Introduction and Epidemiology

The term hallucinogen is misleading. Hallucinogenic compounds rarely produce true hallucinations—but rather, users experience profound distortions in body image, sensory perception, and time perception, in addition to rapid, intense alterations in mood, increased intensity of any emotions, and heightened suggestibility. Hallucinogen is sometimes used interchangeably with the term psychedelic.

Hallucinogens are widely perceived as safe by the public. However, these substances can cause dangerous physiologic effects resulting in serious health consequences. 1–3 The identity, purity, and amount of hallucinogenic compound is usually uncertain, and individual response can be unpredictable.

Hallucinogens in current use consist of both natural and synthetic compounds. 4 The proliferation of “designer drugs”—chemical analogs or derivatives of illicit drugs marketed to circumvent existing drug laws—is a growing problem. Manufacturers of designer drugs try to circumvent U.S. federal drug laws by stamping their product with advisories such as “not intended for human consumption” or by identifying the products as plant food, bath salts, or potpourri. Prosecution through the Federal Analog Act, a section of the Controlled Substance Abuse Act, can occur only if the drug is “intended for human consumption.” Because of this limitation in federal law, some states have moved to ban the sale of such drugs.

Conditions that mimic hallucinogen intoxication include alcohol or benzodiazepine withdrawal, anticholinergic poisoning, thyrotoxicosis, central nervous system infections, structural brain lesions, acute psychosis, hypoglycemia, and hypoxia. 5 Some prescription and nonprescription medications can cause hallucinations. The identity of street drugs is often misrepresented, and substitutions or adulteration of product is common. 6, 7

Drug-induced psychosis may be difficult to distinguish from primary psychotic disorders. 8, 9 A patient with substance-induced psychosis is more likely to have a diagnosis of dependence on any drug, report visual hallucinations, and have a history of parental drug abuse. 9

General Approach to Treatment

Start by assessing the patient’s general medical condition and stabilizing the vital signs. Identify and correct hypoxia and hypoglycemia. Obtain a core temperature to recognize hyperthermia. Obtain serum chemistries and if the patient is agitated, obtain creatine phosphokinase to identify rhabdomyolysis. Obtain an electrocardiogram to identify QT interval prolongation.

Gastric decontamination is not needed in most cases because most hallucinogens are rapidly absorbed and because most patients with adverse effects do not present until several hours after the drug was taken. However, consider administration of oral activated charcoal for ingestions occurring within the previous hour or longer when gastric emptying is delayed, such as with anticholinergic poisonings (e.g., nutmeg ingestion).

Reassurance and a calm, supportive environment can often sufficiently soothe the agitated patient. Pharmacologic sedation and possibly physical restraints may be necessary in order to ensure the safety of the patient and the ED staff and to facilitate evaluation and treatment. Benzodiazepines are the preferred agents for the treatment of hallucinogen-induced agitation and delirium because they possess no significant drug interactions, have no dystonic or anticholinergic adverse effects, do not prolong the QT interval or promote arrhythmias, and are reversible by flumazenil if over sedation occurs. Start with diazepam 5 to 10 milligrams PO or IV, or lorazepam 1 to 2 milligrams PO, IM, or IV. Give repeated doses as needed, and monitor blood pressure and respiration. Tachycardia and hypertension often respond to sedation with benzodiazepines alone. Severe hypertension can be treated with IV nitroprusside. Correct electrolyte abnormalities and treat dehydration and hypovolemia with normal saline infusion. Treat symptomatic arrhythmias using standard antiarrhythmic protocols. Active cooling measures should be initiated for patients with significant hyperthermia. Treatment of severe agitation, hyperthermia, or seizures may require neuromuscular paralysis and endotracheal intubation. Seizures are treated with benzodiazepines or propofol. Patients with rhabdomyolysis require aggressive IV hydration to maintain urine output.

Disposition and Follow-Up

Compared with other abused psychoactive agents, hallucinogens have some of the largest acute safety ratios when lethal doses are measured against the doses customarily used to produce the desired hallucinogenic effects. 10 Most patients seen in the ED due to adverse reactions from hallucinogen use can be discharged into the custody of family or friends if they are lucid and in medically stable condition after a period of observation. Patients with persistent psychotic symptoms or comorbid psychiatric illnesses require psychiatric evaluation.

Common Hallucinogens

Common hallucinogens are listed in Table 182-1.

<table>
<thead>
<tr>
<th>Typical</th>
<th>Duration</th>
<th>Clinical</th>
<th>Specific</th>
</tr>
</thead>
</table>

Table 182-1 Common Hallucinogens

<table>
<thead>
<tr>
<th>Drug</th>
<th>Hallucinogenic Dose</th>
<th>Time of Action</th>
<th>Features</th>
<th>Complications</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lysergic acid diethylamide</td>
<td>20–80 micrograms</td>
<td>8–12 h</td>
<td>Mydriasis, Tachycardia, Anxiety, Muscle tension</td>
<td>Coma, Hyperthermia, Coagulopathy, Persistent psychosis, Hallucinogen persisting perception disorder</td>
<td>Reassurance, Benzodiazepines</td>
</tr>
<tr>
<td>Psilocybin</td>
<td>5–100 mushrooms</td>
<td>4–6 h</td>
<td>Mydriasis, Tachycardia, Muscle tension, Nausea &amp; vomiting</td>
<td>Seizures (rare), Hyperthermia (rare)</td>
<td>Reassurance, Hydration, Benzodiazepines</td>
</tr>
<tr>
<td>Mescaline</td>
<td>3–12 “buttons”</td>
<td>6–12 h</td>
<td>Mydriasis, Abdominal pain, Nausea/vomiting, Dizziness, Nystagmus, Ataxia</td>
<td>Rare</td>
<td>Supportive, Benzodiazepines</td>
</tr>
<tr>
<td>Methylenedioxymethamphetamine (&quot;Ecstasy&quot;)</td>
<td>50–200 milligrams</td>
<td>4–6 h</td>
<td>Mydriasis, Bruxism, Jaw tension, Ataxia, Dry mouth, Nausea</td>
<td>Hyponatremia, Hypertension, Seizures, Hyperthermia, Arrhythmias, Rhabdomyolysis</td>
<td>Benzodiazepines, Hydration, Active cooling, Dantrolene, Specific serotonin antagonists</td>
</tr>
<tr>
<td>Synthetic cathinone derivatives (&quot;bath salts&quot;)</td>
<td>50–300 milligrams of mephedrone</td>
<td>2–4 h</td>
<td>Agitation, Tachycardia, Hypertension, Diaphoresis, Mydriasis</td>
<td>Paranoia, Panic reactions, Hyperthermia, Seizures, Hyponatremia, Rhabdomyolysis</td>
<td>Benzodiazepines, Hydration, Active cooling</td>
</tr>
<tr>
<td>Phencyclidine (&quot;angel dust&quot;)</td>
<td>1–9 milligrams</td>
<td>4–6 h</td>
<td>Small or midsized pupils, Nystagmus, Muscle rigidity, Hypersalivation, Agitation, Catatonia</td>
<td>Coma, Seizures, Hyperthermia, Rhabdomyolysis, Hypertension, Hypoglycemia</td>
<td>Benzodiazepines, Hydration, Active cooling</td>
</tr>
<tr>
<td>Marijuana (cannabis)</td>
<td>5–15 milligrams</td>
<td></td>
<td>Tachycardia</td>
<td>Acute psychosis (rare)</td>
<td>Supportive, Benzodiazepines</td>
</tr>
<tr>
<td>Mushroom Type</td>
<td>Potency (micrograms)</td>
<td>Onset (h)</td>
<td>Effect</td>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>----------------------</td>
<td>-----------</td>
<td>-------------------------------</td>
<td>----------------------------------</td>
<td></td>
</tr>
<tr>
<td><em>Psilocybe</em></td>
<td>Unknown</td>
<td>2–4</td>
<td>Conjourctival injection</td>
<td>Supportive benzodiazepines</td>
<td></td>
</tr>
<tr>
<td><em>Psilocybe</em></td>
<td>Unknown</td>
<td>3–4</td>
<td>Tachycardia, conjurctival injection</td>
<td>Acute psychosis, panic reactions (rare), seizures (rare), arrhythmias (rare)</td>
<td></td>
</tr>
<tr>
<td><em>Bromo-benzodifuranyl-isopropylamine</em></td>
<td>200–800</td>
<td>10–14</td>
<td>Agitation, hallucinations</td>
<td>Seizures, vasoconstrictor with necrosis and gangrene</td>
<td></td>
</tr>
</tbody>
</table>

**Psilocybin**

Psilocybin is a naturally occurring hallucinogenic compound found in at least six genera of mushrooms, but most notably the *Psilocybe* genus. Psilocybin is an indolalkylamine that is metabolized to the pharmacologically active compound psilocin. Both psilocybin and psilocin are believed to act as serotonin type 2 receptor agonists similar to lysergic acid diethylamide.

Psilocybin-containing mushrooms grow naturally in the southern United States and Europe but can also be grown from kits sold over the Internet. Most species of psilocybin-containing mushrooms turn bluish when bruised, but this is not a definitive method of identification or determination of potency. Psilocybin-containing mushrooms may be dried or cooked without losing potency. Hallucinogenic mushrooms sold on the street are often nonpsychoactive mushrooms that have been adulterated with lysergic acid diethylamide or phenylcyclohexylamine. Because of the variation in mushroom size and concentration of psychoactive compounds, there is little correlation between the number of mushrooms ingested and the hallucinogenic effects. A user may ingest as few as five or as many as 100 mushrooms for a single “dose.”

Hallucinogenic effects begin within 30 minutes of ingestion and last 4 to 6 hours. The hallucinogenic effects are similar to, although less powerful than, those produced by lysergic acid diethylamide. Other common effects include mydriasis, tachycardia, nausea, and vomiting. Serious medical complications are extremely rare but include seizures, hyperthermia, rhabdomyolysis, and renal failure. Mistaken identity and ingestion of highly toxic mushrooms is possible and can lead to serious outcomes.
Management is supportive. There is no routinely available screening test for psilocybin or psilocin in the urine. If the patient’s symptoms are not consistent with psilocybin ingestion, consider the possibility that a toxic mushroom (see Chapter 214, Mushroom Poisoning) or other psychoactive substances were ingested.21

Mescaline and Peyote

Mescaline is found in many cacti, most notably the Mexican Peyote cactus (Lophophora williamsii) and the Peruvian San Pedro cactus (Trichocereus pachanoi). Peyote is used in Native American religious ceremonies, and its legal use is restricted to the Native American Church. Mescaline is a phenethylamine, structurally related to amphetamines, making it chemically distinct from lysergic acid diethylamide.22 Mescaline is believed to act as a serotonin type 2 receptor agonist, but is much less potent than lysergic acid diethylamide.

Peyote is most commonly sold as raw cactus or “buttons,” 2- to 3-cm discs sliced off of the top of the cactus. Each button contains approximately 45 milligrams of mescaline. A typical hallucinogenic dose is 200 to 500 milligrams. Pills or capsules sold on the street as “mescaline” are unlikely to be genuine and may instead contain lysergic acid diethylamide or phencyclidine.6

Peyote is bitter tasting and causes uncomfortable physical side effects within an hour of ingestion—including nausea, vomiting, abdominal discomfort, diaphoresis, dizziness, nystagmus, ataxia, and headache—that generally resolve after about 2 hours. Adrenergic stimulation causes mydriasis and mild elevations in pulse, blood pressure, and temperature. Hallucinogenic effects begin several hours after ingestion and persist for 6 to 12 hours. Significant morbidity or mortality caused by the physiologic effects of mescaline has not been observed, but death can result from aberrant behavior while under the influence of the drug.23 Mescaline-intoxicated patients are managed supportively. Routine urine drug screens do not detect mescaline.

Hallucinogenic Amphetamines

More than 50 “designer” amphetamines have been created for their hallucinogenic properties. Best known is methylenedioxymethamphetamine, a synthetic phenethylamine derivative structurally related to both amphetamines and mescaline and commonly known by the street name “Ecstasy.” Other designer amphetamines include methylenedioxymethamphetamine and methylenedioxymethylamphetamine (“Eve”). Methylenedioxymethylamphetamine is known for both its psychedelic properties and unique effects on mood and intimacy, which has led to its reputation as a “love drug” popular in dance clubs.24 Methylenedioxymethamphetamine has complex effects, interacting with dopamine, norepinephrine, acetycholine, and β2-adrenergic and serotonin type 2A receptors, and affecting the release of several hormones, including prolactin, oxytocin, adrenocorticotropic hormone, dehydroepiandrosterone, and anti-diuretic hormone.25

Methylenedioxymethamphetamine is usually ingested as tablets in doses of 50 to 200 milligrams. The drug is colorless and tasteless—properties lending to its use as a date-rape drug.26 Symptoms occur within 30 minutes of ingestion and last about 4 to 6 hours. These include feelings of euphoria, inner peace, enhanced sociability, verbosity, and heightened sexual interest. The drug rarely causes actual hallucinations but can produce sensory effects such as alterations in the intensity of colors or sensation of textures. Other common effects include mydriasis, tachycardia, and elevated blood pressure, as well as nausea, jaw tension, bruxism, dry mouth, muscle aches, and ataxia. Current urinary amphetamine immunoassays incorporate a specific monoclonal antibody for methylenedioxymethamphetamine and should routinely detect this drug.

Methylenedioxymethamphetamine and related amphetamines can produce serious complications and death.27–30 As with other amphetamines, large-quantity overdoses can cause severe hypertension, intracranial hemorrhage, and ischemia in the heart or brain.27 Fatal arrhythmias and sudden cardiac death have been reported, both with and without underlying cardiac disease.27,28 The most frequently cited causes of death are hyperthermia and hyponatremia.31–34 A syndrome of methylenedioxymethamphetamine toxicity manifested by hyperthermia, seizures, disseminated intravascular coagulation, rhabdomyolysis, and hepatotoxicity has been described.35 This pattern shares many features of the serotonin syndrome, and combining methylenedioxymethylamphetamine with selective serotonin reuptake inhibitors (see Chapter 172, Atypical Antidepressants, Serotonin Reuptake Inhibitors, and Serotonin Syndrome) or monoamine oxidase inhibitors (see Chapter 173, Monoamine Oxidase Inhibitors) can precipitate serotonin syndrome.36

Hyponatremia is predominantly due to excessive water consumption and inappropriate antidiuretic hormone secretion.31,32 Excessive water drinking from thirst can occur if the drug is taken at hot and crowded club venues, with vigorous dancing and profuse sweating.31,33 Persistent neurotoxic effects are possible from chronic methylenedioxymethylamphetamine use. Neuropsychiatric studies of habitual users demonstrate long-lasting cognitive impairment and mood dysfunction, including memory impairment, diminished learning ability, and depression.37

Gastrointestinal decontamination with activated charcoal may be useful if the drug was ingested within 60 minutes of ED arrival.38 Hypertension and tachycardia often respond to benzodiazepines. Severe hypertension is treated with IV phentolamine or nitroprusside. Rapid IV titration with high doses of benzodiazepines or propofol may be required to control symptoms in patients with refractory agitation or seizures. Arrhythmias are managed with standard therapy.

Check serum electrolyte concentrations and anticipate and treat abnormalities, especially hyponatremia (see Chapter 19, Fluids and Electrolytes). Hyperthermia is managed with cooling measures and fluid resuscitation.32,33 Patients with temperatures exceeding 40°C (104°F) have increased morbidity and mortality, so rapid cooling is important.39 Although there is no evidence from controlled studies, expert opinion and case reports support the use of dantrolene when methylenedioxymethamphetamine-induced hyperthermia is refractory to sedation and active cooling.38,40–42 Specific serotonin antagonists, such as methysergide or cyproheptadine, have been suggested for patients with features of the serotonin syndrome following...
methyleneoxymethamphetamine use.\textsuperscript{43}

**Synthetic Cathinone Derivatives**

In the fall of 2010, U.S. Poison Control Centers began receiving calls regarding synthetic cathinone derivatives, and use has increased dramatically since then.\textsuperscript{44,45} Cathinone is a naturally occurring alkaloid extracted from the leaves of the *Catha edulis* plant (khat) native to areas of Africa and the Middle East. Cathinone and synthetic derivatives, including methylone, methylethylketonepyrrolvalerone, and methylone, are chemically similar to amphetamines. These drugs likely stimulate the release and inhibit the uptake of biogenic amines such as norepinephrine, dopamine, and serotonin.

Synthetic cathinone derivatives are abused by individuals seeking a “legal” high with stimulatory effects similar to those of cocaine or methylethylketonepyrrolvalerone. These drugs are often labeled as “bath salts” or “plant food,” with fanciful names such as “Vanilla Sky” or “Ivory Wave.” They are often labeled as “not for human consumption” in an attempt to avoid federal regulations.

Synthetic cathinones can be nasally insufflated (“snorted”), ingested, or injected. Duration of effects depends on method of use—1 to 2 hours with nasal insufflation and up to 4 hours if ingested.\textsuperscript{46} Approximately 20\% of users report adverse effects including sweating, palpatations, nausea, headache, and dizziness.\textsuperscript{46} Agitation is common, and paranoia, panic attacks, and aggression—including violent behavior—have been reported. Sympathomimetic toxicity, with dilated pupils, tachycardia, and hypertension, is common. Hyperthermia, seizures, hyponatremia, rhabdomyolysis, and deaths have been reported.\textsuperscript{46–50} Synthetic cathinones are not detected on routine urine toxicology screens.

Treatment is primarily supportive, including cardiovascular monitoring; benzodiazepines as needed for agitation, sympathomimetic effects, or seizures; and cooling for hyperthermia. Admission to a monitored or intensive care unit setting is appropriate for patients with persistent symptoms.

In September 2011 the U.S. Drug Enforcement Administration issued an emergency order to place three synthetic cathinones (mephedrone, methylethylketonepyrrolvalerone, and methylone) temporarily into Schedule 1 under the Controlled Substances Act, making the manufacture, sale, or possession of these agents illegal.\textsuperscript{51}

**Phencyclidine**

Phencyclidine is a synthetic piperidine derivative, structurally related to ketamine. Phencyclidine does not fit easily into a single classification, combining features of hallucinogens, depressants, and stimulants.\textsuperscript{52} Unlike classic hallucinogens, phencyclidine causes a clouding of the sensorium rather than heightened sensory awareness. The primary pharmacologic action is blockade of N-methyl-D-aspartate receptor channels. At high concentrations, phencyclidine also interacts with other receptors and channels, including the opioid, acetylcholine receptor and voltage-gated electrolyte channels, and exhibits sympathomimetic effects by blocking reuptake of norepinephrine and dopamine.

Phencyclidine is easily and inexpensively synthesized. Powdered (“angel dust”) or liquid (“dippers”) drug is often combined with tobacco, marijuana, or other leafy materials and smoked. Phencyclidine can also be ingested orally, snorted, or intravenously injected.\textsuperscript{53} Phencyclidine may be unknowingly ingested, because it is often sold as another drug or used to adulterate another illicit drug product.\textsuperscript{17} The onset of action depends on the mode of administration. With smoking the onset is about 5 minutes and effects generally last 4 to 6 hours. With large doses, effects can persist for days due to its lipid solubility and accumulation in fat stores.\textsuperscript{54,55}

Patients may experience CNS stimulation or depression, with clinical presentations ranging from physically violent to catatonic or comatose states.\textsuperscript{53,56} A combination of cholinergic, anticholinergic, and sympathomimetic effects causes a confusing clinical toxidrome. Phencyclidine is often coadministered with other drugs such as crack cocaine (“beam me up”), marijuana (“crystal supergrass”), or ethanol, which also complicates the clinical picture.\textsuperscript{54} The most common findings in phencyclidine-intoxicated patients are nystagmus and hypertension (generally mild), each occurring in almost 60\% of cases.\textsuperscript{54} Feelings of detachment (dissociation) from the environment and self may give the user feelings of strength, power, and invulnerability. Violent actions, agitation, bizarre and unpredictable behavior, and hallucinations or delusions are frequent. Diaphoresis, tachycardia, muscle rigidity, dystonic reactions, ataxia, and a decreased response to painful stimuli can occur. About 10\% of patients are described as comatose.\textsuperscript{55} Pupil size is variable, but widely dilated pupils are uncommon.\textsuperscript{54}

Medical complications from phencyclidine toxicity are frequent.\textsuperscript{52,56,57} Seizures occur in about 3\% of patients, and rhabdomyolysis, occasionally producing acute renal failure, is reported in up to 70\%.\textsuperscript{55} Hypoglycemia, hypertension causing intracerebral hemorrhage, hyperthermia causing hepatic necrosis, and multiorgan failure can occur.\textsuperscript{54,55,57,58} Violent behavior can result in self-injury.

Evaluate patients with suspected phencyclidine toxicity for occult injury, hypoglycemia, and rhabdomyolysis.\textsuperscript{52,53,56} Phencyclidine can be detected by commercially available urine drug screens up to 8 days after single use and up to several weeks after long-term use.\textsuperscript{59} Cough and cold medications (dextromethorphan, diphenhydramine, and doxylamine), analgesics (ibuprofen, meperidine, and tramadol), and psychotropics (imipramine, mirtazapine, thioridazine, and venlafaxine) cross-react with the drug screen and produce false-positive results.

Sedation and physical restraints are frequently required to control violent and aggressive behavior. Parenteral benzodiazepines are preferable to physical restraints because fighting against restraints may contribute to rhabdomyolysis.

Treatment is generally supportive. Treat seizures with benzodiazepines. Status epilepticus or seizures refractory to benzodiazepines may require intubation and treatment with propofol or barbiturates. Treat hyperthermia with active cooling measures. Hypertension usually responds to sedation, but severe hypertension can be treated with nitroprusside. Rhabdomyolysis is treated with aggressive hydration and close monitoring of urine output.
Patients exhibiting only minor clinical features of phencyclidine intoxication and no medical complications can be discharged when behavior normalizes.\textsuperscript{52,53,55,56}

**Marijuana or Cannabis**

Marijuana or cannabis consists of the dried leaves and flowers of the hemp plant \textit{Cannabis sativa}. Hashish is prepared from the dried resin from the flower tops of this plant. The psychoactive ingredient in marijuana is tetrahydrocannabinol.\textsuperscript{60}

Marijuana is most often smoked\textsuperscript{61} but can also be ingested. Symptoms persist for 2 to 4 hours after smoking, or longer if ingested. Clinical effects include drowsiness, euphoria, heightened sensory awareness, paranoia, and distortions of time and space. Hallucinations do not usually occur at usual doses. Common physiologic effects of marijuana are mild tachycardia, injected conjunctiva, bronchodilation, orthostatic hypotension, and impaired motor coordination.\textsuperscript{62} Medical complications, such as panic reactions, brief toxic psychoses, pneumomediastinum, and pneumothorax, are rare. Acute cardiac events associated with marijuana use have been reported,\textsuperscript{63,64} possibly the result of aging in the population of marijuana users and the increasing availability of medical marijuana.

Marijuana is used for treatment of medical conditions such as glaucoma and chemotherapy-related nausea and to promote weight gain in patients with HIV infection and AIDS.

Chronic cannabis use is associated with psychiatric, respiratory, cardiovascular, and bone effects.\textsuperscript{65} Cyclic vomiting syndrome can be due to marijuana use.\textsuperscript{66–68} Symptoms are often misdiagnosed as gastroparesis or opiate withdrawal, and cannabis cessation results in symptomatic recovery.

Acute psychiatric symptoms due to marijuana use can generally be managed with reassurance alone, but benzodiazepines can be used for severe symptoms. Standard urine drug screens are unreliable indicators of acute marijuana intoxication. High lipid solubility results in extensive deposition within body fat and slow excretion in the urine. After a single use, tetrahydrocannabinol is detected by commercially available urine screens for up to 3 days. With long-term use, cannabinoids can be detected up to 30 days or longer after abstinence.\textsuperscript{69} Ibuprofen, naproxen, pantoprazole, and efavirenz, a non-nucleoside reverse transcriptase inhibitor used to treat HIV infection, can produce false-positive results on the urine cannabinoid screen.

**Synthetic Cannabinoids**

Synthetically produced cannabinoid-receptor agonists have been created for hallucinogenic use and are generally combined with herbal blends and labeled as “Spice” or “K2.”\textsuperscript{47} These products contain a variety of compounds that are active at the cannabinoid receptors but are not structurally related to tetrahydrocannabinol. One of the first synthetic cannabinoids (1-pentyl-1H-indol-3-yl)-1-naphthalenyl-methanone, goes by the term JWH-018 for the initials of J.W. Huffman, who developed this compound to investigate drug-receptor interactions.\textsuperscript{70}

Products containing synthetic cannabinoids are sold in shops and on the Internet labeled as “incense” and “not for human consumption.” The appeal of such products is driven by the desire for a legal “high” that is not detectable by current urine drug assays.

The product is usually rolled in paper and smoked in a manner similar to marijuana. Effects begin within minutes and may last for several hours, generally disappearing within 4 hours.\textsuperscript{47} Most users will not seek or require medical attention, but some have experienced adverse reactions, with anxiety and tachycardia being the most common.\textsuperscript{72} Other reported adverse effects include hypertension, diaphoresis, tremulousness, and agitation.\textsuperscript{72,73} Synthetic cannabinoids can precipitate psychosis in patients with prior mental illness.\textsuperscript{74} Symptoms are usually self-limited and short-lived, and treatment is supportive.

In March 2011 the U.S. Drug Enforcement Administration placed five synthetic cannabinoid compounds (JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol) into Schedule 1, criminalizing their sale or use.\textsuperscript{75} These will likely be replaced in the illegal hallucinogen marketplace by other related molecules in this class.

**Designer Alkaloids**

Bromo-benzodifuranyl-isopropylamine, or Bromo-DragonFLY, is a phenethylamine hallucinogen.\textsuperscript{76} Bromo-DragonFLY stimulates serotonin receptors in the brain, similar to lysergic acid diethylamide. Bromo-DragonFLY was developed as a research chemical to study the relationship between molecular structure and psychedelic activity. The name comes from its chemical structure, two furanyl rings with double bonds and a side amphetamine arm, which gives it the appearance of a dragonfly. In 2005, Bromo-DragonFLY became available in human experimental markets and was soon diverted to hallucinogenic use.

Bromo-DragonFLY is sold as white to pink powder that can be snorted, smoked, or injected. Bromo-DragonFLY may also be sold on blotter paper, similar to lysergic acid diethylamide, which has led to confusion in users mistakenly consuming Bromo-Dragon-FLY instead. The hallucinogenic dose of Bromo-DragonFLY ranges from 200 to 800 micrograms, with the onset of action within 20 to 90 minutes and a duration of hallucinogenic effects up to 10 to 14 hours. Toxicity includes agitation, hallucinations, and tonic-clonic seizures that may be delayed in onset.\textsuperscript{77} Bromo-DragonFLY acts as a long-acting vasoconstrictor that can cause necrosis and gangrene several weeks after use. Bromo-DragonFLY has been associated with fatalities in several countries.\textsuperscript{78} Two similar compounds, 2C-B-FLY and 3C-B-FLY, are also abused as hallucinogens.

Benzylpiperazine and trifluoromethylphenylpiperazine are synthetic phenylolephazaine analogues used as substitutes for amphetamine-derived designer drugs.\textsuperscript{47,79} These two compounds are usually combined and sold as “\textit{Legal X}” in attempt to mimic the effects of methylenedioxymethamphetamine.
These drugs are legally available in many countries. Clinical effects include sympathomimetic effects such as palpitations, agitation, anxiety, confusion, dizziness, headache, tremor, mydriasis, insomnia, urinary retention, vomiting, and seizures.\textsuperscript{47,80} Deaths have been associated, but in most cases, recovery occurs with supportive care and benzodiazepines.\textsuperscript{81}

### Less Commonly Abused Hallucinogens

Other drugs with hallucinogenic properties (Table 182-2) are enjoying increasing popularity because of information disseminated on the Internet that promotes the use of these “natural” psychoactive agents.\textsuperscript{47,82}

#### Table 182-2 Less Commonly Abused Hallucinogens

<table>
<thead>
<tr>
<th>Drug</th>
<th>Typical Route of Use</th>
<th>Onset of Action</th>
<th>Duration of Action</th>
<th>Additional Features of Acute Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salvia divinorum: salvinorin A</td>
<td>Smoking of dried leaves</td>
<td>20–60 s (smoking)</td>
<td>20–30 min (smoking)</td>
<td>Headache</td>
</tr>
<tr>
<td>Toad venom or eggs: bufotoxins</td>
<td>Ingestion of toad venom extract or food made</td>
<td>30–60 min</td>
<td>1–3 d (untreated)</td>
<td>Abdominal pain, vomiting, Sympathomimetic effects, Features similar to cardiac glycoside toxicity</td>
</tr>
<tr>
<td>Ipomoea species (morning glory):</td>
<td>1–2 h</td>
<td>6–10 h</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>lysergic acid amide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutmeg: myristicin</td>
<td>Ingestion of seeds or ground spice</td>
<td>3–6 h</td>
<td>6–24 h</td>
<td>Some features resemble anticholinergic toxicity</td>
</tr>
<tr>
<td>Datura species (Jimson weed and</td>
<td>Ingestion of seeds</td>
<td>1–3 h (ingestion)</td>
<td>24–48 h</td>
<td>Anticholinergic effects</td>
</tr>
<tr>
<td>angel’s trumpet): scopolamine, atropine, and hyoscyamine</td>
<td>Smoking dried plant parts</td>
<td>5 min (smoking)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>Snorting dried powder or smoking of powder</td>
<td>5–15 min (nasal insufflation)</td>
<td>45–60 min (nasal insufflation)</td>
<td>Sympathomimetic effects</td>
</tr>
<tr>
<td>Dextromethorphan</td>
<td>Ingestion of liquid</td>
<td>20–60 min</td>
<td>4–6 h (ingestion)</td>
<td>Nausea, vomiting, and diarrhea</td>
</tr>
<tr>
<td></td>
<td>Nasal insufflation of powder</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Salvia**

*Salvia divinorum* ("salvia," "Sally," "magic mint") is a perennial herb in the mint family.\textsuperscript{83} Salvia is sold as seeds, plant cuttings, whole plants, fresh and dried leaves, and liquid extracts purported to contain the active ingredient salvinorin A. Although salvia and salvinorin A are not currently regulated under the U.S. Controlled Substance Act, a number of states have placed controls on the plant and extract. When chewed, the leaf mass and juice are retained within the mouth, and absorption of the active ingredient is rapid, causing clinical effects within 5 to 10 minutes. Dried leaves, as well as extract-enhanced leaves, can be smoked. Smoking pure salvinorin A at a dose of 200 to 500 micrograms results in effects that begin within 30 seconds
and last up to 30 minutes. Desired effects include perceptions of bright lights, vivid colors and shapes, body movements, and object distortions. Adverse effects may include dysphoria, incoordination, dizziness, and slurred speech. Treatment is supportive.

Bufotoxins

Bufotoxins (bufotenine and 5-methoxy-dimethyltryptamine) are hallucinogenic tryptamines found in the venom, skin, and eggs of many toads (e.g., Bufo alvarius, Bufo marinus). Toad venom has also been used as an aphrodisiac ("love stone" or "rock hard") and in some traditional Chinese medicines (chan su and kyushin). Venom can be obtained by "milking" the toad’s parotid glands and drying the liquid venom to form an extract. 5-Methoxy-dimethyltryptamine is a powerful psychedelic but bufotenine has weaker effects. In addition to psychoactive substances, the venom contains cardioactive steroids (bufagins or bufadienolides), catecholamines (epinephrine and norepinephrine) and noncardiac sterols (e.g., cholesterol). Bufagins are cardioactive steroids that can cause cardiac toxicity similar to digoxin. Toxicity from toad venom varies considerably depending on the toad species and its geographic location.

Symptoms of toad venom poisoning occur almost immediately. Effects may be restricted to local gastrointestinal irritation, with copious salivation, nausea, vomiting, and abdominal discomfort persisting for hours. Systemic toxicity may develop due to sympathomimetic effects. Cardiac toxicity is similar to acute digoxin poisoning, with hyperkalemia, bradycardia, atroventricular conduction block, ventricular tachycardia, ventricular fibrillation, and cardiac arrest. Serum digoxin immunoassay often yields a positive result. Bradycardia is initially treated with atropine and may require pacemaker placement. Antiarrhythmic drugs should be used for ventricular arrhythmias. Digoxin-specific Fab antibody treatment has been effective in animal models and human cases.

Morning Glory Seeds and Ipomoea Species

Morning glory seeds (Ipomoea violacea, Ipomoea tricolor, and others) contain lysergic acid amide (ergine), a compound closely related to lysergic acid diethylamide. The seeds can be ingested for their hallucinogenic effects; typically several hundred seeds are ingested as one “dose.” Physical and psychologic manifestations closely resemble the effects of lysergic acid diethylamide, and patients are managed similarly.

Myristicin

Nutmeg is the dried seed from the tropical Myristica fragrans tree. Accidental or intentional ingestion of large amounts of nutmeg can cause delirium with hallucinations. The hallucinogenic properties of nutmeg may be due to the component myristicin, but the mechanism is not well understood. Ingestion of one to three nutmegs or 5 to 15 grams of the ground spice produces psychologic effects that begin 3 to 6 hours later and lasts for 6 to 24 hours. Symptoms include tachycardia, flushing, dry mouth, nausea, and abdominal pain. Signs and symptoms may resemble anticholinergic poisoning, but pupils are usually small or midsized. Management is supportive care.

Datura Species

Jimson weed (Datura stramonium) and angel’s trumpet (Datura candida) are plants that originated in the United States and Mexico but have spread worldwide throughout other areas with warm and temperate climates. All Datura species contain the anticholinergic alkaloids atropine, scopolamine, and hyoscyamine. Seeds or other parts of the plant can be ingested or smoked and produce delirium, hallucinations, and seizures along with other classic anticholinergic effects, such as mydriasis, tachycardia, dry mouth and skin, blurred vision, urinary retention, and hyperthermia (see Chapter 196, Anticholinergics). Gastric emptying is often delayed, and the small, plentiful seeds can become trapped among the gastrointestinal folds after ingestion; thus gastric decontamination can be an important therapy. Whole-bowel irrigation is also recommended for patients who have ingested a large number of seeds. Medications with anticholinergic properties, such as phenothiazines, should be avoided. Physostigmine, a reversible acetylcholine esterase antagonist, is effective treatment for severe anticholinergic poisoning.

Ketamine and Dextromethorphan

Ketamine and dextromethorphan are chemically related to phencyclidine. Ketamine and phencyclidine are described as dissociative drugs because they distort perceptions of sight and sound and produce feelings of detachment from the environment and self. Ketamine, known by the street names “vitamin K” and “special K,” can be abused by SC or IM injection, nasal insufflation of the dried powder, or smoking of the dried power admixed with marijuana or tobacco. Ketamine abusers may come to the ED because of anxiety, palpitations, and chest pain.

Dextromethorphan, available in over-the-counter cough-suppressant products, has become popular among adolescents. A large quantity must be ingested for the user to experience hallucinogenic effects. Abuse among youths has prompted many states to enact restrictions regarding the age of the buyer and the maximum amount purchaseable, and most retailers and pharmacists keep cough medicines containing dextromethorphan behind the counter. Cold and cough products often contain other ingredients, such as antihistamines and acetaminophen, so investigate for toxic amounts of a co-ingestant in any patient who has ingested hallucinogenic doses of dextromethorphan. Medical care is primarily supportive.

References


