

both epinephrine and norepinephrine while stimulating the presynaptic release of norepinephrine. The net effect is the accumulation of these two neurotransmitters in synapses, resulting in excess stimulation, manifested by *tachycardia*, *hypertension*, and *peripheral vasoconstriction*. Cocaine may also induce *myocardial ischemia* by causing *coronary artery vasoconstriction* and by enhancing platelet aggregation and thrombus formation. Cigarette smoking potentiates cocaine-induced coronary vasospasm. Thus, the dual effect of cocaine, causing increased myocardial oxygen demand by its sympathomimetic action, and, at the same time, decreasing coronary blood flow, sets the stage for myocardial ischemia that may lead to myocardial infarction. Cocaine can also precipitate *lethal arrhythmias* by enhanced sympathetic activity as well as by disrupting normal ion ( $K^+$ ,  $Ca^{2+}$ ,  $Na^+$ ) transport in the myocardium. These toxic effects are not necessarily dose related, and a fatal event may occur in a first time user with what is a typical mood-altering dose.

- **CNS.** The most common acute effects on the CNS are hyperpyrexia (thought to be caused by aberrations of the dopaminergic pathways that control body temperature) and seizures.
- **Effects on pregnancy.** In pregnant women, cocaine may cause acute decreases in blood flow to the placenta, resulting in fetal hypoxia and spontaneous abortion. Neurologic development may be impaired in the fetus of pregnant women who are chronic drug users.
- **Other effects.** Chronic cocaine use may cause (1) perforation of the nasal septum in snorters, (2) decreased lung diffusing capacity in those who inhale the smoke, and (3) development of dilated cardiomyopathy.

### Opiates

In 2010, there were an estimated 13 to 21 million users of opiates worldwide, with the highest levels of use being in North America (an estimated 4% of people between 15 and 64 years of age). Opiate drugs of abuse include synthetic prescription opiates such as oxycodone (OxyContin) and "street drugs," most notably heroin. Heroin is an addictive opioid derived from the poppy plant that is closely related to morphine. Its use is even more harmful than that of cocaine. As sold on the street, it is cut (diluted) with an agent (often talc or quinine); thus, the size of the dose is not only variable but also usually unknown to the buyer. Heroin, along with any contaminating substances, is usually self-administered intravenously or subcutaneously. The effects on the CNS are varied and include euphoria, hallucinations, somnolence, and sedation. Heroin has a wide range of other adverse physical effects related to (1) the pharmacologic action of the agent, (2) reactions to the cutting agents or contaminants, (3) hypersensitivity reactions to the drug or its adulterants (quinine itself has neurologic, renal, and auditory toxicity), and (4) diseases contracted incident to the use of contaminated needles. Some of the most important adverse effects of heroin follow:

- **Sudden death.** Sudden death, usually related to overdose, is an ever-present risk, because drug purity is generally unknown (ranging from 2% to 90%). The yearly mortality among heroin users in the United States is estimated

to be between 1% and 3%. Sudden death can also occur if heroin is taken after tolerance for the drug, built up over time, is lost (as during a period of incarceration). The mechanisms of death include profound respiratory depression, arrhythmia and cardiac arrest, and severe pulmonary edema.

- **Pulmonary injury.** Pulmonary complications include moderate to severe edema, septic embolism from endocarditis, lung abscess, opportunistic infections, and foreign-body granulomas from talc and other adulterants. Although granulomas occur principally in the lung, they are sometimes found in the mononuclear phagocyte system, particularly in the spleen, liver, and lymph nodes that drain the upper extremities. Examination under polarized light often highlights trapped talc crystals, sometimes enclosed within foreign-body giant cells.
- **Infections.** Infectious complications are common. The four sites most commonly affected are the skin and subcutaneous tissue, heart valves, liver, and lungs. In a series of addicted patients admitted to the hospital, more than 10% had endocarditis, which often takes a distinctive form involving right-sided heart valves, particularly the tricuspid. Most cases are caused by *S. aureus*, but fungi and a multitude of other organisms have also been implicated. Viral hepatitis is the most common infection among addicted persons and is acquired by the sharing of dirty needles. In the United States, this practice has also led to a very high incidence of HIV infection in intravenous drug abusers.
- **Skin.** Cutaneous lesions are probably the most frequent telltale sign of heroin addiction. Acute changes include abscesses, cellulitis, and ulcerations due to subcutaneous injections. Scarring at injection sites, hyperpigmentation over commonly used veins, and thrombosed veins are the usual sequelae of repeated intravenous inoculations.
- **Kidneys.** Kidney disease is a relatively common hazard. The two forms most frequently encountered are amyloidosis (generally secondary to skin infections) and focal and segmental glomerulosclerosis; both induce proteinuria and the nephrotic syndrome.

Abuse of oxycodone, an oral opiate available by prescription for treatment of pain, has increased sharply in recent years in the United States. According to the National Institute of Drug Abuse, approximately 5% of high school seniors took oxycodone in the year 2010, sometimes with tragic results due to the potent respiratory suppressant effect of the drug. The overall number of yearly fatalities attributed to abuse of prescription opiates in the United States rose from approximately 3000 in 1999 to approximately 12,000 deaths in 2008. Most of this increase is attributable to abuse of oxycodone, which has surpassed heroin as the leading cause of opiate-related death in the United States.

### Amphetamines and Related Drugs

**Methamphetamine.** This addictive drug, known as "speed" or "meth," is closely related to amphetamine but has stronger effects in the CNS. Methamphetamine use rose rapidly in the United States in the early 2000s, peaking in the year 2005, but has fallen steadily since that time. According