

Proprietary analgesic mixtures of aspirin and phenacetin or its active metabolite, acetaminophen, when taken over several years, can cause tubulointerstitial nephritis with renal papillary necrosis, referred to as *analgesic nephropathy* (Chapter 20).

Injury by Nontherapeutic Agents (Drug Abuse)

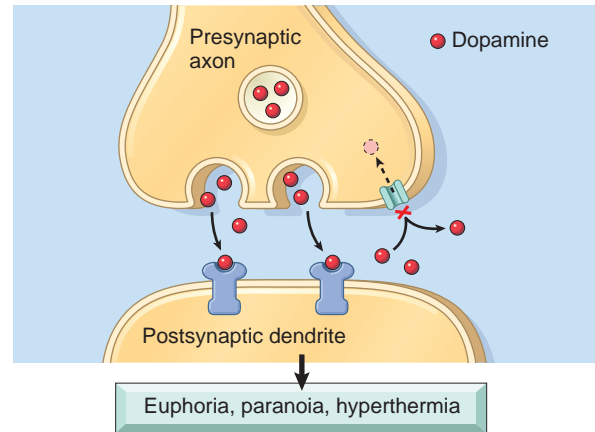
According to the United Nations Office on Drugs and Crime, it is estimated in the year 2010 approximately 153 million to 300 million people between 15 and 64 years of age used an illicit substance at least once. In most instances, occasional users of illicit “recreational” drugs suffer no apparent long-term health effects, but (depending on the drug) acute effects may take a significant toll in the form of accidents, violence, or even fatal drug-related complications. Drug abuse generally involves the repeated or chronic use of mind-altering substances, beyond therapeutic or social norms, and may lead to drug addiction and overdose, both serious public health problems. Common drugs of abuse are listed in Table 9-6. Considered here are cocaine, heroin, amphetamines, and marijuana, among others.

Cocaine

Globally, cocaine use is greatest in North America, Western and Central Europe, Australia, and New Zealand; in each of these countries, it is estimated from 1% to 2% of adults younger than age 65 years used cocaine in 2010. According to national surveys, the numbers of users in the United States has decline substantially in recent years, from approximately 2.4 million in 2006 to approximately 1.5 million in 2010.

Cocaine is extracted from the leaves of the coca plant, and is usually prepared as a water-soluble powder, cocaine

CENTRAL NERVOUS SYSTEM SYNAPSE



SYMPATHETIC NEURON-TARGET CELL INTERFACE

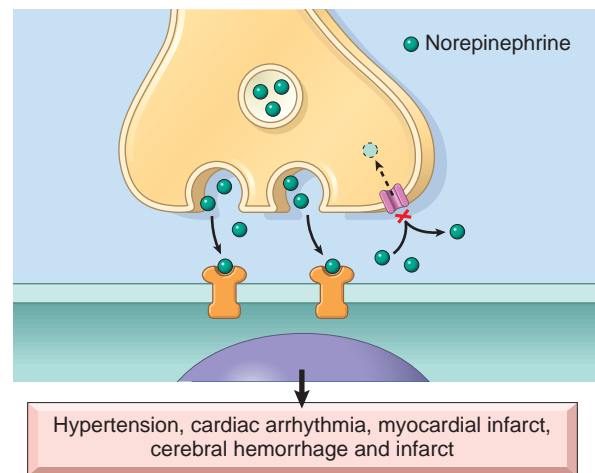


Figure 9-15 The effect of cocaine on neurotransmission. The drug inhibits reuptake of the neurotransmitters dopamine and norepinephrine in the central and peripheral nervous systems.

hydrochloride. Sold on the street, it is liberally diluted with talcum powder, lactose, or other look-alikes. Cocaine can be snorted or dissolved in water and injected subcutaneously or intravenously. Crystallization of the pure alkaloid yields nuggets of *crack*, so called because of the cracking or popping sound it makes when heated to produce vapors that are inhaled. The pharmacologic actions of cocaine and crack are identical, but crack is far more potent.

Cocaine produces an intense euphoria and stimulation, making it one of the most addictive drugs. Experimental animals will press a lever more than 1000 times and forgo food and drink to obtain it. In the cocaine user, although physical dependence generally does not occur, the psychological withdrawal is profound and can be extremely difficult to treat. Intense cravings are particularly severe in the first several months after abstinence and can recur for years.

The acute and chronic effects of cocaine on various organ systems are as follows:

- **Cardiovascular effects.** The most serious physical effects of cocaine relate to its acute action on the cardiovascular system, where it behaves as a sympathomimetic (Fig. 9-15). It facilitates neurotransmission both in the CNS, where it blocks the reuptake of dopamine, and at adrenergic nerve endings, where it blocks the reuptake of

Table 9-6 Common Drugs of Abuse

Class	Molecular Target	Example
Opioid narcotics	Mu opioid receptor (agonist)	Heroin, Hydromorphone (Dilaudid) Oxycodone (OxyContin) Methadone (Dolophine) Meperidine (Demerol)
Sedative-hypnotics	GABA _A receptor (agonist)	Barbiturates Ethanol Methaqualone (Quaalude) Glutethimide (Doriden) Ethchlorvynol (Placidyl)
Psychomotor stimulants	Dopamine transporter (antagonist) Serotonin receptors (toxicity)	Cocaine Amphetamines 3,4-methylenedioxymethamphetamine (MDMA, ecstasy)
Phencyclidine-like drugs	NMDA glutamate receptor channel (antagonist)	Phencyclidine (PCP, angel dust) Ketamine
Cannabinoids	CBI cannabinoid receptors (agonist)	Marijuana Hashish
Hallucinogens	Serotonin 5-HT ₂ receptors (agonist)	Lysergic acid diethylamide (LSD) Mescaline Psilocybin

GABA, γ -aminobutyric acid; 5-HT₂, 5-hydroxytryptamine; NMDA, *N*-methyl *D*-aspartate. From Hyman SE: A 28-year-old man addicted to cocaine. JAMA 286:2586, 2001.