marijuana-induced tachycardia develops rapidly among regular users. However, marijuana smoking may precipitate angina in persons with a history of coronary insufficiency. Exercise-induced angina may increase after marijuana use to a greater extent than after tobacco cigarette smoking. Patients with cardiac disease should be strongly advised not to smoke marijuana or use cannabis compounds.

Significant decrements in pulmonary vital capacity have been found in regular daily marijuana smokers. Because marijuana smoking typically involves deep inhalation and prolonged retention of marijuana smoke, chronic bronchial irritation may develop. Impairment of single-breath carbon monoxide diffusion capacity (DL_{CO}) is greater in persons who smoke both marijuana and tobacco than in tobacco smokers.

Although marijuana has also been associated with a number of other adverse effects, many of these studies await replication and confirmation. A reported correlation between chronic marijuana use and decreased testosterone levels in males has not been confirmed. Decreased sperm count and sperm motility and morphologic abnormalities of spermatozoa following marijuana use have been reported. Prospective studies found a correlation between impaired fetal growth and development and heavy marijuana use during pregnancy. Marijuana has also been implicated in derangements of the immune system; in chromosomal abnormalities; and in inhibition of DNA, RNA, and protein synthesis; however, these findings have not been confirmed or related to any specific physiologic effect in humans. Herbal marijuana alternatives produce many of the effects of marijuana including conjunctival injection and tachycardia.

TOLERANCE AND PHYSICAL DEPENDENCE

Habitual marijuana users may develop tolerance to the psychoactive effects of marijuana, and then smoke more frequently and try to acquire more potent cannabis compounds. Tolerance for the physiologic effects of marijuana develops at different rates; e.g., tolerance develops rapidly for marijuana-induced tachycardia but more slowly for marijuana-induced conjunctival injection. Tolerance for both behavioral and physiologic effects of marijuana decreases rapidly upon cessation of marijuana use.

A distinct withdrawal syndrome has been documented in chronic cannabis users, and the severity of symptoms is related to dosage and duration of use. These symptoms typically reach their peak several days after cessation of chronic use and include irritability, anorexia, and sleep disturbances. Withdrawal signs and symptoms observed in chronic marijuana users are usually relatively mild in comparison to those observed in heavy opioid or alcohol users and rarely require medical or pharmacologic intervention. However, more severe and protracted abstinence syndromes may occur after sustained use of high-potency cannabis compounds. As yet there have been no systematic studies of tolerance and physical dependence to the herbal marijuana alternatives. The large number of synthetic cannabinoids available for combination with about 20 herbs presents a daunting challenge for analysis.

THERAPEUTIC USE OF MARIJUANA

Marijuana, administered as cigarettes or as a synthetic oral cannabinoid (dronabinol), is thought to have a number of clinically useful medicinal properties. These include antiemetic effects in chemotherapy recipients, appetite-promoting effects in AIDS patients, reduction of intraocular pressure in glaucoma, and reduction of spasticity in multiple sclerosis and other neurologic disorders. With the possible exception of AIDS-related cachexia, none of these attributes of marijuana compounds is clearly superior to other readily available therapies.

METHAMPHETAMINE

Methamphetamine is also referred to as "meth," "speed," "crank," "chalk," "ice," "glass," or "crystal." Methamphetamine is a mixed-action monoamine releaser with activity at dopamine, serotonin, and norepinephrine systems. Methamphetamine was considered second only to cocaine as a drug threat to society by the U.S. Department of Justice in 2009. Hospital admissions for methamphetamine treatment more than doubled between 1998 and 2007, and young adults (age 18–25) have the highest use rates. In 2011, an estimated 439,000 people reported current use of methamphetamine in the United States, and emergency room admissions involving amphetamines/methamphetamine totaled 160,000. Persistent abuse of methamphetamine continues despite drug seizures, closures of clandestine laboratories that produce methamphetamine illegally, and an increase in methamphetamine abuse prevention programs.

Methamphetamine can be used by smoking, snorting, IV injection, or oral administration. Methamphetamine abusers report that drug use induces feelings of euphoria and decreased fatigue. Adverse consequences of methamphetamine use include headache, difficulty concentrating, diminished appetite, abdominal pain, vomiting or diarrhea, disordered sleep, paranoid or aggressive behavior, and psychosis. Chronic methamphetamine abuse can result in severe dental caries, described as blackened, rotting, crumbling teeth. Severe, life-threatening methamphetamine toxicity may include hypertension, cardiac arrhythmia or cardiac failure, subarachnoid hemorrhage, ischemic stroke, intracerebral hemorrhage, convulsions, or coma.

Methamphetamines increase the release of monoamine neurotransmitters (dopamine, norepinephrine, and serotonin) from presynaptic neurons. It is thought that the euphoric and reinforcing effects of this class of drugs are mediated through dopamine and the mesolimbic system, whereas the cardiovascular effects are related to norepinephrine. MRS studies of the brain suggest that chronic abusers have neuronal damage in the frontal areas and basal ganglia.

Treatment of acute methamphetamine overdose is largely symptomatic. Ammonium chloride may be useful to acidify the urine and enhance clearance of the drug. Hypertension may respond to sodium nitroprusside or α-adrenergic antagonists. Sedatives may reduce agitation and other signs of central nervous system hyperactivity. Treatment of chronic methamphetamine dependence may be accomplished in either an inpatient or outpatient setting using strategies similar to those described earlier for cocaine abuse.

MDMA is a derivative of methamphetamine also called *Ecstasy* or *Molly*. Reported use of MDMA in the United States has increased from 615,000 persons in 2005, to an estimated 869,000 people in 2012. Emergency ward admissions involving MDMA totaled more than 22,000 in 2011. Ecstasy is usually taken orally but may be injected or inhaled, and its effects last for 3–6 h. MDMA has amphetamine-like effects including vivid visual and auditory hallucinations and other perceptual distortions. Recent studies indicate that MDMA use is associated with cognitive and memory impairment. MDMA can induce hyperthermia and elevated blood pressure, seizures, comma, and death. Withdrawal symptoms after cessation of use may include teeth grinding, anxiety, loss of appetite, insomnia, and fever. The long-term consequences of recreational use of MDMA by young persons are poorly understood.

SYNTHETIC CATHINONES (BATH SALTS)

The rapid emergence of synthetic cathinone abuse during 2010 was accompanied by numerous reports of adverse medical and psychiatric effects, suicides, and deaths. Reports to poison centers and health agencies increased from about 300 in 2010 to over 6000 in 2011. In 2011, the Drug Enforcement Administration classified three commonly abused synthetic cathinones (mephedrone [4-methyl methcathinone], MDPV [3,4-methylenedioxy pyrovalerone], and methylone) as Schedule I compounds with no accepted medical use and a high potential for abuse. However, synthetic cathinones are readily available on the Internet as well as in convenience stores, gas stations, and head shops. These drugs are merchandised under a variety of names such as Vanilla Sky, Purple Wave, Blue Silk, White Lightening, and Snow Leopard. Regulatory constraints are evaded by labeling the products as plant food, insecticides, pond cleaner, and bath salts with the qualifier, "not for human consumption."

Cathinone is the primary psychoactive ingredient in khat leaves. Chewing the leaves of the khat shrub (*Catha edulis*) produces mild