

to national surveys, use of methamphetamine fell to approximately 350,000 users in 2010, a decrease of more than 50% since 2006. Methamphetamine acts by releasing dopamine in the brain, which inhibits presynaptic neurotransmission at corticostriatal synapses, slowing glutamate release. Methamphetamine produces a feeling of euphoria, which is followed by a “crash.” Long-term use leads to violent behaviors, confusion, and psychotic features that include paranoia and hallucinations.

MDMA. MDMA (3,4 methylenedioxymethamphetamine) is popularly known as *ecstasy*. MDMA is used mainly by young people between the ages of 14 and 34 years in North America, Europe, and Australia. It is generally taken orally. Its effects, which include euphoria and hallucinogen-like feelings that last 4 to 6 hours, are partly attributable to an increase in serotonin release in the CNS. As the drug wears off, this increased release coupled with its ability to interfere with serotonin synthesis causes a subsequent a post-use drop in serotonin that is only slowly replenished. MDMA use also reduces the number of serotonergic axon terminals in the striatum and the cortex, and it may increase the peripheral effects of dopamine and adrenergic agents. MDMA tablets may be spiked with other drugs, including methamphetamine and cocaine, which greatly enhance the effects on the CNS.

Marijuana

It is estimated that between 2.6% to 5% of adults worldwide (119 million to 224 million people) used marijuana (or “pot”) in 2010, making it far and away the most widely used illicit drug globally. Several states in the United States have legalized the “recreational” use of marijuana in 2013, and more appear poised to follow; thus, its status as an illicit drug is undergoing reevaluation.

Marijuana is made from the leaves of the *Cannabis sativa* plant, which contain the psychoactive substance Δ^9 -tetrahydrocannabinol (THC). About 5% to 10% of THC is absorbed when it is smoked in a hand-rolled cigarette (“joint”). Despite numerous studies, the central question of whether the drug has persistent adverse physical and functional effects remains unresolved. Some of the untoward anecdotal effects may be allergic or idiosyncratic reactions or possibly related to contaminants in the preparations rather than to the pharmacologic effects of marijuana. Among the beneficial effects of marijuana is its potential use to treat nausea secondary to cancer chemotherapy and as an agent capable of decreasing pain in some chronic conditions that are otherwise difficult to treat. The functional and organic CNS consequences of marijuana smoking have received most scrutiny. Its use distorts sensory perception and impairs motor coordination, but these acute effects generally clear in 4 to 5 hours. With continued use these changes may progress to cognitive and psychomotor impairments, such as inability to judge time, speed, and distance, a potential cause of automobile accidents. Marijuana increases the heart rate and sometimes blood pressure, and it may cause angina in a person with coronary artery disease.

The respiratory system is also affected by chronic marijuana smoking; laryngitis, pharyngitis, bronchitis, cough and hoarseness, and asthma-like symptoms have all been described, along with mild but significant airway

obstruction. Marijuana cigarettes contain a large number of carcinogens that are also present in tobacco. Smoking a marijuana cigarette, compared with a tobacco cigarette, is associated with a threefold increase in the amount of tar inhaled and retained in the lungs, presumably because of the larger puff volume, deeper inhalation, and longer breath holding.

In addition to the use of THC as a recreational drug, a large number of studies have characterized the *endogenous cannabinoid system*, which consists of the *cannabinoid receptors CB1 and CB2*, and the endogenous lipid ligands known as *endocannabinoids*. This system participates in the regulation of the hypothalamic-pituitary-adrenal axis, and modulates the control of appetite, food intake, and energy balance, as well as fertility and sexual behavior.

Other Drugs

The variety of drugs that have been tried by those seeking “new experiences” (e.g., “highs,” “lows,” “out-of-body experiences”) defies belief. These drugs include various stimulants, depressants, analgesics, and hallucinogens (Table 9-6). Among these are PCP (phencyclidine, an anesthetic agent), analgesics such as Vicodin, and ketamine, an anesthetic agent used in animal surgery. Most drugs of abuse are used by males more often than by females. The exception is prescription tranquilizers, which are abused by women about twice as often as by men and which often lead to chronic dependencies.

Chronic inhalation of vapors of spray paints, paint thinners, and some glues that contain toluene (“glue sniffing” or “huffing”) can cause cognitive abnormalities and magnetic resonance imaging–detectable brain damage that ranges from mild to severe dementia. Because inhalants are used haphazardly and in various combinations, not much is known about the long-time deleterious effects of most of these agents. However, their acute effects are clear: they cause bizarre and often aggressive behavior that leads to violence or depressed mood and suicidal ideation.

New drugs of abuse emerge yearly. An example is so-called *bath salts*, intentionally misnamed substances that appeared in 2010 and have nothing to do with bathing. Bath salts usually contain 4-methyl-meth-cathinone and methylenedioxypropylvalerone, chemicals that have amphetamine-like effects when snorted or eaten. Bath salts have been associated with agitation, psychosis, myocardial infarction, and suicide. They will no doubt be declared illegal, only to be replaced by the next generation of illicit “designer” drugs.

KEY CONCEPTS

Drug Injury

- Drug injury may be caused by therapeutic drugs (adverse drug reactions) or nontherapeutic agents (drug abuse).
- Antineoplastic agents, anticoagulants, MHT preparations and oral contraceptives, acetaminophen, and aspirin are among the therapeutic drugs involved most frequently.
- MHT increases the risk of endometrial and breast cancers and thromboembolism and does not appear to protect against ischemic heart disease. Oral contraceptives have a protective effect against endometrial and ovarian cancers