Hallucinogens and Drugs of Abuse
Mark B. Mycyk

KEY POINTS

- The most common chief complaint when patients have hallucinogenic intoxication is altered mental status.
- Optimal treatment depends on symptom-based (rather than drug-based) diagnostic strategies and interventions.
- An elevated temperature is the most important prognostic sign of poor outcome.
- Most new drugs cannot be identified with hospital-based blood or urine tests, and results of urine drug screens should never be considered diagnostic.
- Treatment for drug-induced hypertension should involve generous doses of benzodiazepines before antihypertensive agents are considered.
- Substance abuse counseling and referral are required for all patients before discharge.

EPIDEMIOLOGY

Recreational abuse of hallucinogens and other drugs is common among patients in the emergency department (ED) and is directly responsible for many ED visits. Although the exact prevalence of drug abuse in patients in the ED is unknown because so much drug abuse goes undetected, various surveillance studies all indicate that ED visits related to drug use continue to rise yearly.1-3 Patients who present to an ED immediately after using a drug do so for various reasons: an unfavorable or unanticipated reaction to the drug, an unintentional overdose, a traumatic injury, altered mental status, or suicidal and other dangerous behavior. In addition to the acute complications directly related to drug use, many cardiovascular, neurologic, infectious, psychiatric, and social health problems treated in the ED are linked to chronic drug abuse. Because drug abuse is often not declared by the patient at the time of arrival, recognition and optimal treatment require vigilance from the emergency physician, as well as attention to historical, clinical, and laboratory clues.

Recreational drug use today knows no demographic, age, or socioeconomic boundaries. Drug use is just as common (although perhaps less frequently suspected) in white, employed, and insured individuals as in patients who are nonwhite, unemployed, or homeless.1,4 In the last 2 decades, first-time drug use has become more common among adolescents, and the variety of drugs used has exploded.5,6 Drug use is no longer limited to what can be identified on a standard hospital toxicology screen, and many of the drugs people abuse to become high are not illegal, such as cough and cold products and prescription medications.7-10 The rampant growth of drug use is likely linked to the proliferation of the Internet and the wide availability of unregulated partisan drug sites that enable potential users to learn about drugs, to order the raw ingredients and supplies to manufacture their own drugs, or simply to purchase drugs online in the safety of their own homes.6

PATHOPHYSIOLOGY

The drugs available for recreational abuse are countless and are constantly evolving. In the past, recreational drugs were categorized, for the purposes of discussion, identification, and treatment, somewhat arbitrarily on the basis of structural class, predominant biochemical or neurotransmitter activity (e.g., dopaminergic versus serotonergic versus gamma-aminobutyric acid [GABA]–ergic), or expected clinical effect (e.g., hallucinogen versus stimulant versus entactogen). In reality, most drugs exhibit multiple biochemical effects of varying intensity that are not limited to a particular structural class, and clinical findings vary widely among different individuals even when these persons are exposed to the same drug. Physicians now recognize that clinical variability depends not only on the specific type of drug but also on the dose used, the form of drug (e.g., crystal versus powder versus liquid), the purity of the drug, the route of delivery (e.g., intranasal versus ingestion versus injection), the concomitant use of coingestants, individual genetic polymorphisms, and individual biochemical and physiologic adaptations from long-term exposure.

Most recreational drugs are highly lipophilic and easily cross the blood-brain barrier, so most result in some euphoria; otherwise, patients would have little reason to abuse them.3 Although the exact mechanisms are still incompletely understood, modulation of central dopaminergic activity, which is responsible for pleasure seeking and reward reinforcement, is an important factor in the euphoric response and the development of drug addiction.5 Recreational drugs also affect, to
variable extents, peripheral and central norepinephrine, serotonin (5-HT), N-methyl-d aspartate (NMDA), and GABA activity.

PRESENTING SIGNS AND SYMPTOMS

The most common presenting feature in all patients with recreational drug use is some degree of altered mental status. It may range from seemingly benign giddiness to life-threatening agitation or obtundation. Drug-associated altered mental status may be associated with any kind of vital sign abnormalities or evidence of end-organ damage. Cardiovascular, neurologic, infectious, and psychiatric complaints are also common (Table 150.1). Because the predominant drugs seen in a particular ED vary depending on local geographic preferences and because the types of drugs abused change far more quickly than published medical literature can keep up with, optimal treatment depends on symptom-based (rather than drug-based) diagnostic strategies and interventions.

The following paragraphs discuss some of the more common drugs of abuse historically prevalent in most EDs. Identifying previously undetected drug abuse requires some familiarity with these common drugs and the street slang associated with them (Table 150.2).

<table>
<thead>
<tr>
<th>SIGN OR SYMPTOM</th>
<th>RESPONSIBLE DRUG(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered mental status</td>
<td>All</td>
</tr>
<tr>
<td>Agitation</td>
<td>Amphetamine, Cocaine, Dextromethorphan, Jimsonweed, MDMA, Mephedrone, Methamphetamine, PCP, Prescription medications</td>
</tr>
<tr>
<td>Obtundation</td>
<td>GHB, Opioids, Prescription medications</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Opiates, GHB</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>Amphetamine, Cocaine, Jimsonweed, MDMA, Mephedrone, Methamphetamine, PCP</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Amphetamines, Cocaine, Jimsonweed, Ketamine, LSD, Mephedrone, MDMA, Methamphetamine, PCP, Prescription medications</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>GHB, Opioids, Prescription medications</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Amphetamine, Cocaine, Jimsonweed, Ketamine, LSD, Methamphetamine, MDMA, PCP, Prescription medications</td>
</tr>
<tr>
<td>Hypotension</td>
<td>GHB, Opioids, Prescription medications</td>
</tr>
<tr>
<td>Seizures</td>
<td>Amphetamines, Cocaine, Dextromethorphan, GHB, Jimsonweed, MDMA, Methamphetamine, Prescription medications</td>
</tr>
</tbody>
</table>

GHB, Gamma-hydroxybutyrate; LSD, ∆-lysergic acid diethylamide; MDMA, methylenedioxymethamphetamine; PCP, phencyclidine.

AMPHEATMIN

Commonly referred to as “crank” or “speed,” amphetamine is a specific drug first synthesized in 1887 and initially marketed as a decongestant and appetite suppressant. Many other drugs with a similar chemical structure, such as methylenedioxymethamphetamine (MDMA) and methamphetamine, are collectively called amphetamines, even though their clinical effects vary. More precisely, these drugs are all derived from
stimulation, medical complications such as acute coronary syndrome, seizures, cerebral vascular accidents, intracranial hemorrhage, renal failure, and rhabdomyolysis are common. Cocaine washout syndrome occurs after cocaine binging. Affected patients typically have a depressed mental status ranging from lethargy to obtundation that lasts up to 24 hours until depleted neurotransmitters are regenerated.

**DEXTROMETHORPHAN**

Also known as DXM, dextromethorphan is a common antitussive agent found in over-the-counter and prescription medications in liquid or tablet form. It is a synthetic analogue of codeine but does not have the same analgesic effect because its activity is primarily at NM2 and 5-HT receptors. Hallucinations are commonly reported, and in addition to some opioid features, patients may exhibit ataxia, slurred speech, nystagmus, tachycardia, hypertension, dystonia, and seizures.

**GAMMA-HYDROXYBUTYRATE**

Gamma-hydroxybutyrate (GHB), also known as “Georgia Home Boy” and “Liquid G,” has been variously used as an exercise supplement, for treatment of narcolepsy, for obtaining chemical submission of victims, and for euphoria. GHB works primarily at GABA receptors and the still poorly defined GHB receptor. The analogues gamma-butyrolactone (GBL), 1,4-butanediol (1,4-BD), gamma-hydroxyvalerate methyl-GHB (GHV), and gamma-valerolactone 4-pentanolide (GVL) work similarly because they are all converted to GHB through various pathways after ingestion. GHB easily crosses the blood-brain barrier and produces loss of consciousness within 15 to 30 minutes of ingestion. Bradycardia, vomiting, myoclonic jerks, and hyperthermia are commonly associated. Duration of unconsciousness lasts 2 to 6 hours in most cases.

**JIMSONWEED**

Jimsonweed is the common name of plants in the *Datura* genera. Intoxication with jimsonweed was first reported in 1676. The plants grow throughout the United States, and all parts of it—the fruit, flower, and seeds—can be abused for their hallucinogenic properties. Because these plants contain the alkaloids atropine, scopolamine, and hyoscyamine, clinical effects associated with jimsonweed hallucinations include anticholinergic findings such as dilated pupils, dry mouth, warm and flushed skin, diminished bowel sounds, and urinary retention. Cardiovascular instability, hyperthermia, and seizures have been reported after large ingestions.

**KETAMINE**

Also known as “Special K,” “Kitty Valium,” and “Kiddie Valium,” ketamine is a structural and functional analogue of phencyclidine (PCP) and also works primarily at NMDA receptors. Ketamine can be ingested or injected. Patients with ketamine abuse have symptoms similar to those of PCP intoxication, including rotatory nystagmus, excessive salivation, muscle rigidity, tachycardia, and hypertension, although the effects tend to last a shorter time.

**LSD**

D-Lysergic acid diethylamide (LSD) was first synthesized in 1938. It is available in tablets, liquid, powder, and gelatin
squares, although the most commonly abused form of LSD is “blotter” acid (sheets of paper sprayed with LSD, dried, and then perforated into small squares). Effects occur within 30 minutes, can last for 16 to 24 hours, and cause powerful hallucinations from serotonergic (5-HT) and dopaminergic activity. Time is distorted, and visual hallucinations of bright colors are common. Tachycardia, hypertension, anxiety, and paranoia are frequently seen in patients who seek treatment in the ED as a result of LSD use. Significant medical complications are uncommon.18

MARIJUANA
Also known as “grass,” “weed,” or “pot,” marijuana is considered the most commonly used illegal substance in the United States. Marijuana is primarily smoked; its effects occur within 15 minutes and can last up to 4 hours. The psychoactive substance, delta-9-tetrahydrocannabinol, is derived from the plant Cannabis sativa.3 Clinical effects are variable and seem to occur as a result of cannabinoid receptor activity in the brain. Inappropriate laughter, excessive hunger, anxiety, paranoia, ataxia, and tachycardia are commonly seen. Various synthetic cannabinoids (known by names such as Spice, K2, and Sky Incense) have become available to users in herb shops.19 The duration of symptoms has reportedly been longer than for naturally growing marijuana. Medical complications associated with cannabinoid abuse alone are uncommon.

METHYLENEDIOXYMETHAMPHETAMINE
MDMA is better known as “Ecstasy,” “X,” “XTC,” and “ADAM” and is also discussed in Chapter 149, Sympathomimetics. It was first synthesized in 1914 but became wildly popular at rave parties and on college campuses in the 1980s and 1990s.13 Although it is a phenylethylamine like amphetamine, MDMA’s strong serotonergic activity has clinical effects that are primarily hallucinogenic and entactogenic.3 Variable tachycardia and hypertension can also occur from some stimulant activity. Hyperthermia has been reported as a complication of excessive dancing in warm rave clubs without adequate hydration, although other individual variabilities and drug contaminants are also likely responsible.3 Hyponatremia, another common occurrence with MDMA use, results from excessive ingestion of water or from MDMA-induced syndrome of inappropriate antidiuretic hormone secretion.

METHAMPHETAMINE
Also known as “meth,” “crystal,” “chicken feed,” and “white man’s crank,” methamphetamine has become one of the most popular drugs of abuse in the twenty-first century.20,21 Its popularity is related to its multiple forms (crystal, powder, liquid, and tablet), its ease of manufacture from decongestants such as pseudoephedrine, and its low street cost (less than one third the cost of cocaine). Methamphetamine has strong norepinephrine activity and, of all the phenylethylamines, is the most quickly addictive because of its strong dopaminergic action. It can be ingested, snorted, smoked, injected, or administered rectally. Clinical findings are similar to those associated with other stimulant intoxications, and acute coronary syndrome and cerebrovascular accident have been reported. Other hallmark features of methamphetamine are poor dentition, known as “meth mouth,” from poor hygiene and bruxism and dermatologic lesions called “crank bugs” or “meth mites,” from compulsive scratching that is likely delusional in origin.

OPIOIDS
Naturally occurring or synthetic drugs with opium-like or morphine-like activity have always been popular. The poppy plant, Papaver somniferum, is the source of opium and contains the alkaloids morphine and codeine. Opioid effects are primarily modulated throughout the peripheral and CNS by interacting at three main opioid receptors: μ, κ, and δ.5 The classic opioid toxidrome comprises CNS depression, respiratory depression, and miosis, although the intensity of each of those features varies among the different synthetic opioids. Prehospital deaths typically occur from untreated apnea.22 Abuse of prescription opioids continues to rise, especially abuse of methadone and fentanyl patches. Data indicate that the abuse of combination acetaminophen-opioid analgesics is directly related to rising rates of acetaminophen-induced hepatic failure.23

OTHER NATURAL PRODUCTS
Naturally found herbs, plants, and other related products have become especially popular during the Internet drug era. Adolescents and young adults have been reported to use morning glory seeds for LSD-like effects, nutmeg for myristicin-associated hallucinogenic effects, and the plant Salvia divinorum (known also as “Sally D” and “Diviner’s mint”) for κ-opioid–mediated hallucinogenic effects.24 Naturally occurring recreational drugs are popular because they are considered “naturally” safe and can be used in various ways by users, including ingesting, insufflation, smoking, injection, and even tea consumption. Effects typically last 2 to 6 hours, and medical complications are uncommon, although long-term effects are still unknown.

PRESCRIPTION MEDICATIONS
Nonmedical abuse of prescription drugs has been identified as a national epidemic. In 2005, nearly 15 million U.S. residents abused prescription drugs, including prescribed opioids, sedatives, antidepressants, and stimulants.1 One of the reasons for the rapid rise of prescription drug abuse is the perception that these agents are safer than traditional street drugs. The growing rates of prescriptions written for analgesia, for mood disorders, and for attention-deficit hyperactivity disorder have resulted in experimentation with easily available tablets by the family members or friends of the person for whom the agents were prescribed.9,11

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING
Drug intoxication should always be considered in the differential diagnosis of any patient presenting to the ED with altered mental status. Infectious, metabolic, neurologic, endocrinologic, structural, and psychogenic causes should also be considered in the evaluation of the patient with suspected drug intoxication. The history of events immediately preceding onset of symptoms, if available to the clinician from the patient or witnesses, is most helpful in narrowing the diagnosis.

Asymptomatic patients with drug intoxication who have normal vital signs and normal physical findings do not require diagnostic testing. Patients with mild symptoms should undergo rapid blood glucose measurement because
hypoglycemia or hyperglycemia may cause altered mental status. Ethanol measurement should be obtained if alcohol is suspected as a coingestant or to exclude alcohol ingestion as a cause of altered mental status. Patients who are agitated, hyperthermic, or seizing or were found after prolonged obtundation are all at risk for the development of rhabdomyolysis and should be evaluated with a basic metabolic profile, renal function tests, measurements of calcium, phosphorus, total creatine phosphokinase levels, and urinalysis.

Electrocardiography should be performed in all patients with tachycardia or bradycardia, and telemetry monitoring should be instituted. Patients with altered mental status inconsistent with their reported drug use, new-onset seizure, or signs of traumatic injury or suspected trauma should be evaluated with computed tomography of the head (Table 150.3).

The toxicology drug screen has limited utility in the ED setting and should be used only for a patient in whom mental status is altered and the diagnosis is not clear. Several studies confirm that a careful patient history and attention to clinical signs make toxicology screens unnecessary in most cases of drug intoxication.\textsuperscript{26,27} For example, a patient with depressed respirations, depressed mental status, and pinpoint pupils consistent with an opioid toxidrome who completely awakens after the administration of naloxone does not need a costly urine drug screen to confirm opioid toxicity. Furthermore, waiting for the results of a urine drug screen before administering lifesaving naloxone is impractical in cases of severe intoxication.

The drug screens available in most hospitals have a limited panel, and many of the nontraditional, emerging, and Web-based drugs (new drugs, including prescription medications and club drugs) cannot be detected by such hospital screens.\textsuperscript{5} Toxicology screens are limited by what they cannot detect, and they can yield false-positive results related to contaminants. For example, over-the-counter decongestants used appropriately for an upper respiratory infection can yield a falsely positive amphetamine screen result, and quinolones can cause falsely positive opioid screen results.\textsuperscript{28} Finally, urine drug screen results are not forensically defensible because most hospitals analyze urine with only one laboratory technique, and the chain of custody is not enforced from patient to laboratory (Box 150.1).

Table 150.3  Diagnostic Testing for Suspected Recreational Drug Use

<table>
<thead>
<tr>
<th>TEST</th>
<th>INDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid blood glucose measurement</td>
<td>Altered mental status</td>
</tr>
<tr>
<td>Blood chemistry panel</td>
<td>M eth ylenedioxyamphetamine intoxication or suspected rhabdomyolysis</td>
</tr>
<tr>
<td>Serum acetaminophen measurement</td>
<td>Prescription opioid ingestion</td>
</tr>
<tr>
<td>Blood alcohol evaluation</td>
<td>Suspected coingestant</td>
</tr>
<tr>
<td>Serum creatine phosphokinase (total)</td>
<td>Agitation or suspected rhabdomyolysis</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>Suspected rhabdomyolysis</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>Prescription opioid ingestion</td>
</tr>
<tr>
<td>Electrocardiogram</td>
<td>Tachycardia, bradycardia, or dysrhythmia</td>
</tr>
<tr>
<td>Computed tomography of the head</td>
<td>Suspected trauma or mental status inconsistent with reported ingestion</td>
</tr>
</tbody>
</table>

RED FLAGS

- An elevated temperature is prognostic of poor outcomes.
- Focal neurologic findings are indicative of seizure activity or intracranial lesion.
- Rhabdomyolysis can occur in cases of agitation or prolonged obtundation.
- Renal insufficiency or creatine phosphokinase elevation requires adequate fluid resuscitation to prevent renal failure.

DOCUMENTATION

- Amount ingested?
- Route of ingestion (oral, intravenous, subcutaneous, dermal, sublingual, rectal)?
- Time of ingestion?
- Coingestants?
- History of trauma?
- Previous emergency department visits for drug abuse?
- Previous detoxification or other treatment programs?
- Referral for counseling, treatment program, or detoxification

TREATMENT

Because the clinical presentation of drug intoxication varies widely, optimal treatment must be symptom based. Attempts to confirm identification of the drug should be postponed until the patient is stabilized. As with any patient in the ED,
attention to airway management is the top priority in all patients with drug intoxication. Obtunded patients with a poor respiratory effort should receive either naloxone, in an effort to reverse potential narcosis, or dextrose and thiamine for hypoglycemia. Intubation should be performed for persistent hypoxemia or the inability to protect a patient’s airway. Intra- venous fluids should be administered to treat hypotension. Dysrhythmias should be treated according to standard Advanced Cardiac Life Support guidelines. A thorough examination must be completed to exclude concomitant traumatic injuries that require emergency management.

Patients who are agitated or difficult to control should receive liberal benzodiazepine treatment for their own safety, as well as staff safety, and to ensure a complete examination. Butyrophenones, such as haloperidol, may be considered if benzodiazepines do not successfully control the difficult patient. Although physical restraints may be needed temporarily for patient and staff safety, chemical sedation with benzodiazepines must be given top priority, to minimize the duration of potentially harmful physical restraints.

Drug-induced hypertension and tachycardia should also be treated first with benzodiazepines because these clinical findings primarily result from direct stimulant effects and are effectively managed in most cases with liberal benzodiazepine sedation. Short-acting antihypertensive agents with minimal beta-blocker activity may be considered only after sufficient doses of benzodiazepines have been administered.

Hyperthermia must be aggressively treated with external cooling measures and, if the patient is agitated, with liberal benzodiazepine therapy as well. Close monitoring of the patient’s core temperature is critical because an elevated temperature is the only vital sign abnormality consistently associated with poor outcomes in cases of drug intoxication.

Renal insufficiency or an elevated creatine phosphokinase value requires adequate fluid resuscitation. Drug-induced rhabdomyolysis results in renal failure and hemodialysis in 10% of patients hospitalized for drug intoxication and associated rhabdomyolysis.

**FOLLOW-UP, NEXT STEPS OF CARE, AND PATIENT EDUCATION**

Most patients with single-drug intoxication who have improved can be safely discharged after 4 to 6 hours of ED observation. In patients with multiple drug ingestion, prolonged clinical effects of long-acting agents such as methadone, or medical complications, admission to a monitored hospital bed is appropriate. Attention to signs of withdrawal is important before such a patient is discharged. Whether being discharged from the ED or from an inpatient bed, all patients with drug intoxication require substance abuse counseling and referral for support groups, detoxification, and other outpatient treatment.

**SUGGESTED READINGS**


**REFERENCES**

References can be found on Expert Consult @ www.expertconsult.com.
REFERENCES

11. Setlik J, Bond GR, Ho M. Adolescent prescription ADHD medication abuse is rising along with prescriptions for these medications. Pediatrics 2009;124:875-80.