



# Medical Complications of Cocaine Abuse

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## Substance Abuse Update

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### Abstract

*Cocaine use has increased dramatically in the past ten years and brings with it a broad range of medical complications. Cardiac, pulmonary, neurologic, and infectious complications are common. They may present during evaluation in the emergency department or during psychiatric evaluation of comorbid conditions. Sudden death and severe morbidity are possible during periods of intoxication and withdrawal. Other conditions create long-term health problems that must be addressed in cocaine abusing patients. By understanding the range and significance of possible medical problems, psychiatrists can ensure timely and appropriate evaluation, treatment, and referral to other specialists. Published 1997 by Elsevier Science Inc. MEDICAL UPDATE FOR PSYCHIATRISTS 2;2:34-38, 1997.*

### Introduction

The use of cocaine has expanded dramatically in the past ten years, with 5 million individuals using it on a routine basis. There has also been a marked increase in the use of the more rapidly absorbed "crack" form of freebase cocaine. Cocaine use can lead to a variety of medical problems that include cardiac, pulmonary, neurologic, infectious, and other conditions. Polysubstance use and comorbid psychiatric disorders complicate evaluation and treatment.

Pregnant women represent a special risk group, with more than a third of some population subgroups having drug screens positive for cocaine use.

Cocaine users frequently present to emergency departments with medical complaints, but may also report symptoms of illness during psychiatric evaluation and treatment. In the course of providing care for cocaine users it is important to understand the medical risks associated with its use and to ensure that medical conditions and medical complaints are appropriately addressed and consultation obtained when necessary. The evaluation must be tailored to the individual's risk factors and presenting signs and symptoms. Sudden death is possible, as are cases complicated by potentially fatal medical problems. Rapid and thorough intervention may make a significant difference in outcome.

### Extent of Problem

Cocaine use has increased dramatically during the past decade. It is estimated that 30 million Americans have used cocaine and that 5 million use it regularly. Each day another 5,000 use it for the first time (1). Up to 7% of adults be-

tween the ages of 18 and 34 have used cocaine in the past year (2). It is estimated that in 1990 up to 4.5% of pregnant women between ages 12 and 34 used cocaine; in some populations up to 36% of pregnant females presenting to hospitals had positive urine toxicology screens for cocaine (3). Polydrug use, involving the abuse of cocaine with alcohol, opiates, and nicotine also appears to be rising in several population subgroups, including minority women of childbearing age (4). In one study more than half of all cocaine dependent outpatients presenting for treatment also met criteria for current alcohol dependence (5). Cocaine is also commonly abused concurrently with heroin; intravenous abusers of this combination account for a major new group becoming infected with HIV in several large American cities (4).

### Patterns of Use

Cocaine can be used orally, intranasally, by injection, or by smoking, depending on its chemical form (4). The various forms of cocaine vary in their bioavailability and addictive potential. Cocaine hydrochloride is the form of cocaine that is used intranasally. It cannot be smoked because it decomposes upon heating (1). It is often cut with adulterants: mannitol and lactose provide bulk, caffeine boosts the stimulant effect, and lidocaine or procaine boosts its local anesthetic effect (2). To be smoked, cocaine HCl has to be transformed into its alkaloid forms: "freebase" and "crack." Historically, intranasal use of cocaine has been the most common route of administration. It is estimated that 90% of cocaine users "snort" cocaine. About 30% of cocaine users have smoked crack and less than 10% have injected the drug intravenously. The majority of hospitalized cocaine users report using crack (5).

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## Pharmacology and Pathophysiology

The route of administration alters the rate of absorption, bioavailability, and rate of distribution, which affect the rapidity of onset and intensity and duration of the drug's effects (6). Pulmonary absorption results in the fastest onset, because cocaine is then immediately distributed to peripheral sites and the CNS. Cerebral effects ("rush," "flash") occur within 6 to 8 seconds after smoking cocaine and last 20 min. Peak blood levels are 60% of the same dose given intravenously. Intravenous cocaine reaches the brain in 15 seconds (delayed by passage through the peripheral venous system and pulmonary arterial and venous systems before entering the peripheral arterial system). In intravenous administration 100% of the dose is absorbed. Intranasal insufflation, "Snorting," results in slower, but more sustained absorption. It produces a "high" in 5 min that is not as intense as the "high" produced by smoking or injecting. Blood levels peak in 30 to 60 min and last 90 min. Blood levels achieved are about 20% to 60% of the same dose given intravenously (7).

The reinforcing properties of cocaine, the short duration of action, and rapid absorption all lead to patterns of uncontrollable, compulsive use. Compulsive use leads to tolerance, transition to more dangerous routes of administration, and higher doses of the drug. This pattern greatly increases the possibility of adverse medical complications occurring (1).

Regardless of the route of administration, all forms of cocaine are metabolized similarly. The biologic half-life of cocaine is approximately 1 hour; less than 5% of cocaine is excreted unchanged in the urine. There are two major metabolites of cocaine that account for more than 80% of its breakdown products, benzoylecgonine and ecgonine methyl ester. Benzoylecgonine, produced by spontaneous nonenzymatic hydrolysis in the blood, is found in the urine in high concentrations, and is the major metabolite used in drug testing (2). In chronic users, the metabolites can be detected in urine for up to three weeks. Although previously considered inactive metabolites, they are capable of increasing blood pressure in rats and this effect may contribute to the toxicity of cocaine (8). Less than 10% of

cocaine undergoes oxidative metabolism in the liver to form norcocaine, the only metabolite of cocaine with significant pharmacologic activity. When cocaine is consumed in close proximity with ethanol, a novel metabolite, cocaethylene, is formed in the liver (9). Cocaethylene may be the metabolite responsible for the large, prolonged increase in heart rate that is seen when cocaine and alcohol are consumed together. It may also lengthen cocaine-induced euphoria (4). The biologic effects of this metabolite are currently under intense scrutiny to determine its possible role in deaths associated with cocaine and ethanol abuse (9).

Cocaine serves as a local anesthetic and it blocks reuptake of the monoamine neurotransmitters. Local anesthetic action is mediated by reduced sodium channel conduction during depolarization. Cocaine blocks the reuptake of monoamine neurotransmitters (norepinephrine, dopamine, and serotonin) at the synaptic junctions, resulting in increased neurotransmitter levels. Increased norepinephrine levels result in sympathetic stimulation of the CNS, vasoconstriction, tachycardia, mydriasis, and hyperthermia. In the CNS elevated levels of catecholamines result in increased alertness, increased talkativeness, increased energy, and decreased appetite. Dopamine is the neurotransmitter most frequently implicated in the addictive properties of cocaine, with elevated concentrations in the mesocorticolimbic pathway leading to euphoria, positive reinforcement, and consequent addiction. Long-term use of cocaine may deplete dopamine stores and contribute to the dysphoria that develops during withdrawal and the subsequent craving for the drug.

### Categories of Medical Problems

Cocaine abuse has been associated with cardiac, pulmonary, neurologic, infectious, gastrointestinal, hematologic, and obstetric medical problems, as well as homeostatic disturbances. The method of administration strongly influences the types of medical complications that develop. Most of the knowledge about cocaine toxicity comes from case reports, small series of observed patients, and autopsy studies of cocaine abusers.

Chest pain is a common symptom in cocaine users presenting to the emergency room. Cocaine leads to tachycardia,

hypertension, an increase in myocardial oxygen demand and vasoconstriction, which increases coronary vascular resistance. The combination sets the stage for myocardial ischemia (10, 11). Cocaine users are at increased risk of atherosclerotic coronary artery disease despite their relatively young age. Those with normal coronary arteries are also at increased risk of myocardial infarction, probably caused by vasospasm or thrombosis (12). Myocardial ischemia related to cocaine also appears to occur during the withdrawal period, with a high incidence of asymptomatic ST segment elevation seen during the first few weeks of abstinence (13). Other cardiac complications include depressed myocardial contractility, predisposition to aortic dissection, increased automaticity, and tachyarrhythmias (11).

Pulmonary complications of cocaine use are seen in patients who smoke crack cocaine. Cough, black sputum, hemoptysis, and pleuritic chest pain are the most common complaints (6, 14). Chest pain is often reported within one hour of smoking and is usually worse on deep inspiration. Pulmonary granulomatosis and pulmonary hypertension may result from intranasal and intravenous cocaine use (15). Adulterants such as talc and microcrystalline cellulose may become embedded in the pulmonary interstitium by inhalation or embolize to arterioles and capillaries by intravenous injection. The term "crack lung" has been applied to lung disease characterized by diffuse alveolar infiltrates on chest x-ray, eosinophilia, and alveolar hemorrhage that manifest as chest pain, hemoptysis, and dyspnea. Pneumothorax, pneumomediastinum, and pneumopericardium may occur after smoking using prolonged inspirations with Valsalva's maneuver (16). Acute exacerbations of asthma have been described in both crack and intranasal cocaine users (17).

The most common neurologic complaint among cocaine users is a headache that can occur during intoxication or withdrawal (2). Seizures can also occur at the time of drug use, usually within the first 90 min. Unlike alcohol related seizures, a significant portion of patients with cocaine induced seizures (40%) report that they occurred with their first use of the drug (18). Seizures have been reported to occur in up to 8% of patients seen in emergency departments for cocaine toxicity (19). The seizures are predominantly single, and

generalized, but 20% are focal in onset. Status epilepticus can occur.

Subarachnoid hemorrhage, intracerebral bleed, ischemic stroke, and transient ischemic attacks can also occur with cocaine use (20). The type of cocaine used and the presence of any vascular pathology appear to influence the type of stroke syndrome. Only hemorrhagic stroke has been reported with intravenous cocaine use. Nasal insufflation is associated with hemorrhagic events more often than ischemic events. Ischemic stroke is more common among crack users. Underlying cerebral saccular aneurysms or vascular malformations may be present in up to 50% of cocaine-associated hemorrhagic strokes (21). Concurrent use of alcohol may also contribute to hemorrhagic strokes.

Some infectious diseases are increased in cocaine users. Among these are the sexually transmitted diseases, including HIV infection, gonorrhea, and syphilis. Risk of acquiring HIV infection is especially high among cocaine injectors and crack users. Compared to heroin injectors, cocaine injectors have a higher frequency of use in shooting galleries, increased number of needle sharing partners, less consistent use of bleaching injection paraphernalia, more frequent injection, and more frequent "booting" (drawing blood back into the syringe during injection and then re-injecting it into the vein). They are also more likely to have multiple sexual partners. Crack users are more likely to have multiple sexual partners and to exchange sex for money or drugs (22). All of these behaviors put these two groups of cocaine users at very high risk for acquiring HIV infection as well as other STDs. Additionally, because crack is often smoked in crowded rooms, the potential for transmission of tuberculosis exists (2). Needle sharing also increases the risk of hepatitis and bacterial sepsis (16). Injections can also lead to skin abscesses, phlebitis, cellulitis, septic emboli resulting in pulmonary abscesses, subacute bacterial endocarditis, pneumonia, ophthalmologic infections, and fungal cerebritis (23).

Gastrointestinal complications occur infrequently with cocaine use. An increased incidence of perforated gastroduodenal ulcers in crack users and sporadic cases of colitis in cocaine users has been reported (5). Intestinal ischemia has been reported in several patients

who ingested large quantities of cocaine. The diagnosis of intestinal ischemia should always be considered when a cocaine abuser presents with severe abdominal pain and an elevated white blood cell count. Among individuals who ingest packets of cocaine in smuggling operations there is a high mortality when the packets rupture (16).

The major hematologic complication seen in cocaine users is thrombocytopenia, which may present as an acute, immunopathic, thrombocytopenic purpura-like syndrome that develops from 1 to 21 days after the last cocaine use. Treatment with steroids or splenectomy normalizes platelet counts, supporting the likelihood of an immune etiology (24).

Head and neck problems are common among cocaine users. Dental complications include erosions of the dental enamel and gingival ulceration at the site of application of oral cocaine (2). Additionally, neglect of self care can occur, resulting in multiple dental caries and periodontitis exacerbated by bruxism (23). Intranasal users of cocaine can present with chronic rhinitis, sinusitis, ulceration of the nasal septum, aspiration of nasal septum, midline granuloma, altered olfaction, and optic neuropathy (2, 16). Smoking cocaine can result in laryngeal burns, manifested as hoarseness, stridor, or dysphagia (16). Ophthalmologic complications, such as infectious keratitis and corneal ulcers, may result from frequent eye rubbing because of irritation from crack vapors (5).

Cocaine is used during 10% to 15% of all pregnancies. Its use can cause a host of obstetric complications, to include placental abruption, ruptured ectopic pregnancy, ruptured uterus, maternal seizures, maternal subarachnoid or intracerebral hemorrhage, spontaneous abortion, and a clinical picture that mimics pre-eclampsia (1, 23, 25-27). Decreased uterine and placental blood flow cause fetal hypoxia and acidosis. Cocaine diffuses across the placenta, causing sympathetic stimulation and fetal hypertension (27). The most common perinatal findings associated with cocaine use are prematurity, reduced birth weight, and intrauterine growth retardation. Other findings include necrotizing enterocolitis, bowel ischemia, ileal atresia, limb reduction defects, seizures, cerebral infarcts, brain atrophy, cystic brain lesions, brain atrophy, brain edema, sudden infant death syndrome,

cardiac structural defects, and renal defects (25). Infants without detectable lesions may display developmental delays, learning disabilities, and difficulties maintaining attention. Infants born to mothers who use cocaine prenatally are also at increased risk for acquiring the HIV infection and syphilis (27).

Rhabdomyolysis is present in approximately one-fourth of all cocaine users reporting to emergency rooms with cocaine-related problems and can occur in the absence of muscle symptoms; nephrotoxicity because of rhabdomyolysis is a significant factor in death because of cocaine poisoning (28). Although the exact etiology of cocaine-induced rhabdomyolysis is not known, several studies suggest a close relationship between drug-induced hyperthermia and rhabdomyolysis (28, 29). In one series of patients who developed rhabdomyolysis after cocaine use, hyperthermia was more common in those patients who developed renal failure than in those who did not (28).

Cocaine intoxication and its medical complications lead to a variety of acid-base disturbances. In one series of patients visiting an emergency room for cocaine-related problems, half had abnormal arterial blood gasses. Acidosis was more common than alkalosis. Both respiratory and metabolic etiologies were identified (30).

## Evaluation

Evaluation begins with a careful history of recent and past drug and alcohol use. A specific checklist is often useful to assess for polydrug use, because patients often fail to spontaneously report the full degree of use. Nicotine, caffeine, and over-the-counter medication use should also be assessed because of the tendency of these substances to enhance the effects of cocaine. Past medical history, careful review of systems, and a physical examination with careful attention to the mental status and neurologic components are part of the evaluation of all patients with cocaine-related complaints. Further evaluation will be dependent on the specific problems identified. Because of the potential for sudden death, patients should be initially screened soon after presenting for care.

## Problem Specific Management

### Chest Pain

Any patient presenting with chest pain following cocaine use should be evaluated for the presence of myocardial infarction (MI). Given that silent MI has been demonstrated during the cocaine withdrawal period, some authors suggest admission to a monitored bed for a period of observation (10). Ischemic chest pain should be treated with vasodilators such as nitroprusside and nitroglycerine [(8-13) for reviews]. Cocaine induced hypertension is usually transient, but should be treated when MI is suspected. Propranolol should be avoided because it can paradoxically increase hypertension through unopposed alpha-receptor stimulation. Mixed alpha-1 and beta blockers such as labetalol and pure alpha antagonists such as phentolamine are preferable.

Nitroglycerine is also beneficial through its inhibition of platelet aggregation, endothelial adhesion, macrophage adhesion, and its anticoagulant and fibrinolytic effects (31). Aspirin may also be used to reduce thrombus formation. The use of thrombolytics in these patients is controversial. Although there is a risk of intracerebral hemorrhage after receiving therapy, patients with thrombus formation benefit from treatment and the treatment is generally safe (32).

Management of pulmonary chest pain, cough, hemoptysis, pneumothorax, pneumomediastinum, pneumopericardium, and pulmonary edema is generally supportive. Supplemental oxygen, observation, chest x-ray, and possible bronchoscopic evaluation are the mainstays of treatment. Bronchoalveolar lavage may benefit diagnosis of HIV-related opportunistic infections (14).

### Neurologic Problems

Traditional anticonvulsant agents are less effective in cocaine induced seizures. Intravenous diazepam, phenobarbital loading, and pentobarbital anesthesia may be useful (1, 18). Focal seizures, multiple seizures, prior seizures, and prolonged periods of postictal confusion point to an underlying brain lesion and warrant a full evaluation, including CT scan. The patient with an apparent first cocaine-related seizure also deserves a full work-up and neurology consultation (18).

Cocaine needs to be considered in

the evaluation of stroke in anyone under the age of 40. Symptoms that would warrant neurologic consultation include focal weakness, aphasia, and cranial nerve abnormalities.

The classic presentation for subarachnoid hemorrhage is the worst headache of ones life, possibly accompanied by photophobia, nuchal rigidity, or a third nerve palsy. An emergent CT is the imaging study of choice to show fresh hemorrhage. If the CT does not reveal acute blood, and the clinical presentation suggests a subarachnoid hemorrhage, a lumbar puncture is indicated. A new ischemic event may not be seen on CT. A follow-up MRI would better define the extent of the infarct and any possible edema. Aggressive treatment of systemic hypertension is not warranted in the acute stroke period and could further compromise cerebral perfusion. Neurologic consultation is warranted during this period.

### Obstetric Problems

The most important intervention for pregnant women is education and treatment of their addiction(s). Infections and other medical complications should be evaluated and treated in consultation with an obstetrician.

### Infectious Problems

All cocaine using patients should be carefully questioned concerning their usage patterns, mode of drug administration, and sexual practices. Anyone suspected of needle sharing or unprotected sex should be tested for HIV and other sexually transmitted diseases. History, review of systems, and physical examination would suggest whether testing for hepatitis, tuberculosis, sepsis, endocarditis, or opportunistic infections is indicated.

### Gastrointestinal Problems

Major concern is indicated for individuals who attempt to smuggle cocaine by swallowing packages. Treatment consists of activated charcoal and sorbitol to absorb the released cocaine and facilitate expulsion. Nonstimulant laxatives should be used to prevent rupturing the packets. Endoscopy can be used to remove packets that were recently swallowed. Surgical removal should be re-

served for cases of severe intoxication or gastrointestinal obstruction (23).

### Homeostatic Disturbances

As discussed earlier, hypertension should be treated if myocardial infarction is suspected. Severe hyperthermia may be a harbinger of pending delirium or sudden death and warrants close monitoring and rapid intervention. Treatment includes the use of cooling blankets, infusion of cooled intravenous fluids, gastric lavage, and treatment of agitation using benzodiazepines. In severe cases, intubation and paralysis can provide airway protection and reduce hyperthermia. Rhabdomyolysis may also be present, even in the absence of muscle pain, tenderness, or weakness. In cases of severe intoxication, serum creatinine kinase is indicated, with elevations of more than 1,000 U/L suggestive of clinically significant rhabdomyolysis. Aggressive fluid resuscitation and diuresis may reduce the potential for renal or hepatic damage and other metabolic disturbances. Arterial blood gas abnormalities are usually a marker for metabolic or respiratory disturbances. They signal the need for thorough evaluation of toxic, infectious, or traumatic causes. Respiratory alkalosis may be because of agitation and may respond to benzodiazepine sedation. Respiratory acidosis warns of respiratory suppression and CNS depression, possibly because of other drugs or progressive intracerebral hemorrhage or infarction. Toxicology screen, careful serial mental status, and neurologic examination are indicated, along with CT scan, neurology consultation, and probable transfer to an intensive care setting.

### Conclusions

Cocaine use has expanded in this country during the past decade and has resulted in increased direct and indirect medical complications. Cocaine users are at risk for both short-term and long-term morbidity and mortality. Their medical problems span multiple organ systems, requiring careful history gathering, physical examination, and diagnostic studies. Proper management may require consultation to internists (cardiologists, pulmonologists, and infectious dis-

ease), neurologists, and intensive care specialists. Awareness of common problems and thorough initial assessment will identify patients with a potentially difficult clinical course and ensure appropriate recognition and treatment of their medical problems.

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