Chapter 187: Cocaine and Amphetamines

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INTRODUCTION

Historical records of indigenous cultures in South America describe early stimulant use by chewing leaves of the *Erythroxylum coca* plant, a practice that continues today. Cocaine was first used therapeutically in 1884 for ophthalmologic procedures. Amphetamines were first synthesized in 1887, and in 1932 they were first marketed medicinally in an inhaler form as a bronchodilator. Use of methamphetamine to enhance physical and intellectual performance began in the 1930s. These drugs have limited therapeutic roles but are widely used as drugs of abuse. Clinical effects and toxicity are due to sympathetic nervous system stimulation.

PHARMACOLOGY

COCAINE

Cocaine is the naturally occurring alkaloid found in *E. coca*, a plant indigenous to South America. The water-soluble hydrochloride salt is absorbed across all mucosal surfaces, including oral, nasal, GI, and vaginal epithelium; thus, cocaine can be topically applied, swallowed, or injected IV. The hydrochloride (salt) form is most often insufflated (snorted) or injected IV. The freebase form of cocaine can be prepared in several ways. A common method uses an alkali, such as sodium bicarbonate, to produce "crack cocaine," a freebase form that is stable to pyrolysis that, when smoked, produces the popping sound that characterizes its name. The onset and duration of action vary with the route of administration (*Table 187-1*).
TABLE 187-1

Pharmacokinetics of Cocaine

<table>
<thead>
<tr>
<th>Route of Exposure</th>
<th>Onset of Action</th>
<th>Peak Action</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>&lt;1 min</td>
<td>3–5 min</td>
<td>30–60 min</td>
</tr>
<tr>
<td>Nasal insufflation (snorting)</td>
<td>1–5 min</td>
<td>20–30 min</td>
<td>60–120 min</td>
</tr>
<tr>
<td>Inhalation (smoking)</td>
<td>&lt;1 min</td>
<td>3–5 min</td>
<td>30–60 min</td>
</tr>
<tr>
<td>GI</td>
<td>30–60 min</td>
<td>60–90 min</td>
<td>Unknown</td>
</tr>
</tbody>
</table>


When cocaine is insufflated nasally, the delayed and prolonged effect is a result of vasoconstrictive properties that limit mucosal absorption as well as the swallowing of a portion of the insufflated cocaine, which is then absorbed from the stomach. GI absorption is also delayed by vasoconstriction, producing delayed peak effect.

Cocaine is primarily metabolized to ecegonine methyl ester by plasma cholinesterase. Relative deficiency of this enzyme may predispose affected patients to life-threatening toxicity.\(^1\) Benzoylecgonine is the other major metabolite excreted in the urine and is the target compound detected in routine urine toxicology screens. Cocaethylene is a long-acting metabolite formed when cocaine is used in combination with ethanol. Cocaethylene has vasoconstrictive properties similar to those of cocaine.

Cocaine is both a CNS stimulant and a local anesthetic.\(^2,3\) Central effects are mediated by enhancement of excitatory amino acids and blockade of presynaptic reuptake of norepinephrine, dopamine, and serotonin. The excess of neurotransmitters at postsynaptic receptor sites leads to sympathetic activation, producing the characteristic physical findings of mydriasis, tachycardia, hypertension, and diaphoresis, and predisposing to dysrhythmias, seizures, and hyperthermia. Cocaine use produces a euphoria associated with enhanced alertness and a general sense of well-being. It is thought that the psychological addiction, drug craving, and withdrawal effects are mediated by interference with dopamine and serotonin balance in the CNS. Subsequent dopamine depletion at the nerve terminals may account for the dysphoria and depression associated with long-term abuse.

Like other local anesthetics, cocaine inhibits conduction of nerve impulses by blocking fast sodium channels in the cell membrane. Cocaine also has quinidine-like effects on conduction, causing QRS-complex widening and QT-interval prolongation. Thus, in large doses, cocaine may exert a direct toxic effect on the myocardium, resulting in negative inotropy and wide-complex dysrhythmia.
AMPHETAMINES

Amphetamines comprise a broad class of structurally similar derivatives of phenylethylamine. The derivative methamphetamine, also known as "ice," is abused by ingestion, IV injection, inhalation, or nasal insufflation. Absorption and peak effects vary with the route (Table 187-2). Modification of the basic amphetamine structure produces substances with additional psychoactive properties. Over 50 such "designer" amphetamines have been created (Table 187-3), primarily for hallucinogenic effects (see chapter 188, "Hallucinogens"). Methamphetamine and the designer amphetamines may have effects that persist for up to 12 hours or longer.

TABLE 187-2
Pharmacokinetics of Methamphetamine

<table>
<thead>
<tr>
<th>Route of Exposure</th>
<th>Onset of Action</th>
<th>Peak Action</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>15–30 s</td>
<td>30 min</td>
<td>10–12 h</td>
</tr>
<tr>
<td>Nasal insufflation (snorting)</td>
<td>3–5 min</td>
<td>1–2 h</td>
<td>10–12 h</td>
</tr>
<tr>
<td>Inhalation (smoking)</td>
<td>10–30 s</td>
<td>5–10 min</td>
<td>8–12 h</td>
</tr>
<tr>
<td>GI</td>
<td>15–20 min</td>
<td>2–3 h</td>
<td>10–12 h</td>
</tr>
</tbody>
</table>
### TABLE 187-3

**Commonly Abused Designer Amphetamines**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Chemical Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDMA</td>
<td>3,4-methylenedioxymethamphetamine</td>
</tr>
<tr>
<td>MDA</td>
<td>3,4-methylenedioxyamphetamine</td>
</tr>
<tr>
<td>MDEA</td>
<td>3,4-methylenedioxyethamphetamine</td>
</tr>
<tr>
<td>PMA</td>
<td>Paramethoxyamphetamine</td>
</tr>
<tr>
<td>DOB</td>
<td>4-bromo-2,5-dimethoxyamphetamine</td>
</tr>
<tr>
<td>2CB</td>
<td>4-bromo-2,5-dimethoxyphenylethylamine</td>
</tr>
<tr>
<td>STP or DOM</td>
<td>4-methyl-2,5-dimethoxyamphetamine</td>
</tr>
</tbody>
</table>

Synthetic (or substituted) cathinones, often termed "bath salts," are designer drugs derived from naturally occurring amphetamine analogs found in the *Catha edulis* plant. Cathinones stimulate the release and block the reuptake of norepinephrine, dopamine, and serotonin at synapses in the brain, producing stimulant effects similar to cocaine and amphetamines.  

Commonly abused substituted cathinones include mephedrone, methylenedioxypyrovalerone, and methylone, although the composition in bath salts sold for use by abusers varies widely. Stimulant medications for attention-deficit disorder, such as methylphenidate and dextroamphetamine, are available in both immediate- and extended-release formulations. Abusers may crush the extended-release tablet to separate the active agent from the extended-release matrix to achieve a rapid onset of action after insufflation or injection.

Amphetamines enhance the release and block the reuptake of catecholamines at the presynaptic terminal and may also directly stimulate catecholamine presynaptic and postsynaptic receptors. Some amphetamine metabolites inhibit monoamine oxidase, increasing cytoplasmic concentrations of norepinephrine. Certain amphetamine derivatives can also induce release of serotonin and affect central serotonin receptors. These serotonergic effects account for the hallucinogenic properties of some amphetamine derivatives such as MDMA (3,4-methylenedioxymethamphetamine) and mescaline (3,4,5-trimethoxyphenethylamine). Downregulation of dopamine receptor activity with long-term use may contribute to the withdrawal phenomenon. Mortality from amphetamine toxicity is a result of hyperthermia, dysrhythmias, seizures, hypertension (intracranial hemorrhage or infarction), and encephalopathy.
Stimulants such as methylphenidate, ephedrine, pseudoephedrine, and phenylpropanolamine produce toxic syndromes similar to those caused by cocaine and amphetamines. Ephedrine is derived from ephedra or ma huang (Ephedra sinica) and is an indirect-acting sympathomimetic that was advertised as a "natural" stimulant in health food supplements and promoted for dieting, energy, and maintenance of alertness. Cardiovascular and neurologic toxicity associated with psychosis, severe hypertension, and several deaths prompted the U.S. Food and Drug Administration in 2004 to ban the sale of ephedra in dietary supplements.

**CLINICAL FEATURES**

The clinical features of cocaine and amphetamine toxicity are the result of their sympathomimetic, vasoconstrictive, psychoactive, and local anesthetic properties affecting a variety of organ systems.

**CARDIOVASCULAR**

Cocaine induces dysrhythmias, myocarditis, cardiomyopathy, and acute coronary syndromes. Other vascular complications include aortic rupture and aortic and coronary artery dissection. Even at relatively low doses, cocaine induces vasoconstriction in coronary arteries, contributing to cocaine-induced chest pain. Coronary vasoconstriction is exacerbated by β-adrenergic blockade and antagonized by phentolamine, which suggests mediation through stimulation of α-adrenergic receptors. This effect is further potentiated by cigarette smoking. In addition to promoting vasospasm, cocaine potentiates acute coronary syndrome by increasing atherogenesis through increased platelet aggregation, thrombogenesis, and accelerated atherosclerosis.

The patient most at risk for cocaine-associated acute coronary syndrome is a male between 20 and 40 years old, who is a cigarette smoker and who regularly uses cocaine. All routes of cocaine administration are associated with chest pain, acute coronary syndrome, ST-elevation myocardial infarction, and non–ST-elevation myocardial infarction. Atypical chest pain is common.

Acute coronary syndromes and aortic dissection are also reported in association with ephedrine, phenylpropanolamine, and amphetamine use. Mitral and aortic valve abnormalities associated with use of the amphetamine combination phentermine-fenfluramine prompted a voluntary recall of these drugs. Cardiopulmonary toxicity from other amphetamine diet aids has also been reported.

Dysrhythmias induced by cocaine can result from sympathomimetic stimulation, blockade of the sodium channel during depolarization, inhibition of the potassium channel during repolarization, and effects on calcium channel current. Sympathomimetic-induced dysrhythmias are tachycardias, such as sinus tachycardia, reentrant supraventricular tachycardia, and atrial fibrillation and flutter. Sodium channel blockade produces a rightward shift of the terminal portion of the QRS complex as seen on the frontal plane ECG leads, a pattern similar to that of cyclic antidepressants. Progressive toxicity may induce a complete...
right bundle-branch block or a prolonged QRS >120 ms that, when combined with sinus tachycardia, produces a wide-complex tachycardia. Cocaine can induce the ECG appearance of the Brugada pattern, although it is not clear whether this is strictly a toxic effect or if the sodium channel–blocking effect of cocaine unmasked an underlying genetic predisposition to the Brugada syndrome.  

Potassium channel blockade impairs repolarization, prolonging the QT interval on the ECG.  The effects of cocaine on calcium channel current are dose dependent and complex, but at concentrations associated with clinical toxicity, prolongation of both depolarization and repolarization is seen, as well as enhanced dispersion in repolarization. Delayed repolarization and enhanced dispersion promote early afterpotentials that can trigger reentrant dysrhythmias, such as ventricular tachycardia and a variant, torsades de pointes.

Takotsubo syndrome, transient apical ballooning of the left ventricle, has been associated with cocaine use. The physiology is not clearly understood but has been attributed to the effects of a sympathomimetic surge on the myocardium after cocaine use.

CNS

Neurologic syndromes associated with cocaine abuse include seizures, intracranial infarctions, and hemorrhages. Hyperadrenergic tone induces severe transient hypertension, hemorrhage, or focal vasospasm, and, sometimes, exacerbation of underlying abnormalities of cerebral blood vessels. Cerebral vasoconstriction following cocaine administration has been observed using magnetic resonance angiography.

Other CNS manifestations reported after cocaine use include spinal cord infarctions, cerebral vasculitis, and intracranial abscesses. Chorea and repetitive movements (termed "crack dancing") are associated with cocaine and amphetamine intoxication and appear related to dopamine dysregulation. Acute dystonic reactions following cocaine use and withdrawal are also observed. Unilateral blindness has been reported secondary to central retinal artery occlusion, and bilateral blindness can be caused by diffuse vasospasm. A syndrome of corneal abrasions and ulcerations secondary to smoke and irritation is known as "crack eye." Keratitis caused by methamphetamine use has been described as well.

"Cocaine washout" is a syndrome that may occur in patients after a prolonged crack binge and results from depletion of neurotransmitters. Patients have a depressed level of consciousness but can be aroused to normal with stimulation. Resolution of lethargy can take up to 24 hours.

Amphetamine, phenylpropanolamine, and ephedrine use are associated with intracranial hemorrhage, infarction, encephalopathy, and seizures. Amphetamines can also cause a CNS vasculitis resulting in focal neurologic deficits. A profound paranoid psychosis can be seen with long-term amphetamine abuse and withdrawal.

PULMONARY
Respiratory effects of cocaine use are more common in patients who smoke crack cocaine. Pulmonary hemorrhage, barotrauma, pneumonitis, asthma, and pulmonary edema have been observed. Pneumomediastinum, pneumothorax, and pneumopericardium result from barotrauma secondary to performance of the Valsalva maneuver after inhalation or nasal insufflation in an attempt to enhance drug effect. Pneumonitis, asthma, and bronchiolitis may be an immunologic phenomenon or may result from numerous adulterants in illicit preparations.

Inhalation of crack cocaine is associated with new-onset bronchospasm, likely the result of local airway irritation. Acute lung injury associated with cocaine use is multifactorial and may be catecholamine-mediated because a similar syndrome has been described in patients with adrenergic excess from pheochromocytoma and intracranial hemorrhage. Upper airway irritation and a "thermal" uvulitis can occur in patients smoking crack cocaine.

GI

Cocaine-induced mesenteric vasospasm may produce intestinal ischemia, bowel necrosis, ischemic colitis, and splenic infarctions. In addition, GI ulceration, bleeding, and perforation occur in association with cocaine use. Advanced tooth decay (termed "meth mouth") is common in habitual methamphetamine users. The reasons are presumably multifactorial and are related to poor oral hygiene, persistent dry mouth, consumption of high-carbohydrate carbonated beverages, jaw clenching, and tooth grinding. The belief that contamination with acidic or corrosive substances from the manufacturing process is responsible for this condition is not supported by analysis of illicitly produced methamphetamine.

ENDOCRINE

MDMA users may develop hyponatremia due to drug-induced secretion of vasopressin in the setting of overhydration with water. There is limited evidence suggesting that synthetic cathinones may cause similar effects, and they have been associated with several deaths.

RENAI

Cocaine or amphetamine use may cause traumatic and nontraumatic rhabdomyolysis. In cocaine-induced rhabdomyolysis, up to one-third of patients develop acute kidney failure. Risk factors for rhabdomyolysis include altered mental status, seizures, dysrhythmias, and hemodynamic instability. Stimulants may further exacerbate renal injury by producing hyperthermia, vasoconstriction, hypotension, and hypovolemia. Renal infarction has been described following IV cocaine use.

PREGNANCY

Cocaine is a potent vasoconstrictor that affects uteroplacental blood flow. Cocaine abuse during pregnancy is associated with an increased incidence of spontaneous abortions, abruptio placentae, fetal prematurity,
and intrauterine growth retardation.\textsuperscript{32,33} Both spontaneous abortions and abruptio placentae appear to occur from placental vasoconstriction and increased uterine contractility, with concomitant maternal hypertension. A breastfed infant can become intoxicated secondary to maternal cocaine use. Methamphetamine abuse during pregnancy has detrimental effects on fetal growth.

**DIAGNOSIS**

Cocaine or amphetamine intoxication can usually be suspected based on the symptoms and signs of the sympathomimetic toxidrome: agitation, mydriasis, diaphoresis, tachycardia, tachypnea, hypertension, and possibly hyperthermia. Mental status can range from normal to severely agitated and paranoid. Lethargy or coma suggests a postictal state or intracranial hemorrhage. Symptoms such as chest pain, palpitations, dyspnea, headache, or focal neurologic complaints suggest end-organ toxicity. Without a history of cocaine or other stimulant use, it may be difficult to distinguish this presentation from other conditions with catecholamine excess, such as withdrawal from alcohol or sedative-hypnotic drugs (Table 187-4). Lactic acidosis may be present following seizures or as a result of vasoconstriction and hypoperfusion. As with all intoxicated patients, consider occult trauma and hypoglycemia.
TABLE 187-4

Differential Diagnosis of Cocaine or Amphetamine Toxicity

<table>
<thead>
<tr>
<th>Toxicologic</th>
<th>Phencyclidine toxicity</th>
<th>Hallucinogen toxicity</th>
<th>Anticholinergic toxicity</th>
<th>Sedative-hypnotic withdrawal</th>
<th>Serotonin syndrome</th>
<th>Neuroleptic malignant syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial</td>
<td>Ischemic stroke</td>
<td>Intracranial hemorrhage</td>
<td>Traumatic brain injury</td>
<td>Encephalitis or meningitis</td>
<td>Cerebral vasculitis</td>
<td>Neoplasm</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Hypoglycemia</td>
<td>Pheochromocytoma</td>
<td>Hyponatremia</td>
<td>Thyrotoxicosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Acute psychosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Heat stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Concomitant use of alcohol and other drugs frequently alters the clinical presentation. For example, a patient using both opioids and stimulants may present with a decreased level of consciousness and few if any other diagnostic features of catecholamine excess. When the opioid effects are reversed with naloxone, the stimulant effects are unmasked, often with impressive findings.

LABORATORY EVALUATION

Laboratory studies and imaging are directed by clinical findings. Obtain a chemistry panel and creatine kinase level in a patient with agitation or elevated temperature to evaluate for possible metabolic acidosis, renal failure, or rhabdomyolysis. Hyponatremia, often with altered mental status, occasionally occurs after the use of hallucinogenic amphetamines such as MDMA or mescaline. For chest pain, obtain an ECG and serum levels of cardiac biomarkers. If the patient is hyperthermic (>104°F or 40°C), coagulation and liver function studies should be performed. Altered mental status typically requires CT of the head.
Urine drug screens to confirm cocaine or amphetamine use are readily available, but interpretation requires knowledge of pharmacology and the testing method. Most of the rapid urine screening tests for cocaine are highly specific for cocaine metabolites (such as benzoylecgonine) and exhibit little cross-reactivity to the parent compound or other metabolites. Commonly available urine drug screens for the cocaine metabolite benzoylecgonine are sensitive at very low levels, and cocaine use within the past 24 to 72 hours is typically detected, depending on dose. Cocaine can be detected in habitual users by more sensitive techniques (radioimmunoassay, gas chromatography) for up to 2 weeks after last use of the drug.

Most urine amphetamine screens detect amphetamine, dextroamphetamine, methamphetamine, and, with decreasing sensitivity, 3,4-methylenedioxyamphetamine, MDMA, and 3,4-methylenedioxyamphetamines. Synthetic cathinones may be detected, but results are too variable to be clinically useful due to variation in both laboratory analyzers as well as "bath salt" preparations. Commercial urine drug screens for amphetamine are sensitive to 1000 nanograms/mL, and amphetamine use within the past 48 hours is usually detected. However, interfering substances and other phenylethylamine compounds cross-react with amphetamine immunoassays, which limits their specificity. For example, excessive use of certain nasal inhalers that contain cross-reacting stimulant-class drugs may lead to positive results on immunoassays. Patients who take the nonprescription decongestants pseudoephedrine or phenylephrine or use prescription stimulants for attention-deficit disorder or narcolepsy can have a positive urine amphetamine result. Many drugs, such as bupropion, chlorpromazine, promethazine, thioridazine, trazodone, desipramine, and doxepin, have metabolites that react with the amphetamine immunoassay. Other drugs, such as labetalol, isomethetepine, ranitidine, ritodrine, and trimethobenzamide, possess enough structural similarity to the basic amphetamine form to react with the immunoassay as well.

**TREATMENT**

Follow the standard protocol for poisoned patients (see chapter 176, "General Management of Poisoned Patients"). Establish IV access, and provide oxygen administration for hypoxia. The cornerstone of therapy is monitoring of vital signs, treatment of medical complications, supportive care, and adequate sedation to prevent self-harm and allow for testing and imaging (Table 187-5). Treat hyperthermia with cool-mist spray and fans or cooling blankets (see chapter 210, "Heat Emergencies"). Aggressive IV hydration is the primary treatment for rhabdomyolysis (see chapter 89, "Rhabdomyolysis"). Seizures are initially treated with benzodiazepines, and status epilepticus requires aggressive treatment (see chapter 171, "Seizures"). Obtain head CT to identify intracranial pathology as the cause of seizures.
Abbreviation: ACS = acute coronary syndrome.

**TABLE 187-5**

**Management of Sympathomimetic Toxicity**

<table>
<thead>
<tr>
<th>Vital sign monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supportive care and prevent self-harm</td>
</tr>
<tr>
<td>Benzodiazepines for sedation</td>
</tr>
<tr>
<td>Aggressive cooling for hyperthermia</td>
</tr>
<tr>
<td>IV fluid for rhabdomyolysis</td>
</tr>
<tr>
<td>Anticonvulsants for seizures</td>
</tr>
<tr>
<td>Evaluate chest pain and treat ACS</td>
</tr>
<tr>
<td>Phentolamine for uncontrolled hypertension</td>
</tr>
<tr>
<td>Targeted therapy for dysrhythmias</td>
</tr>
<tr>
<td>IV lipid emulsion for refractory dysrhythmias</td>
</tr>
</tbody>
</table>

**SEDATION**

Benzodiazepines are the cornerstone of therapy for sedation. Lorazepam, 2 milligrams IV, or diazepam, 5 milligrams IV, can be administered and titrated with repeated doses to decrease the excess autonomic and neural stimulation. Antipsychotics such as haloperidol, droperidol, and chlorpromazine are not first-line therapy because they may lower the seizure threshold, contribute to hyperthermia, and increase QT prolongation and the risk of ventricular dysrhythmias. However, if benzodiazepines are ineffective, antipsychotics are often necessary to control agitation and destructive and dangerous behavior.

**CHEST PAIN**

Chest pain characteristics in cocaine users are no different than in patients with atherosclerotic heart disease. Question chest pain patients about the use of cocaine. Cocaine users with suspected acute coronary syndrome are managed with aspirin and nitroglycerin (see chapter 49, "Acute Coronary Syndromes"). Additional therapy is guided by the ECG. Oral or intravenous calcium channel blockers (diltiazem, 20 milligrams IV) are recommended in patients with ST-segment elevation or depression. Use of β-adrenergic antagonists ("β-blockers") in the management of cocaine-associated myocardial ischemia or infarction is controversial. Case reports suggested that β-blockers may create the potential for unopposed stimulation of α-adrenergic receptors that worsens coronary and peripheral vasoconstriction, hypertension, and possibly ischemia. Conversely, large observational studies of patients with cocaine-related chest pain did not find an increased incidence of adverse effects in patients
Dysrhythmias

Target antidysrhythmic therapy according to the probable pathogenesis of the dysrhythmia. Sinus tachycardia is generally responsive to sedation, cooling, and intravenous fluid rehydration, and specific β-blocker therapy is rarely necessary. Use a calcium channel blocker to treat reentrant supraventricular tachycardia as well as to control the ventricular rate in atrial fibrillation or flutter.

A wide-complex tachycardia with clinical evidence of cocaine toxicity can be assumed to be due to sodium channel blockage and treated with sodium bicarbonate, a 1 to 2 mEq/L IV bolus followed by either intermittent boluses or an infusion. The frequency of boluses or the rate of infusion is guided by clinical response and serum pH; do not alkalinize the serum above a pH of 7.55 with sodium bicarbonate. Lidocaine in standard doses can be used in refractory cases of wide-complex tachycardia; theory and animal models suggest harmful interaction, but clinical experience has documented safety.

Magnesium, lidocaine, and overdrive pacing have all been reported to be successful in cocaine-induced torsades de pointes. It seems reasonable, although unproven, to administer magnesium in patients with a prolonged corrected QT interval to prevent torsades from occurring.

In cases of severe cocaine toxicity, with persistent cardiovascular instability and/or refractory wide-complex tachycardias, intravenous lipid emulsion therapy has been reported to rapidly terminate the dysrhythmia and stabilize the cardiovascular system, although failure has been reported also. No recommendations on dose can be made from such limited clinical experience, so it seems reasonable to use the standard IV 20% lipid protocol developed for local anesthetic systemic toxicity: 100 mL (1.5 mL/kg) IV bolus over 2 to 3 minutes followed by an infusion of 18 mL (0.25 mL/kg) per minute until clinical improvement is seen or a total dose of 10 mL/kg has been given.

Hypertension
Treat severe hypertension not responding to sedation with a sodium nitroprusside infusion (initial dose, 0.3 microgram/kg per minute) or phentolamine (initial dose, 2.5 to 5.0 milligrams IV). Blood pressure may be lowered aggressively if the patient does not have chronic hypertension. Treatment for refractory hypertension is similar to that for hypertensive emergencies except that β-adrenergic blockers are not used (see chapter 57, "Systemic Hypertension").

**BODY STUFFERS AND BODY PACKERS**

Cocaine and other drugs can be internally concealed. Patients who swallow cocaine following police pursuit to conceal the evidence are termed "body stuffers." The swallowed packets are often poorly wrapped and can leak or perforate. "Body packers" swallow a large number of well-sealed packets in order to smuggle drugs across international borders. Both methods can result in severe toxicity and death.

Management of an asymptomatic cocaine body packer brought in by police or customs officials is a treatment dilemma. CT is the best imaging modality to identify the packets. If the patient shows no signs of toxicity, give single-dose activated charcoal and institute whole-bowel irrigation with polyethylene glycol electrolyte solution to gently hasten packet elimination. Continue whole-bowel irrigation until passage of the last packet, and then obtain a confirmatory CT to ensure that all containers have passed. For symptomatic patients, provide sedation and symptomatic care, and obtain immediate surgical consultation for operative removal of the packets. Do not consult for endoscopy or colonoscopy because endoscopic manipulation may rupture the packets.

**DRUG INTERACTIONS**

Because cocaine is metabolized by plasma cholinesterase, co-administration of drugs such as succinylcholine and mivacurium that are also metabolized by plasma cholinesterase may lead to unpredictable rates of metabolism, leading to foreshortened or prolonged effects.

Both lidocaine and cocaine are local anesthetics and act as sodium channel antagonists. It is thought that the neurotoxic effects of both occur by similar mechanisms. Despite theoretical risk in treating cocaine-induced dysrhythmias with lidocaine, it has been used safely in patients with cocaine-associated myocardial infarction.

Monoamine oxidase inhibitors block the degradation of intracellular catecholamines, increasing adrenergic neurotransmitters in the presynaptic terminals. Amphetamines are indirect-acting sympathomimetic amines that induce the release of stored catecholamines and are also weak inhibitors of monoamine oxidase. Thus, patients taking monoamine oxidase inhibitors who subsequently use amphetamines or phenylpropanolamine (and to a lesser extent cocaine) may precipitate an acute syndrome of excessive catecholamine release that results in severe hypertension, tachycardia, hyperthermia, agitation, tremors, and possible severe neurotoxicity.
WITHDRAWAL

Cocaine withdrawal is characterized by irritability, paranoid ideation, and depression. Although symptoms during cocaine withdrawal are generally milder than those during amphetamine withdrawal, psychological addiction may be particularly strong. Methamphetamine withdrawal is characterized by drowsiness, lethargy, hunger, tremor, and chills. There is considerable potential for long-term depression and suicide. Symptoms of withdrawal are strongest during the first 48 hours, but milder symptoms can last up to 2 weeks. Although pharmacologic adjuncts, such as antidepressants, adrenergic antagonists, or dopaminergic agents, are sometimes used during cocaine or amphetamine withdrawal, there are no data confirming efficacy.

DISPOSITION AND FOLLOW-UP

Disposition depends on initial patient presentation, response to therapy, the nature of the stimulant involved, and expected duration of effect. Patients demonstrating resolution of toxicity and clear sensorium in the absence of focal complaints or end-organ damage should be advised of the medical risks of drug abuse and referred to appropriate detoxification, counseling, and social support services.

Patients who present with adrenergic excess following recent cocaine use and who respond to initial sedation may be expected to improve completely during a period of observation in the ED because of the relatively limited duration of cocaine effects. In contrast, amphetamines have a longer duration of effect and produce prolonged toxicity, which necessitates observation or hospitalization.

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[PubMed: 8874243]

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[PubMed: 2221520]

[PubMed: 9929522]

[PubMed: 9547762]

[PubMed: 18174009]

[PubMed: 19865578]

[PubMed: 24176476]


