

Treatment of cocaine overdose is a medical emergency that is best managed in an intensive care unit. Cocaine toxicity produces a hyperadrenergic state characterized by hypertension, tachycardia, tonic-clonic seizures, dyspnea, and ventricular arrhythmias. IV diazepam in doses up to 0.5 mg/kg administered over an 8-h period has been shown to be effective for control of seizures. Ventricular arrhythmias have been managed successfully by administration of 0.5–1.0 mg of propranolol IV. Because many instances of cocaine-related mortality have been associated with concurrent use of other illicit drugs (particularly heroin), the physician must be prepared to institute effective emergency treatment for multiple drug toxicities.

Treatment of chronic cocaine abuse requires the combined efforts of primary care physicians, psychiatrists, and psychosocial care providers. Early abstinence from cocaine use is often complicated by symptoms of depression and guilt, insomnia, and anorexia, which may be as severe as those observed in major affective disorders. Individual and group psychotherapy, family therapy, and peer group assistance programs are often useful for inducing prolonged remission from drug use. Although psychotherapy may be helpful, no specific form of psychotherapy or behavioral modification is uniquely beneficial.

A number of medications used for the treatment of various medical and psychiatric disorders have been administered to reduce the duration and severity of cocaine abuse and dependence. The search for a medication that is both safe and highly effective for cocaine detoxification or maintenance of abstinence is continuing. Clinical trials of buspirone (BuSpar), a nonbenzodiazepine anxiolytic with dopamine D₃ and D₄ receptor antagonist properties, are ongoing. Buspirone reduced use of cocaine, nicotine, and cocaine plus nicotine in combination in a nonhuman primate model of stimulant addiction.

Another approach to reducing cocaine abuse is the development of vaccines to actively immunize against cocaine or to functionally antagonize cocaine by preventing it from reaching the brain. Cocaine is converted into inactive metabolites by the plasma enzyme, butyrylcholinesterase (BChE). When this enzyme is modified to increase its catalytic efficiency and accelerate cocaine metabolism, it can both prevent and reverse cocaine-induced toxicity in animals. Importantly, it remains effective even when high doses of cocaine are administered. Ongoing development of this approach includes cocaine hydrolase gene therapy. Vaccines for both cocaine and nicotine have been designed and shown to be safe and somewhat effective in clinical trials. Individual variability in antibody titers and difficulties in determining the optimally effective antibody titer that will neutralize responses to increasing doses of cocaine and have a relatively long duration of action are among the challenges that remain to be resolved.

MARIJUANA AND CANNABIS COMPOUNDS

Cannabis sativa contains >400 compounds in addition to the psychoactive substance, delta-9-tetrahydrocannabinol (THC). Marijuana cigarettes are prepared from the leaves and flowering tops of the plant, and a typical marijuana cigarette contains 0.5–1 g of plant material. The usual THC concentration varies between 10 and 40 mg, but concentrations <100 mg per cigarette have been detected. Hashish is prepared from concentrated resin of *C. sativa* and contains a THC concentration of between 8 and 12% by weight. “Hash oil,” a lipid-soluble plant extract, may contain THC between 25 and 60% and may be added to marijuana or hashish to enhance its THC concentration. Smoking is the most common mode of marijuana or hashish use. During pyrolysis, <150 compounds in addition to THC are released in the smoke. Although most of these compounds do not have psychoactive properties, they may have physiologic effects.

THC is quickly absorbed from the lungs into blood and then rapidly sequestered in tissues. THC is metabolized primarily in the liver, where

it is converted to 11-hydroxy-THC, a psychoactive compound, and >20 other metabolites. Many THC metabolites are excreted through the feces at a relatively slow rate of clearance compared with most other psychoactive drugs.

Specific cannabinoid receptors (CB₁ and CB₂) have been identified in the central and peripheral nervous system. High densities of cannabinoid receptors have been found in the cerebral cortex, basal ganglia, and hippocampus. T and B lymphocytes also contain cannabinoid receptors, and these appear to mediate the anti-inflammatory and immunoregulatory properties of cannabinoids. A naturally occurring THC-like ligand has been identified and is widely distributed in the nervous system.

Herbal marijuana alternatives are also available. These are usually a combination of several herbs and synthetic cannabinoids. “Spice” and “K2” are among the best known, but many formulations exist, and marijuana is undetectable by the usual methods. These compounds are marketed on the Internet as containing no illegal ingredients. However a number of synthetic cannabinoids are now classified as Schedule I by the Drug Enforcement Administration due to reports of toxicity.

PREVALENCE OF USE

Marijuana is the most commonly used illegal drug in the United States. In 2012, an estimated 18.9 million people reported using marijuana within the past month. An estimated 7.2% of adolescents age 12 to 17 years reported current use of marijuana. Marijuana is relatively inexpensive and is often considered to be less hazardous than other controlled drugs and substances. Very potent forms of marijuana (sinsemilla) are widely available, and concurrent use of marijuana with other drugs such as cocaine is not uncommon. Due in part to the difficulty of detecting herbal marijuana alternatives, the prevalence of use is unknown.

ACUTE AND CHRONIC INTOXICATION

Acute intoxication from marijuana and cannabis compounds is related to both the dose of THC and the route of administration. THC is absorbed more rapidly from marijuana smoking than from orally ingested cannabis compounds. Acute marijuana intoxication may produce a perception of relaxation and mild euphoria resembling mild to moderate alcohol intoxication. This condition is usually accompanied by some impairment in thinking, concentration, and perceptual and psychomotor function. Higher doses of cannabis may produce more pronounced impairment in concentration and perception, as well as greater sedation. Although the acute effects of marijuana intoxication are relatively benign in normal users, the drug can precipitate severe emotional disorders in individuals who have antecedent psychotic or neurotic problems. Like other psychoactive compounds, both the user’s expectations and the environmental context are important determinants of the type and severity of the effects of marijuana intoxication.

As with abuse of cocaine, opioids, and alcohol, chronic marijuana abusers may lose interest in common socially desirable goals and devote progressively more time to drug acquisition and use. However, THC does not cause a specific and unique “amotivational syndrome.” The range of symptoms sometimes attributed to marijuana use is difficult to distinguish from mild to moderate depression and the maturational dysfunctions often associated with protracted adolescence. Chronic marijuana use has also been reported to increase the risk of psychotic symptoms in individuals with a past history of schizophrenia. Persons who begin marijuana smoking before the age of 17 may have more pronounced cognitive deficits and also may be at higher risk for polydrug and alcohol abuse problems in later life, but the role of marijuana in this sequence is uncertain.

The acute effects of herbal marijuana alternatives are based primarily on case reports and include anxiety, agitation, delusions, paranoia, and psychosis. The extent to which these symptoms reflect drug effects or exacerbation of an underlying psychiatric disorder is often difficult to determine.

PHYSICAL EFFECTS

Conjunctival injection and tachycardia are the most frequent immediate physical concomitants of smoking marijuana. Tolerance for