469e Cocaine and Other Commonly Abused Drugs

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The abuse of cocaine and other psychostimulants reflects a complex interaction between the pharmacology of the drug, the personality and expectations of the user, and the environmental context in which the drug is used. Polydrug abuse involving the concurrent use of several drugs with different pharmacologic effects is increasingly common. Sometimes one drug is used to enhance the effects of another, as with the combined use of cocaine and nicotine, benzodiazepines and methadone, or cocaine and heroin in methadone-maintained patients. Some forms of polydrug abuse, such as the combined use of IV heroin and cocaine, are especially dangerous and account for many hospital emergency room visits.

Chronic cocaine and psychostimulant abuse may cause a number of adverse health consequences and may exacerbate preexisting disorders such as hypertension and cardiac disease. The combined use of two or more drugs may accentuate medical complications associated with abuse of one drug. Chronic drug abuse is often associated with immune system dysfunction and increased vulnerability to infections, including risk for HIV infection. In addition, concurrent use of cocaine and opiates (the "speedball") is frequently associated with needle sharing by IV drug users. IV drug abusers continue to be the largest single group of persons with HIV infection in several major metropolitan areas in the United States as well as in many parts of Europe and Asia.

Stimulants and hallucinogens have been used to induce euphoria and alter consciousness for centuries. Cocaine and marijuana are two of the most commonly abused drugs today. Synthetic variations of marijuana and a variety of hallucinogens have become popular recently, and new drugs are continually being developed. This chapter describes the subjective and adverse medical effects of cocaine, marijuana, and lysergic acid diethylamide (LSD), as well as methamphetamine, 3,4-methylenedioxy-*N*-methamphetamine (MDMA), synthetic cathinones (bath salts), phencyclidine (PCP), *Salvia divinorum*, and other drugs of abuse (flunitrazepam, γ-hydroxybutyric acid [GHB], ketamine). Some options for medical management of severe adverse effects are also described.

COCAINE

Cocaine is a stimulant and a local anesthetic with potent vasoconstrictor properties. The leaves of the *coca* plant (*Erythroxylum coca*) contain ~0.5–1% cocaine. The drug produces physiologic and behavioral effects after oral, intranasal, IV, or inhalation/smoking routes of administration. The reinforcing effects of cocaine are related to activation of dopaminergic neurons in the mesolimbic system (Chap. 465e). Cocaine increases synaptic concentrations of the monoamine neurotransmitters dopamine, norepinephrine, and serotonin by binding to transporter proteins in presynaptic neurons and blocking reuptake.

PREVALENCE OF COCAINE USE

Cocaine is widely available and is abused in virtually all social and economic strata of society. In 2012, an estimated 1.6 million persons in the United States used cocaine, and 1.1 million abused or were dependent on cocaine. Emergency room admissions involving cocaine totaled 505,224 in 2011. Cocaine abuse is prevalent in the general population and in heroin-dependent persons, including those in methadone maintenance programs. IV cocaine is often used concurrently with IV heroin in a combination called a "speedball." This combination purportedly attenuates the postcocaine "crash" and substitutes a cocaine "high" for the heroin "high" blocked by methadone.

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ACUTE AND CHRONIC INTOXICATION

There has been an increase in both IV administration and inhalation of pyrolyzed cocaine via smoking. Following intranasal administration, changes in mood and sensation are perceived within 3–5 min, and peak effects occur at 10–20 min. These effects rarely last more than 1 h. Inhalation of pyrolyzed materials includes inhaling crack/cocaine or smoking coca paste, a product made by extracting cocaine preparations with flammable solvents, and cocaine free-base smoking. Free-base cocaine, including the free-base prepared with sodium bicarbonate (crack), has become increasingly popular because of its relative high potency and rapid onset of action (8–10 seconds following smoking).

Cocaine produces a brief, dose-related stimulation and euphoria and an increase in cardiac rate and blood pressure. Body temperature usually increases following cocaine administration, and high doses of cocaine may induce lethal pyrexia or hypertension. Because cocaine inhibits reuptake of catecholamines at adrenergic nerve endings, it potentiates sympathetic nervous system activity. Cocaine has a short plasma half-life of approximately 45–60 min. Cocaine is metabolized by plasma esterases, and cocaine metabolites are excreted in urine. The brief duration of the euphorigenic effects of cocaine reported by chronic abusers is probably due to both acute and chronic tolerance. Cocaine may be used as often as two to three times per hour. Alcohol is often used to modulate both the cocaine high and the dysphoria associated with the abrupt disappearance of cocaine's effects. A metabolite of cocaine, cocaethylene, has been detected in blood and urine of persons who concurrently abuse alcohol and cocaine. Cocaethylene induces changes in cardiovascular function similar to those of cocaine alone, and the pathophysiologic consequences of the concurrent abuse of alcohol plus cocaine may be additive.

Cocaine may cause serious medical consequences by any route of administration. The prevalent assumption that cocaine inhalation or IV administration is relatively safe is contradicted by reports of death from respiratory depression, cardiac arrhythmias, and convulsions associated with cocaine use. In addition to generalized seizures, neurologic complications may include headache, ischemic or hemorrhagic stroke, or subarachnoid hemorrhage. Disorders of cerebral blood flow and perfusion in cocaine-dependent persons have been detected with magnetic resonance spectroscopy (MRS). Inhalation of crack cocaine may lead to severe pulmonary disease due to the direct effects of cocaine and to residual contaminants in the smoked material. Hepatic necrosis may occur following chronic crack/cocaine use. Protracted cocaine abuse may also cause paranoid ideation and visual and auditory hallucinations, a state that resembles alcoholic hallucinosis.

Although men and women who abuse cocaine may report that the drug enhances libidinal drive, chronic cocaine use causes significant loss of libido and adversely affects sexual function. Impotence and gynecomastia have been observed in male cocaine abusers, and these abnormalities often persist for long periods following cessation of drug use. Cocaine abuse may produce major derangements in menstrual cycle function including galactorrhea, amenorrhea, and infertility in women and in a rhesus monkey model of cocaine self-administration. Chronic cocaine abuse may cause persistent hyperprolactinemia as a consequence of disordered dopaminergic inhibition of prolactin secretion by the anterior pituitary. Cocaine abuse by pregnant women, particularly crack smoking, has been associated with both an increased risk of congenital malformations in the fetus and perinatal cardiovascular and cerebrovascular disease in the mother. However, cocaine abuse per se is probably not the sole cause of these perinatal disorders, because maternal cocaine abuse is often associated with poor nutrition and prenatal health care as well as polydrug abuse that may contribute to the risk for perinatal disease.

Psychological dependence on cocaine, indicated by inability to abstain from frequent compulsive use, has been reported. Although the occurrence of withdrawal syndromes involving psychomotor agitation and autonomic hyperactivity remains controversial, severe depression ("crashing") following cocaine intoxication may accompany drug withdrawal.