioner from excessive regulatory scrutiny if a patient is found to be diverting prescribed medications. While practitioners are not expected to act as police detectives, or take extraordinary means to regulate patient behavior, they are expected by virtue of their federal and state licensing status to exercise professional due diligence in prescribing controlled substances for all of their patients, including those considered to be at a high risk for diverting drugs.

To measure substance abuse, the federal government established a system about 30 years ago, called the Drug Abuse Warning Network (DAWN), which is currently managed by the Department of Health and Human Services. DAWN was originally designed to track hospital emergency department admissions for drug-related overdose conditions and currently monitors admissions data in a representative sample of about 500 participating hospitals in 21 metropolitan areas. DAWN data do not reflect the prevalence of drug abuse in society as a whole but only the frequency of drug-related

DAWN ED Mentions* for Analgesics and Analgesic Combinations 1996 to 2001

DRUG	1996	1997	1998	1999	2000	2001
Codeine	1208	1033	1420	894	1155	930
Acet/codeine	5907	6598	5049	3845	3849	2641
Fentanyl	34	203	286	337	576	710
Hydrocodone	1574	904	1907	2074	2240	2214
Acet/hydrocodone	9845	10667	11686	13043	17538	19058
Hydromorphone	609	604	937	1313
Meperidine	806	731	495	512	706	519
Methadone	4129	3832	4810	5426	7819	10725
Morphine	864	1299	1954	2213	2478	3403
Oxycodone	100	372	1034	1804	3792	11100
Acet/oxycodone	2839	4353	3841	4503	6637	7190
Aspirin/oxycodone	251	287	335	121	396	119
Propoxyphene	1065	1166	1109	816	593	684
Acet/propoxyphene	4822	5337	4714	4816	4891	4675

Relative Standard Error (RSE) > 50%, data suppressed

Figure 1. Drug Abuse Warning Network (DAWN) data: emergency department mentions.⁶⁶

*Mentions include any formal reports on record regarding overdose of opioid narcotics requiring an emergency room visit at participating institutions. This includes, but is not limited to, intentional and/or accidental overdose and use of concomitant medications with opioids that synergistically may have intentionally or unintentionally resulted in an overdose.

emergencies and the substances mentioned by patients admitted for such emergencies. Despite this and other limitations, DAWN data may be useful for the practitioner and regulator alike in helping to identify specific types of drugs more likely to be encountered in emergency overdose situations. In fact, state and federal policy makers often consider DAWN data when crafting regulatory and penal laws or when designing drug-abuse prevention strategies.

In addition to using the written treatment agreement, practitioners with high-risk pain patients should consider prescribing medications with relatively low levels of abuse potential. The government's DAWN database, while not a precise indicator of drug abuse prevalence in the general population, is a useful guide for choosing drugs with relatively low abuse potential. Figure 1 provides DAWN data for selected opioid analgesics commonly used in chronic pain treatment. It is important to note in Figure 2 that following a period of decline from 1990 to 1996, the abuse of opioid analgesics increased rapidly over the next 6 years.

According to DAWN, the mentions of prescription analgesics in emergency department admissions for drug-related overdoses doubled between the second half of 1997 and the first half of 2002.³⁸ For the purpose of clarification, "mentions" include any formal reports on record regarding overdose of opioid narcotics requiring an emergency room visit at participating institutions. This includes, but is not limited to, intentional

and/or accidental overdose and use of concomitant medications with opioids that synergistically may have intentionally or unintentionally resulted in an overdose. Close examination of DAWN data in Figure 1 suggests that most abuse occurs with a relatively small number of drugs and specific formulations. Figure 3 illustrates DAWN's reformatted abuse data to show the frequency of mentions for selected opioid analgesics as a percentage of all narcotic analgesics mentioned in the database for the years indicated. As is demonstrated, 3 drugs—hydrocodone, oxycodone, and methadone—accounted for more than half (51%) of all the DAWN mentions of narcotic analgesics in 2001.

Knowing which opioid analgesics account for the majority of mentions in the DAWN database can be informative for the practitioner and pharmacist concerned about diversion and abuse. Taking into account these data, along with the predictors noted previously (Tables 2 and 3), practitioners may be better equipped to deter or detect the rare patient who is attempting to obtain drugs by fraud. While the numbers of such patients remain remarkably low, the social damage that even a few can cause is significant. A recent report by Florida medical examiners of 5816 drug-overdose deaths in 2002 revealed that prescription drugs outpaced illegal drugs by a 2-to-1 margin as the cause of death. The principal prescription drugs identified in this study were benzodiazepine, hydrocodone, oxycodone, and methadone.³⁹ Not surprisingly, the

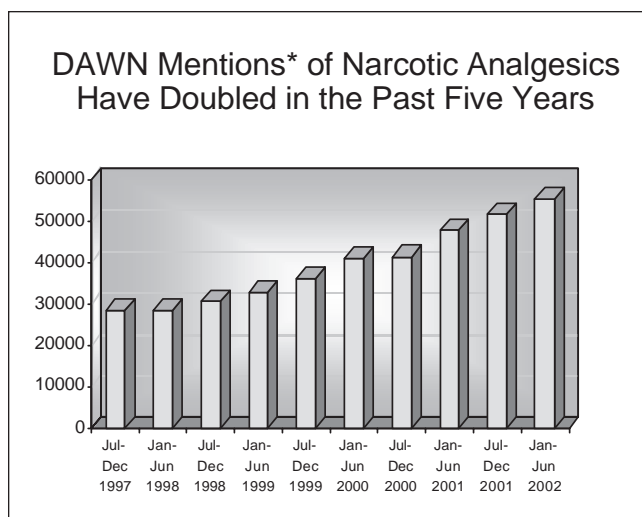


Figure 2. Drug Abuse Warning Network (DAWN) data: narcotic analgesic use mentions.⁶⁷

*Mentions include any formal reports on record regarding overdose of opioid narcotics requiring an emergency room visit at participating institutions. This includes, but is not limited to, intentional and/or accidental overdose and use of concomitant medications with opioids that synergistically may have intentionally or unintentionally resulted in an overdose.

opioids noted in the Florida report, namely, hydrocodone, oxycodone, and methadone, were cited as the top 3 most frequently mentioned drugs in the DAWN hospital admissions data for 2001 (Figure 1).

Perhaps the most promising development in the past several years has been the growing alliance between

practitioners and regulators, as they begin to see their missions—protecting health and safety—as compatible interests. The adversarial relationship between the medical and regulatory communities that existed for most of the past century has given way to a new, cooperative relationship that seeks to reduce the diversion and abuse of drugs while ensuring that patients in need are adequately treated for their conditions. In October 2001, the DEA and some 21 health care organizations, including the American Medical Society, the American Pain Society, and the American Pharmaceutical Association, issued a “consensus statement” on the use of controlled substances. The following statement expresses the concept of collaboration between these 2 important groups: “Preventing drug abuse is an important societal goal, but there is consensus, by law enforcement agencies, health care practitioners, and patient advocates alike, that it should not hinder patients’ ability to receive the care they need and deserve.”⁴⁰

In addition to the above, a team of researchers recently reported that “the attitudes and practices of medical boards toward physicians’ practice of prescribing opioids have changed for the better over the last several years.”⁴¹ This team surveyed 38 medical boards and found that “opioid quantity as a marker of questionable practice”⁴¹ no longer prevails and that, instead, medical boards are more inclined to look at whether the practitioner has “appropriately evaluated the patient, prescribed consistent with board guidelines, and appropriately documented their prescribing.”⁴¹

Figure 3. Drug Abuse Warning Network (DAWN) data: trends in opioid analgesic use mentions.⁶⁸

*Mentions include any formal reports on record regarding overdose of opioid narcotics requiring an emergency room visit at participating institutions. This includes, but is not limited to, intentional and/or accidental overdose and use of concomitant medications with opioids that synergistically may have intentionally or unintentionally resulted in an overdose.

Drug	1994 Total Mentions (est.)	1994 Total DAWN Narcotic Mentions	Ratio of 1994 Mentions to Total DAWN 1994 Narcotic Mentions	2001 Total Mentions (est.)	2001 Total DAWN Narcotic Mentions	Ratio of 2001 Mentions to Total DAWN 2001 Narcotic Mentions	D of Ratio of Total DAWN Mentions 1994 v 2001
Codeine	9439	44518	21.2%	3720	99317	3.7%	- 17.5%
Fentanyl	28	44518	0.06%	710	99317	0.71%	+0.65%
Hydrocodone	9320	44518	20.9%	21567	99317	21.7%	+0.80%
Meperidine	925	44518	2.0%	665	99317	0.67%	- 1.33%
Methadone	3252	44518	7.3%	10725	99317	10.8%	+ 3.5%
Morphine	1099	44518	2.5%	3403	99317	3.4%	+ 0.9%
Oxycodone	4069	44518	9.1%	18409	99317	18.5%	+ 9.4%
Propoxyphene	6731	44518	15.1%	5361	99317	5.4%	- 9.7%

For their part, medical practitioners are becoming more knowledgeable about drug diversion and substance abuse. To complement this, regulators and regulatory policy, as illustrated by the above examples, are moving away from interventions based solely on chronicity and quantity of prescribing and are coming closer to understanding the complicated but vital role of the pain management specialist in treating patients with chronic pain. The end result of this collaboration is, of course, better patient care.

THE CLINICAL MANAGEMENT OF CONTROLLED MEDICATION

As mentioned thus far, disconcerting substance use behaviors are neither mutually exclusive nor totally overlapping and thus make a thorough psychiatric or psychological assessment vitally important to the successful categorization of these behaviors among individuals without a prior history of substance abuse and those with a history of substance abuse who are known, statistically speaking, to present with greater psychiatric comorbidity.^{27,31} Aberrant substance use among medically ill patients, with or without a prior history of substance abuse, represents a serious and complex clinical issue. Perhaps most difficult is the management of patients who are actively abusing illicit substances concomitant with medical therapy. The following guidelines apply irrespective of whether a patient is an active substance abuser, has a past history of substance abuse (is currently in a state of remission), or is not complying with the prescribed therapeutic regimen (is misusing prescription medication). The principles that follow are designed to help the practicing clinicians to establish structure, control, and close monitoring so that they can prescribe freely and without naiveté, prejudice, or an elevated risk of revocation of the license to prescribe.

Interdisciplinary Treatment: The Optimal Approach to Managing Chronic Pain

A multidisciplinary team approach, with an interdisciplinary focus (ie, collaborative, holistic/focused on the mind-body relationship, and embodying the tenets of the biopsychosocial model⁴²⁻⁴⁵) is recommended for the management of substance abuse and misuse in the medical care setting. Mental health professionals with specialization in the area of addiction are usually instrumental here given their expertise in developing and executing strategies for behavioral

management and treatment compliance. Unfortunately, these skilled professionals are not often readily available to clinicians working in private practice or other medical agencies. Therefore, it is beneficial for clinicians in independent practice to establish a collective of complementary practitioners in their geographical locale with whom they can refer patients for the purpose of receiving supplementary services for pain control and maintain a modicum of team-based support. Clinicians practicing in isolation can quickly experience feelings of anger, defensiveness, and frustration in relation to medical patients with chronic pain. Such feelings can unintentionally compromise the level and quality of health care and contribute to a perceived sense of alienation, hopelessness, and rejection felt on the part of the patient. Structured, interdisciplinary treatment (ie, to include addiction, behavioral medicine, rehabilitation medicine, social work, and/or psychiatry team members, etc) is the most effective approach toward facilitating staff understanding of each patient's needs, provides a forum for necessary venting and strategizing, and aids in the development and administration of efficacious and empathic interventions for optimizing pain control and minimizing aberrant substance use. Regular staff meetings can also help to establish both patient-specific and team-based treatment goals, facilitate consistency and confidence in the provision of services, foster patient compliance, and maximize the likelihood that clinical objectives are met.

The Important Elements of a Clinical Assessment

The first person to suspect problematic substance use, or to confirm a history of past or current substance abuse, should alert the entire medical team, thus beginning the process of interdisciplinary communication, assessment, and management.⁴⁶ Obtaining a very detailed history of the duration, frequency, desired effect, and function of problematic substance use is crucial (ie, in the practice of behavioral medicine, this is known as a functional analysis and reflects the assessment of the pros and cons of the target behavior in the long and short term). Too often, clinicians avoid directly asking patients about substance use, misuse, or abuse due to concerns that they might "put-off" the patient or risk "losing face" in the event that their suspicions are wrong. However, a direct, assertive approach to communication, with particular focus on employing active listening skills, is most likely to engender confidence and a favorable rapport with patients; the oppo-

site most certainly contributes to problems of treatment compliance, lack of treatment efficacy, and staff frustration. Empathic and candid communication is, by all means, the best approach to establishing a favorable working alliance. In tandem, the use of a comprehensive, graduated interview can be instrumental in reducing the common symptom of denial or resistance among patients as well as clinicians.

The funnel approach to graduated assessment begins the clinical interview with broad questions about the role of substances (eg, nicotine, caffeine) in the patient's life and gradually becomes more specific in focus (ie, moves toward a discussion about the use of illicit substances or prescription misuse). Such an approach is also helpful for detecting the presence of a coexisting psychiatric disturbance or disorder known to significantly contribute to aberrant prescription medication behavior. For example, studies suggest that 37% to 62% of individuals with alcohol abuse or dependence have 1 or more coexisting psychiatric disorder, with anxiety, mood, and personality being those most commonly encountered.⁴⁷ The assessment and treatment of comorbid psychiatric or psychological disorder can greatly enhance medication adherence, behavioral modification plans, and reduce the risk of substance-related relapse among vulnerable individuals. Of note, the desired effects of illicit substances can also serve as clues as to the nature of the comorbid disturbance present (ie, drinking to quell panic, worry, or social anxiety symptoms; taking amphetamine to foster energy in the presence of depression, etc).

Development of an Interdisciplinary Treatment Plan: A Harm Reduction Approach

Substance abuse is most often a chronic, progressive disorder.⁴⁸ Therefore, the development of clear and thorough treatment goals is essential for chronic pain management involving pharmacologic intervention with controlled substances. During treatment, team members should not expect the abrupt cessation of substance-related problems among individuals who are so predisposed. The distress associated with attempts to cope with a life-threatening or life-compromising illness, coupled with the availability of potentially abusable prescription medication for symptom control, can make this goal or expectation unrealistic.²⁸ Rather, a harm-reduction approach should be employed with the aim of enhancing social support, maximizing treatment compliance, and containing further insult or injury through episodic relapse. The guidelines listed in Table 5 are recommended for the man-

agement of patients with a comorbid substance use disorder or history of substance-related problems.

Recommendations for Outpatient Medication Management

There are a number of strategies for promoting treatment compliance among patients in an outpatient medical setting. A written treatment agreement between the team and the patient provides structure to the treatment plan, establishes clear expectations about the roles of all involved, and outlines the consequences of aberrant substance use (both prescription and illicit). The inclusion of specifications for random, on-the-spot urine toxicology screens and/or serum levels in the agreement can be extremely useful in further maximizing treatment compliance. Expectations regarding attendance at scheduled visits and the management of a personal supply of medication should also be explicit. For example, a clinician may wish to limit the amount of medication dispensed per prescription and make renewals contingent on clinic attendance. In addition, it is helpful to solicit a patient's agreement to fill prescriptions at a single pharmacy and obtain his or her consent to share information with, or receive information from, retail pharmacists with particular attention to the fact that a controlled substance agreement is active and on file. While prescribing pain and other medication used for symptom control, the delivery of clear instructions about the parameters of responsible use is essential. This practice can help to reduce a clinician's hesitation to prescribe medication and optimizes the chance that patients will take their medication responsibly.

A clinician may also wish to consider recommending participation in a substance abuse program, with documented attendance a possible precondition for ongoing prescription treatment. With a patient's informed consent and apparent willingness, it is also recommended that a clinician interface with as many people as possible within his or her personal sphere (ie, sponsors, family, and friends) to inform them of the treatment plan to reduce the potential for stigmatization in relation to noncompliance and to engender necessary support.

In the unfortunate case whereby a patient is noncompliant with, or resistant to, the medication and other prescriptions for treatment following the multiple receipt of detailed expectations for behavioral compliance, it may be necessary to consider discharge. In this case, thorough discussion on the part of all treating parties involved should be initiated and then followed

Table 5
Managing Chronic Pain With Opioids: A Harm Reduction Approach⁶⁸

Step	Description
Step 1: Establish a working relationship and make clear your acceptance of the patient's subjective report of pain.	Focus on developing rapport with the patient. Use empathy, active listening, and nonjudgmental comments and body language.
Step 2: Use nonopioid therapies and behavioral interventions where possible but not as substitutes for appropriate pain control.	Consider anticonvulsants for neuropathic components of pain. Consider nonsteroidal anti-inflammatory drugs (NSAIDs) for swelling and muscle tension. Consider relaxation training, pacing, biofeedback, guided imagery, distraction, and so forth.
Step 3: Evaluate opioid use history.	Consider tolerance, routes of administration, duration of action, and medication side effect profile. Avoid undermedication, which can lead to attempts to self-medicate and other problematic behavior.
Step 4: Choose an opioid.	Consider the results of Step 3. Choose long-acting versus short-acting medication whenever possible. Limit rescue medication.
Step 5: Continually reassess the adequacy of your pain and symptom control plan with the patient and team members.	Document behavior and revisit issues on a regular basis. Reassess effectiveness of treatment regimen, being aware of need to avoid undertreatment. Evaluate whether the patient is engaging in other parts of therapy (ie, psychosocial interventions, physical therapy, prescribed NSAIDs, etc) and not just focusing solely on opioids.
Step 6: Know your opioids.	Stay apprised of the relative costs and trends of diversion and methods of concealment.

up with the patient. In some cases, the patient may be willing and able to engage in corrective action per the provision of detailed contingencies for his or her behavior (ie, "if you do this [desirable/undesirable behavior], then we will do that [consequence]"; here it may be beneficial to have the patient sign a formal agreement to capitalize on their commitment to reengage the therapy). This is, of course, an area where motivational interventions promoting the opportunity for reward or mastery experiences will yield the most favorable outcomes.⁴⁹⁻⁵¹ The decision to discharge must be handled sensitively and therapeutically as it will have both important ethical and legal implications.

Recommendations for Inpatient Medication Management

The management of a patient with substance use problems, who has been admitted to the hospital for the treatment of a life-threatening or life-compromising illness, must entail adherence to the guidelines listed for the outpatient setting. These guidelines aim to promote the important element of safety for patient and staff, contain or diminish patient behavioral problems, foster the appropriate use of medication, and communicate to patients that treating clinicians possess an understanding of, and facility with, pain and substance abuse management. As mentioned previously, the first point of or-

der is to discuss a patient's substance use in an open and direct manner. In addition, it is necessary to reassure the patient that concrete steps will be taken to avoid adverse events such as medication withdrawal. In specific situations, such as preoperatively, patients should be admitted to the hospital several days in advance for stabilization of a medication regimen. Also, it is important to provide a patient with a private room near the nurses' station to aid in monitoring and to discourage attempts to leave for the purpose of purchasing or otherwise obtaining illicit or unsanctioned substances. The treatment team should require visitors to check in with nursing staff prior to visitation because it may be necessary to search their packages to prevent patient access to substances. As a final point, the team may wish to consider collecting daily or random urine specimens for toxicology analysis and continually reassess all relevant aspects of pain and related symptoms.

Recommendations for the Management of Patients in Substance-Related Recovery

Pain management with patients who are actively engaged in recovery (ie, those maintaining continuous abstinence) presents a unique challenge to the practicing clinician. Depending on the structure of the recovery program (eg, Alcoholics Anonymous, methadone

maintenance), a patient may worry about ostracism from other program members or sponsors about their use of certain medications and may thus experience increased apprehension about susceptibility to relapse (ie, resumption of problematic use). Consequently, it is often helpful to inform patients of the difference between psychological and physical dependence and addiction and to explore the viability of nonopioid therapies. This may include consideration of referral to a specialty pain center to tailor a patient-centered treatment plan.⁵² Alternate therapies may include the use of nonsteroidal anti-inflammatory drugs, anticonvulsants (for neuropathic components), antidepressants, antiarrhythmics, biofeedback, electrical stimulation, neuroblative techniques, acupuncture, and behavioral management. If the pain condition warrants the prescription of opioids, care must be taken to provide adequate education, structure opioid use with signed agreements pertaining to their management, and, last, to solicit random urine toxicology screens and tablet/capsule counts. This may also be the optimal time to employ a longer acting medication with different route of delivery, such as transdermal fentanyl whereby the patient is required to return used patches prior to being issued a new prescription. If possible, attempts should be made as well to include the patient's recovery program sponsor and/or important family members and friends to garner their cooperation and aid in successful monitoring of the condition.

As with the provision of pharmacotherapy regimens, behavioral or contingency management approaches should be tailored to address the nature, function, and severity of substance abuse or misuse. Once again, fostering an environment of open and honest communication among all parties provides reassurance that guidelines are well established and will engender a focus on mutually expressed goals. In some cases, enforcement of these guidelines may fail to curtail aberrant substance use despite repeated intervention by staff. In the most recalcitrant of cases, discharge should be considered. In an outpatient setting, medically responsible practice at this point in time would involve the provision of appropriate guidelines and enough opioid medication (without option for renewal) to initiate a reasonable taper so as to prevent a patient from experiencing withdrawal. For obvious reasons, clinicians should engage all members of the treatment team including administrators in a discussion about the ethical and legal implications of such a decision and follow up with the patient as to the rationale for discharge or termination.

Recommendations for the Management of Patients Actively Abusing or Misusing Substances

Prescribing clinicians must aspire to monitor and control substance use among all patients in a manner that is consistent, relatively unbiased, and thoughtful. Sometimes, the major problem is patient compliance with medical treatment prescribed for an underlying disease state whereby the substance abuse actually shortens life expectancy by preventing the effective administration of primary (medical) therapy (ie, a patient engaging in intravenous heroine abuse with contaminated needles while increasing the risk of right-sided endocarditis or HIV disease). Treatment prognosis may also be moderated by the use of substances in a manner that negatively interacts with therapy or predisposes patients to other serious morbidity (eg, renal or liver dysfunction). The goals of health care can be very difficult to define when poor compliance and risky behavior appear to contradict a reported desire for the receipt of disease-modifying therapy.

Turning now to 1 of a set of potential solutions, urine toxicology screening can be a very useful tool to the practicing clinician for its diagnostic utility as well as for its stimulus value as a deterrent and monitoring mechanism for patients with an established history of abuse. However, recent work suggests that urine toxicology screens are employed infrequently in tertiary care centers.⁵³ In addition, when ordered, documentation tends to be vague about the rationale and often absent of concrete recommendations for follow-up. A recent survey found that nearly 40% of medical charts reviewed listed no reason for obtaining urine toxicology screening, and nearly 30% of the time, the ordering physician was unidentifiable.⁵³ Staff education efforts can help to address this apparent problem and may ultimately make urine toxicology screens a vital part of treating chronic pain in the medical care setting.

Facts That You Might Not Know About Toxicology Screening

One of the most important points to remember about toxicology screening is that tests are qualitative, not quantitative. A toxicology screen list is offered in Table 6 as an example and denotes the various opioid medications and their corresponding "cutoff" levels. A cutoff is defined as the level warranted to detect the presence of a given chemical.⁵⁴⁻⁵⁷ If, for a given substance, the value of a medication is measured below the cutoff,

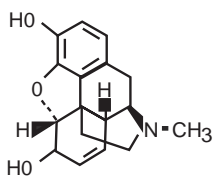
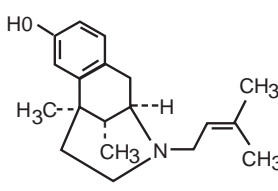
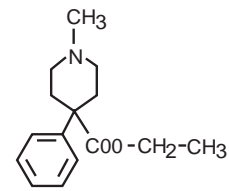
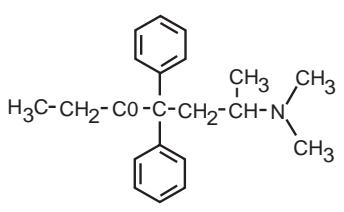
			
MORPHINE	PENTAZOCINE	MEPERIDINE	METHADONE
morphine codeine hydrocodone* hydromorphone* levorphanol* oxycodone* oxymorphone* buprenorphine* nalburphine butorphanol* naloxone* heroin (diacetyl-morphine)	pentazocine diphenoxylate loperamide	meperidine fentanyl sufentanil remifentanil	methadone propoxyphene
PROBABLE	POSSIBLE	LOW RISK	LOW RISK

Figure 4. Chemical classes of opioids.⁶⁹

Medication examples of each chemical class are listed below their prototypical examples. The likelihood of intolerance to a medication after not tolerating morphine is listed above for each chemical class as probable, possible, or low risk.

*These agents lack the 6-OH group of morphine, possibly decreasing cross-sensitivity within the phenanthrene group.

the results will be reported as “negative,” meaning that a particular chemical was not detected within the chosen cutoff range. If, for a given substance, the value is measured as equal to or above the cutoff, the results will be reported as “positive,” meaning that a particular chemical was detected. The concept of threshold is important to consider here because a patient’s urine screen result may be reported as negative when in fact the patient is taking a medication as prescribed for therapeutic purposes but the medication fell below the level of detection.

By way of example, if a patient is receiving a very low as needed (ie, prn) dose of oxycodone, the urine screen may be reported as negative, suggesting that the dose consumed was too low to be reported as positive, or that the urine was too dilute, or both. If the practitioner prescribing the oxycodone deems discussion (confrontation would be contraindicated) with the patient a necessary course of action due to concerns about diversion, it would be prudent to initially contact the laboratory and obtain the corresponding cutoff values used and quantitative report obtained for that test.

Table 6
Sample Urine Toxicology Screen
With Corresponding Cutoff Levels^{54,55}

Screen	Cutoff (ng/mL)
Amphetamine	1000
Barbiturate	200
Benzodiazepine	200
Cocaine	300
Opiates	2000
Cannabinoids	50
Methadone	300
PCP (phencyclidine)	25

A Case Example

A patient is receiving oxycodone 5 mg by mouth 4 times daily as needed (ie, oxycodone 5 mg po qid prn). A urine screen is completed and is reported as negative. When inquiring about the interpretation of this result with the laboratory, you are told that the cutoff for

opiates is 2000 ng/mL. At this point, you should ask the laboratory for the “actual” opioid value measured for the specific patient in question. If the measured amount was 1950 ng/mL, the laboratory would have reported the test as negative because it is below the 2000 ng/mL mark. Many laboratories use a rather high cutoff for opioids to limit the potential of a false positive result associated with the consumption of poppy seeds (eg, found on bagels). If a residual question regarding compliance remains, the practitioner could consider ordering a blood serum level, the complementary quantitative test that yields the amount of actual chemical present and can be theoretically calculated from a given oral dose.^{58,59}

Typical Chemicals Included in Toxicology Panels: Opioid Chemistry and Urine Screening

Urine toxicology panels do not often test for the presence of all opioids in a given screen but do include several classes of related chemicals. Although the screens and/or cutoffs may vary somewhat among laboratories, phenanthrenes (those chemicals listed in the first column of Figure 4) and a single phenylpiperidine (meperidine only) are the most common classes included in the standard urine toxicology panel. Medications that are not routinely tested include the diphenylheptanes (methadone, propoxyphene), other phenylpiperidines (fentanyl and its derivatives such as sufentanil, alfentanil, remifentanil), and benzomorphans (diphenoxylate, loperamide, pentazocine). It is important to note as well that although amphetamines are usually included in the standard panel, a negative urine test will not rule out usage of methylphenidate (Ritalin) or catecholamines (such as phenylephrine or pseudoephedrine). Consequently, these chemicals must be ordered separately.

Typical Questions

1. If a patient is receiving sustained release oxycodone (at low doses), the urine screen may not always be reported as positive. Why? One needs to consider the dose and manner in which the patient is taking the medication. It is possible that the amount excreted did not reach, or fell below, the cutoff level of 2000 ng/mL. Consider whether the patient used prn medication regularly or just prior to providing a urine sample. Inquire about the laboratory’s assigned cutoff level and make a definitive determination after obtaining the quantitative report. By way of example, if the laboratory’s cutoff is 2000 ng/mL and the patient’s actual quantitative measurement was 1999 ng/mL, the urine screen will be reported as negative.
2. If a patient is receiving fentanyl or methadone and is not using a breakthrough medication, then one should expect the results to be reported as negative. Why? A positive result would indicate that the patient is likely using other medications including those in the phenanthrene class and/or meperidine (a phenylpiperidine). Note that meperidine is generally the only phenylpiperidine identified in routine urine screens.

Action Recommended Following Test Interpretation: Contingency-Based Medication Management

As recommended previously, clinicians should clearly inform patients about all procedures and expectations (eg, “no-show/no-call” policy, required signature on treatment and controlled substance use agreements, random toxicology screening) for medication use during the period of prescribed enrollment in opioid treatment. In particular, matters pertaining to illicit substance use, the receipt of pain medication from multiple providers, requests for early refills, and/or the inappropriate use of medication should be strictly delineated and enforced in a written and signed agreement. By way of example, a policy pertaining to toxicology screening might, in part, read as follows:

If random, routine toxicology screening results are . . .

1. . . . positive for cocaine and/or heroin, then the clinic will appropriately discontinue opioid therapy and refer the patient to a treatment program. After successful completion of said program, and consistently negative random urine screens for more than 3 to 6 months, the patient may be reevaluated within the clinic for eligibility to receive long-term opioid therapy.
2. . . . positive for cannabinoids (ie, marijuana), nonprescribed otherwise legal opioids, amphetamines, barbiturates, and/or benzodiazapines, then the patient will be counseled during the visit and receive repeat urine toxicology screening (with 30 days lapse in time from date of last use). If the toxicology screen is positive a second time, then the clinic will discontinue opioid therapy, provide recommendations for the use of nonopioid treatment and substance-related referral, and refer the patient back to the primary care clinician with additional recommendations for future management.
3. . . . consistently negative (note here: 3 data points are required to determine an actual trend in behavior) fol-

lowing a history of prior positives with consequent action to discontinue opioids, then the clinic will resume opioid therapy with planned random medication screening to monitor future compliance.

4. . . . variably positive (for nonprescribed controlled substances as determined by DEA regulation), then this will be cause for discontinuation of opioid therapy and the provision of recommendations for non-opioid treatment for pain management.

In summary, if a patient consistently demonstrates behavior of addiction (eg, with the use of ethyl alcohol, opioids, benzodiazepines, or other substances), the clinic will recommend (1) cessation of opioid therapy with appropriate taper; (2) initiation of nonopioid therapy; (3) enrollment in, and successful completion of, a substance use treatment program; and/or (4) successive urine toxicology screens with negative results for a period of ≥ 3 to 6 months prior to reevaluation of candidacy for therapy with controlled substances. Recommendations are thus made on a case-by-case basis and are tailored to meet patients' individualized needs.

CONCLUSION: UNDERSTANDING THE RANGE OF ISSUES ASSOCIATED WITH THE PRESCRIPTION USE OF POTENTIALLY ABUSABLE MEDICATION

While the most prudent actions on the part of clinicians cannot obviate the risk of all aberrant substance use, we must recognize that virtually any medication that acts on the central nervous system and any route of administration has the potential for abuse. Herein, the problem lies not with the medication but rather is influenced by variables within and among the individuals taking them. The effective management of patients with chronic pain who engage in aberrant substance use necessitates a comprehensive treatment approach that recognizes the interaction between biological, chemical, social, and psychiatric or psychological aspects of substance abuse and misuse. Furthermore, treatment plans should provide the practical means to manage risk, target pain, and ensure patient and staff safety.

Treating medically ill patients who are experiencing chronic pain and substance-related problems is clearly complex and challenging because one sphere can significantly complicate the other. However, to provide treatment that maximizes the chance of favorable outcomes, substance use issues involving the presence of an elevated risk of abuse or misuse must be identified and managed directly. While previous studies have

shed light on the particular diagnostic meanings of various behaviors and have afforded clinicians the opportunity to recognize those that are truly aberrant, far too often clinicians are prejudiced in their perceptions of these behaviors due to anecdotal accounts of patient-related problems and to a lack of experience or confidence in prescribing controlled substances. Some behaviors (eg, occasional unsanctioned changes in dosage, requests for specific opioid medications) are universally judged as aberrant regardless of limited data substantiating their aberrancy or contribution to addiction, while other behaviors (multiple episodes of prescription "loss," borrowing medication from others) may not seem aberrant at face value but indeed may have predictive value for the development or presence of true addiction.

Without a doubt, the future holds several challenges regarding the state of pain management in medically ill patients with past or present histories of substance abuse or misuse. Data are needed to understand which aberrant substance-related behaviors are normative among the medically ill. These studies will likely need to target specific medical conditions to maximize our future clinical understanding. For instance, aberrant behavior common among cancer patients (such as increasing medication dose once or twice in frequency) may or may not be similar to those behaviors found in patients with other disorders such as sickle cell anemia or chronic lower back pain. In conclusion, we collectively call for future programmatic study involving epidemiological research on the nature, function, and form of the behavioral correlates of chronic pain among multiple disease categories and across varied patient populations, including those with comorbid substance abuse or related vulnerability.

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