The use and abuse of psychoactive substances are not unique to our country or century. People used hallucinogenic plants to achieve altered states of consciousness in prehistoric times, and psychoactive substances have been used in all eras and cultures. As Osler remarked, “The desire to take medicine is, perhaps, the great feature which distinguishes man from other animals.” 1 The human cost of substance abuse is high, and deaths secondary to the use of psychoactive substances are common. In the United States, illicit drug use results in thousands of deaths each year (Box 186-1).

A major barrier to appropriate recognition and treatment of substance abuse is the lack of a precise definition. The American Psychiatric Association defines it as a maladaptive pattern of drug use associated with some manifest harm to the user or others. 2 Physicians have a difficult time recognizing such abuse when up to 44% of emergency department (ED) patients report underlying chronic pain syndromes. 3 Chronic pain may not manifest the typical overt sympathetic changes or physical findings of acute pain. 5 Therefore, emergency physicians constantly walk a tightrope between undertreating legitimate pain and inappropriately rewarding substance abusers with controlled medications.

A variety of stereotypes come to mind in compiling the profile of a substance abuser. These stereotypes pose dangerous traps for the clinician. Physicians are likely to ignore the possibility of drug intoxication in the well-dressed businessman or in those at the extremes of age. Yet children may ingest psychoactive substances they find in homes where drugs are used.

Abuse of prescription and over-the-counter (OTC) drugs by adolescents is on the rise. According to the 2005 Partnership for a Drug-Free America’s 18th annual self-administered study of 7300 teenagers in grades 7 to 12, one in five (19%, or 4.5 million) report abusing prescription medications and one in ten (10%, or 2.4 million) report abusing cough medications to “get high.” This use is on par with or higher than the abuse of illegal drugs such as ecstasy and cocaine. 6 Dextromethorphan abuse has become epidemic in the last decade. Increasing numbers of teens are ingesting dextromethorphan-containing OTC products such as Coricidin HBP Cough & Cold tablets, 7 known on the streets as triple C, red devils, red C, red box, or skittles. Other dextromethorphan compounds include cough medicines, such as NyQuil and Robitussin DM, that provide the sought-after high known as the robo-buzz. Adolescents may also abuse medication used to treat obsessive-compulsive disorder and attention-deficit/hyperactivity disorder. Methylphenidate and related compounds have been a particular concern. Tablets can be abused orally, or they can be crushed and the powder injected or snorted. Despite its abuse potential, experts disagree about the extent to which methylphenidate is diverted from therapeutic use to abuse in preteens and adolescents. 8 In addition, some parents deliberately give psychoactive substances to their children to calm or to abuse them.

The emergence of “legal highs” has become a concerning trend. Numerous synthetic and naturally derived psychoactive substances are easy to obtain from Internet websites, “head shops,” and local suppliers. One such example is known as bath salts. These products are available in small quantities, with packaging that usually includes the disclaimer “not for consumption” to avoid regulation. 9 Bath salts contain synthetic cathinones, which are pharmacologically similar to methamphetamine and MDMA (ecstasy) and produce similar clinical effects. 10 A variety of adverse effects have been reported from cathinone derivatives, including tachycardia, hypertension, agitation, hyponatremia, hallucinations, paranoia, and suicide. 5-11 The legal status of bath salts is rapidly changing. The U.S. Department of Justice Drug Enforcement Administration has temporarily placed three of the synthetic stimulants under Schedule I of the Controlled Substances Act; however, numerous other synthetic cathinones have been found in these products. 7

The elderly also abuse substances, and geriatric patients may suffer new-onset psychosis as a result of sympathomimetic abuse or drug withdrawal. Drug use is frequent among pregnant women, resulting in both maternal and fetal morbidity. A study of an inner-city population reported that 19% of women had a positive urine toxicology screen for at least one of seven substances at the time of admission for delivery. 12 Manifestations of abuse may be acute, as in abruptio placentae or premature birth, or insidious, producing growth restriction and birth defects. Drug problems are more prevalent among the disadvantaged minority and lower socioeconomic groups. As a result, these groups are disproportionately affected by drug-related problems, such as incarceration, acquired immunodeficiency syndrome, and tuberculosis.

The Drug Alert Warning Network (DAWN) collects data from hospital EDs and medical examiners that include drug-related visits or deaths. The data consist of patients who abuse illegal drugs or use legal substances for a nonmedical purpose. According to DAWN, the drugs of misuse or abuse most commonly involved in deaths are cocaine, opioids, antidepressants, benzodiazepines, stimulants, and club drugs. 13 For 2005, DAWN estimated that 816,696 ED visits involved an illicit drug; cocaine was involved in 448,481, marijuana in 242,200, heroin in 164,572, and stimulants (including amphetamines and methamphetamine) in 138,950 ED visits. Other illicit drugs (phenycyclidine [PCP], ecstasy, and γ-hydroxybutyric acid [GHB]) were much less frequent. 14 Despite efforts to control nonmedical

**Perspective**

**Epidemiology**
use of prescription drugs in the United States, the estimated number of ED visits for nonmedical use of opioid analgesics increased 111% during 2004-2008 (from 144,600 to 305,900 visits) and increased 29% during 2007-2008. The highest numbers of these ED visits were recorded for oxycodone, hydrocodone, and methadone, all of which showed statistically significant increases during the 5-year period. The estimated number of ED visits involving nonmedical use of benzodiazepines increased 89% during 2004-2008 (from 143,500 to 271,700 visits) and 24% during 2007-2008. In 2008, the number of ED visits involving nonmedical use of prescription or OTC drugs matched the number of ED visits involving illicit drugs.18

Illicit drug use generates significant costs to the health care system. In 2001, the hospital and ambulatory care costs of illicit drug use as a whole were estimated at $1.34 billion. The cost for illicit drug–related skin and soft tissue infections alone was estimated to be more than $193 million.16 More recently in 2008, the cost of hospital days stemming from drug overdoses without alcohol involvement was estimated to be $737 million.17

PHARMACOLOGY

Knowledge of drug interactions assists in the diagnosis and care of substance abuse victims. A careful medication history for all legal and illegal drugs, including ethanol, may pinpoint the source of an adverse reaction. For example, a variety of agents can increase the effects of cocaine. The coingestion of ethanol and cocaine may result in an active metabolite, cocaethylene, that also enhances cocaine’s effects. Serum syndrome, manifested by muscle rigidity, hyperthermia, diarrhea, and seizures, may result when sympathomimetic drugs are taken concurrently with selective serotonin reuptake inhibitors such as fluoxetine. Amphetamines elevate serotonin either directly or by reversible inhibition of monoamine oxidase. In fact, a selective serotonin reuptake inhibitor can result in flashbacks in prior amphetamine users. Monoamine oxidase inhibitors can provoke hypertensive crisis in patients taking sympathomimetics. Interactions between medications commonly prescribed for patients with human immunodeficiency virus (HIV) infection and recreational drugs may be associated with serious clinical consequences because protease inhibitors and non-nucleoside reverse transcriptase inhibitors (NNRTIs) can inhibit or induce the cytochrome P450 system, which could result in either drug accumulation or toxicity or withdrawal reactions.19 For example, patients maintained with methadone who are subsequently treated with NNRTIs are at risk for development of methadone withdrawal by NNRTI-mediated enzyme induction.18

Household products and medications also have abuse potential. For example, dextromethorphan in common cough medications is converted into a substance (dextrorphan) similar to ketamine and PCP, which causes dissociative effects by antagonizing the N-methyl-D-aspartate (NMDA) receptor. Recreational users describe mild hallucinations and an “out-of-body” state.19 Some common chemicals in the home and workplace have an intoxicating effect that may be unexpected. Solvents, paint, lacquers, glues, aerosols, refrigerants, and other propellants (Fig. 186-1) are readily accessible for abuse among children and teens. Inhaled hydrocarbons, such as toluene, are rapidly absorbed and easily pass through the lipophilic blood-brain barrier to give an inexpensive high.

Illicit drug laboratories have poor quality control, and many drugs are combined or “cut” with other substances to increase profits. Up to 50% of street samples lack the alleged drug. Some additives, such as local anesthetics or sugars, may be innocuous, but others, such as strychnine, may be lethal. Levamisole, a widely available anthelmintic agent, is now a common cocaine adulterant and can result in life-threatening agranulocytosis, leukoencephalopathy, and cutaneous vasculitides.20 Other drugs, such as PCP, are misleadingly sold as a different drug, such as lysergic acid diethylamide (LSD). During the 1990s, many doses of purported ecstasy (MDMA) actually contained amphetamine drug mixtures or even simple caffeine or ephedrine.21,22 Drug combinations and unanticipated additives or substitutions may produce a clinical picture discordant with what the patient claims to have taken.

“Look-alike” drugs may also have toxic effects. Teens in particular may take look-alike or “knock-off” drugs that look like a desired product, such as Ritalin or Coricidin, in the hope of getting high, when in reality they may suffer unanticipated effects from an unrelated medication sold by an unscrupulous dealer. Teenagers can present with dystonias after unsuspectingly taking haloperidol instead of diazepam (each can have a “letter” inscribed in the middle of the pill).
**CLINICAL FINDINGS**

**History**

A drug history should be obtained from patients reporting drug reactions, acute anxiety or other psychiatric problems, and acute cardiopulmonary or neurologic symptoms. This information should include use of legal and illegal substances, prescription and OTC medications, vitamins, herbs, tonics, and potions. When it is appropriate, the physician should specifically ask if the patient is suicidal. A physician who is neutral and nonjudgmental in approach is more likely to obtain accurate information.

Parents should be asked what they believe their son or daughter took and when. The “street name” may be unfamiliar to the emergency physician; there are numerous websites available for reference information, such as [www.whitehousedrugpolicy.gov/pdf/street_terms.pdf](http://www.whitehousedrugpolicy.gov/pdf/street_terms.pdf). Regardless, there is no guarantee that the purported ingestant is pure or unadulterated; therefore, a careful examination may provide the most reliable clues about the exposure. Prehospital personnel, family members, and friends may be able to offer additional information. Patients who were brought from the scene of a club, “rave,” or circuit party with altered mental status may be under the influence of a club drug such as MDMA (ecstasy), GHB, flunitrazepam (Rohypnol), or ketamine. Other club drugs, such as Verve and Jolt, contain γ-butyrolactone (GBL) and are sold on the Internet as precursor molecules to GHB. These dangerous drugs are especially appealing to teens.

The RAFFT questionnaire may be useful in detection of substance abuse in adolescents. Each yes response receives a score of 1, and each no response receives a score of 0. The scores for the five questions are added together, and a RAFFT total score of 3 or more indicates that an individual needs further assessment.

- Relax: Do you drink/use drugs to relax, feel better about yourself, or fit in?
- Alone: Do you ever drink/use drugs while you are by yourself, alone?
- Friends: Do any of your closest friends drink/use drugs?
- Family: Does a close family member have a problem with alcohol or drugs?
- Trouble: Have you ever gotten into trouble from drinking or using drugs?

Injection drug abusers often have infectious complications, such as septic pulmonary emboli, skin or brain abscesses, endocarditis, and HIV-related disease. Wound botulism can also be a complication of injection drug use.

**Physical Examination**

Documentation of vital signs is essential. Temperatures are frequently neglected in violent or agitated patients, and external skin temperature can be misleading. Because rapid mouth breathing, dry mucous membranes, and agitation may produce unreliable oral temperatures, a rectal temperature can confirm suspected alterations in temperature. Patients should be undressed and completely examined, with particular attention paid to the skin, pupils, and mental status, and evaluated for signs of trauma. Needle marks and track marks may be found in unusual areas, such as the supraclavicular space.

Physical examination includes evaluation for specific toxic syndromes. The presence of diaphoresis, mydriasis, tachycardia, hypertension, abnormal mental status, and urinary retention suggests sympathomimetic toxicity. In comparison, the anticholinergic (antimuscarinic) syndrome has these same features with the exception of dry skin and mouth. Also, patients with antimuscarinic delirium tend to be less violent and paranoid than those with sympathomimetic toxicity. The mental status evaluation should address both the level of consciousness and appropriateness of affect. Specific physical findings, such as dental disease, skin abscesses, cardiac murmur, or focal neurologic abnormalities such as tremor or ataxia, can assist in identification of chronic drug abuse. Dental disease, with extensive caries, has traditionally been attributed to methamphetamine use, but it is common with other forms of chemical dependency. The skin provides important clues to substance abuse, such as residue of chemicals or drugs on the hand or face or track marks from injection drug use.

**DIFFERENTIAL DIAGNOSIS**

It is unreliable to assume that abnormal behavior or altered mental status in the unkempt young patient is due to drug intoxication. Many serious illnesses can be manifested as an overdose, including sepsis, meningitis, encephalitis, head trauma, unintentional poisoning (e.g., carbon monoxide), hypothermia, heatstroke, intracranial hemorrhage, complex seizures, and drug withdrawal. Hypoglycemia and other metabolic and endocrine derangements are important considerations. Similarly, drug intoxication should be considered in the differential diagnosis of altered mental status or abnormal vital signs regardless of age. Although patients with decompensated psychiatric disease can present similarly to those with drug intoxication, the hallucinations from psychiatric disease are usually auditory in nature, whereas hallucinations from drug intoxication or withdrawal tend to be visual hallucinations. Otherwise, the behavior and agitation associated with drug abuse can be similar to those of decompensated psychiatric disease.

**COMPLICATIONS**

Illicit drugs produce a wide variety of complications involving all major organ systems. Neurologic complications are especially prominent. Up to 10% of strokes are secondary to drug abuse. Cerebral infarction, cerebral and cerebellar hemorrhage, and subarachnoid bleeding are often secondary to use of cocaine and amphetamines and, occasionally, PCP or heroin. Single generalized tonic-clonic seizures are common with substance abuse, and status epilepticus can occur. Although sympathomimetics such as cocaine and amphetamines are responsible for the majority of seizures, heroin, tricyclic antidepressants, and PCP are high risk. Withdrawal from benzodiazepines and alcohol can also result in seizures, including status epilepticus.

The dangers of substance abuse extend far beyond the toxic effects of a particular drug. Associated hazards include HIV infection, not only secondary to injection but also from the promiscuous lifestyle associated with the drug culture. The prevalence of HIV infection in injection drug users is approximately 12 to 17%.

Recent declines in the incidence of HIV infection among injection drug abusers are encouraging, but resurgence has been associated with needle sharing and inadequate methadone treatment. Accompanying this phenomenon is a decrease in hepatitis B and hepatitis C among injection drug users in some U.S. cities. This is probably due to increases in preventive measures, such as needle-exchange programs, condom use, and vaccination for hepatitis B. Almost 20% of cocaine abusers have a positive tuberculosis skin test result. Sexually transmitted disease is common, especially in the sex-for-drugs culture of crack cocaine. Syphilis, in particular, is endemic among crack abusers.

The lungs are target organs for impurities in intravenous drugs, and pyrogens become trapped in this massive filter. This can produce “cotton fever,” characterized by high fever, tachycardia, and tachypnea 10 to 20 minutes after injection. This self-limited illness contrasts with the long-term restrictive and obstructive lung diseases with the prolonged intravenous abuse of methylphenidate. Right-sided endocarditis is a frequent sequela of chronic injection drug abuse, and the nonspecific influenza-like symptoms that accompany this disease can mislead the clinician. In addition
to endocarditis and HIV infection, injection drug abusers have septic pulmonary emboli, cellulitis, botulism, tetanus, and other infectious complications. They may have unusual sites of osteomyelitis or septic arthritis involving the spine or sternoclavicular or sacroiliac joints.

Psychiatric complications of substance abuse are frequent and include anxiety, depression, suicidal ideation, mood swings, paranoia, and panic attacks. Paranoia and depression and associated suicide attempts are common among stimulant abusers, and hallucinations of parasites under the skin (formation) are frequent in those addicted to amphetamine derivatives and cocaine. Symptomimetics are strongly associated with aggressive behavior and street crime. Traumatic injuries are endemic among substance abusers and arise from both assault and motor vehicle collisions. Psychedelic drugs, such as LSD and PCP, can prompt extreme behavioral changes that can in turn lead to traumatic injuries. On occasion, trauma can be occult, and the unwary physician may overlook a stab wound in a patient whose clinical picture is predominantly drug-induced agitation.

**DIAGNOSTIC ADJUNCTS**

All patients with acute alterations in mental status in whom hypoglycemia is possible require either a finger-stick glucose test or the empirical administration of 50% dextrose solution. Patients who are unstable or with altered mental status may need evaluation of electrolytes, blood urea nitrogen, and creatinine. The electrocardiogram will occasionally diagnose a myocardial infarction in patients with drug-related chest pain as well as changes specific to certain drugs and medications, such as prolongation of the QRS or QTc interval. A complete blood cell count is of little value, except to follow serial hemoglobin values if occult trauma or hemolysis is suspected. Arterial blood gas analysis may be useful in assessment of acid-base status as well as in measurement of oxygenation and ventilation. Rhabdomyolysis, most often seen with psychostimulant abuse or prolonged periods in the same body position after abuse of sedatives (e.g., barbiturates), is best detected by measurement of serum creatine kinase or myoglobin. Rhabdomyolysis is usually defined as creatine kinase levels more than five times the upper limit of normal, but absolute levels may not correlate with renal dysfunction. Dipstick urinalysis may screen positive for hemoglobin without accompanying red blood cells but is insensitive for this condition.

The use of qualitative toxicology screens is less important than the patient’s history and clinical status. Although unsuspected drugs may be detected on a urine toxicology screen, this knowledge rarely affects acute management of the patient. Quantitative levels of suspected substances, such as acetaminophen, acetylsalicylic acid, lithium, and certain anticonvulsants, may be valuable in certain circumstances. A new generation of rapid bedside “drug of abuse” urine toxicology screens may provide timely information, but their use requires further study. There are some special circumstances in which rapid qualitative urine toxicology screening may have some utility. For example, positive urine screens for sympathomimetics can occasionally be found in children presenting with bizarre or abnormal behavior or new-onset convulsions if they have been exposed to these substances in the home environment where they are being used or manufactured. These findings in older children may also assist parents in assessing changing behavior or school performance in some situations.

**MANAGEMENT**

**Agitation**

Few antidotes exist for psychoactive drug intoxication, and with a few notable exceptions, treatment is supportive. Violent or agitated patients require rapid sedation. Benzodiazepines such as lorazepam (Ativan) can best sedate patients with sympathomimetic symptoms, whether they are due to drug intoxication or withdrawal. For other patients, intramuscular or intravenous butyrophenones, such as haloperidol (Haldol) and droperidol (Inapsine), are rapidly effective and generally safe. Droperidol has a box warning from the Food and Drug Administration (FDA) for QT prolongation and potentially torsades de pointes. However, in September 2007, the FDA added a warning that “torsades de pointes and QT prolongation have been observed in patients receiving haloperidol, especially when the drug is administered intravenously or in higher doses than recommended. Haloperidol is not approved for intravenous use.” Most reported cases of butyrophenone-induced dysrhythmias have been in individuals receiving large doses for prolonged periods, such as hours to days, or in elderly populations (older than 60 years). These medications lack the respiratory depression potentially caused by other agents and may be beneficial in some cases when sedation is required. For these reasons, the butyrophenones remain safe and effective agents for treatment of drug-induced agitation. In cases of cocaine or methamphetamine toxicity, in which hyperthermia or convulsions have occurred or can occur, benzodiazepines may be preferred. Phenothiazines, such as chlorpromazine, are not generally recommended in the drug-intoxicated patient because of their strong anticholinergic effects and potential to produce hypotension and lower the seizure threshold.

**Body Packers and Stuffers**

The body *stuffer* swallows loosely packaged drugs, or the raw drug itself, in an attempt to conceal contraband during arrest. The body *packer* (a “mule”) delivers professionally packaged drugs in his or her intestinal tract, usually on a flight from another country. In many cases, these packets can be visualized radiographically.

There is considerable debate about the best approach to these patients. Some sources recommend activated charcoal for body stuffers and whole-bowel irrigation for body packers, but others adopt a less aggressive approach. In severe cases of body packing in which packet rupture occurs, surgical removal may be considered. In asymptomatic cases, the patient’s right to refuse care usually supersedes local laws for forcible removal of such evidence, but patients who are significantly confused from drug effects (or comatose) are incapable of refusing lifesaving interventions.

**Referral**

After acute medical issues have been managed, substance abusers should be asked whether they would like help in overcoming their addiction. Studies show that intervention may be most successful for abusers of heroin, nonprescribed methadone, and benzodiazepines. Users of crack cocaine appear to be more resistant to treatment. Offering symptomatic relief from withdrawal with short courses of medications including antiemetics, antidiarrheals, and benzodiazepines, when indicated, may improve the patient’s ability to sustain sobriety.

**Drug Seeker**

As the front line in medical care, EDs are frequently confronted by patients with drug-seeking behavior, typically for pain medication or benzodiazepines. Although only 1% of ED patients have a formally recorded diagnosis of substance abuse, as many as 27% of ED patients are actually in need of substance abuse treatment. This drug-seeking behavior is described as a compulsion for seeking and taking drugs after prolonged use of a certain drug. Although health care providers should not facilitate drug-seeking
behavior, inadequate pain management is internationally considered unethical.\(^4^4\) Drug diversion has also become an increasing problem. The street value of prescription opioids such as oxycodone is greater than that of marijuana and heroin.\(^4^5\)

Emergency physicians need to judiciously provide pain medication to avoid long-term problems from undertreatment of genuine acute pain. However, an overly liberal approach can contribute to addictive behavior. It is difficult for the individual health care provider to screen effectively for drug seeking or abuse on just a single encounter. Self-admission would be the easiest screen, but 90% of patients who abuse opioids deny it.\(^4^2\) Although it is not sensitive, a prior history of drug or alcohol abuse may identify patients at risk for abuse of opioids, the most commonly abused agents of the prescription drug seeker.\(^4^6\) Repeated visits for the same complaint, rapid dose escalation, unusual and multiple allergies, and demands for specific agents (often in specific milligram amounts) are all warning signs of potential drug seeking.\(^4^7\) Unfortunately, there is no reliable finding that can consistently identify drug seeking while not penalizing those in true need of analgesics.

In response to this problem, both individual hospitals and some states are starting to track patients who habitually receive opioid prescriptions.\(^4^8\) The effectiveness of such programs is not known. Some locales have had success with pain guidelines that restrict the use of opioids to proven conditions, with electronic flagging of habitual visitors who present for medical care.\(^4^9\) Such approaches may work if they are done in conjunction with referral to chronic pain clinics or detoxification centers. A multifaceted approach that combined counseling, denial of narcotic prescriptions in the ED, and referral to a single pharmacy resulted in a 72% decrease in ED visits by frequent users.\(^4^9\) Restriction or removal of meperidine from EDs can decrease visits from substance-abusing patients.\(^5^0\)

Beyond facility-wide policies, individual physicians and other health care providers can attenuate drug-seeking behaviors. In addition, the conservative use of long-acting opioids, such as specialized forms of oral morphine, may decrease the reinforcement of drug-seeking behavior while providing compassionate pain alleviation.\(^5^1\) Finally, pain contracts or explaining to the patient that opioids or other controlled substances are not appropriate may be helpful, but only if other physicians in the group or community agree on such a strategy for a particular patient.\(^4^5\)

### KEY CONCEPTS

- Substance abuse can affect people from all socioeconomic groups and all ages.
- For the majority of patients with toxin-induced violent behavior, intramuscular butyrophenones such as haloperidol (Haldol) are safe and rapidly effective sedating agents. With suspected sympathomimetic (e.g., cocaine and amphetamines) intoxication, benzodiazepines such as lorazepam (Ativan) should be used.
- Presentation to an ED with a complication of substance abuse may be a “teaching moment.” Substance abusers should be offered drug treatment services.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.
References