proximity to the ingestion of ethanol produce the metabolite cocaethylene, which has also been implicated in cocaine-related deaths.

Cocaine blocks the presynaptic reuptake of norepinephrine and dopamine, producing an excess of these neurotransmitters at the site of the postsynaptic receptor. Thus, cocaine acts as a powerful sympathomimetic agent, resulting in tachycardia, hypertension, tachypnea, hyperthermia, agitation, pupillary dilation, peripheral vasoconstriction, and seizures. Cocaine causes potent vasoconstriction of cerebral arteries and, therefore, may result in a stroke. It is associated with myocardial ischemia and arrhythmias and, in rare cases, with myocardial infarction in young persons with normal or only minimally diseased coronary arteries. The principal mechanisms of ischemia and infarction are coronary arterial vasoconstriction, thrombosis, platelet aggregation, tissue plasminogen activator inhibition, increased myocardial oxygen demand, and accelerated atherosclerosis (Fig. 126-5).

For patients with cocaine-induced hypertension or tachycardia, labetalol and benzodiazepines are usually effective in lowering systemic arterial pressure and heart rate. Patients with acute myocardial infarction should receive aspirin, heparin, nitroglycerin, and, if indicated, reperfusion therapy (with a thrombolytic agent or primary coronary intervention). The use of β-adrenergic blockers should be avoided, since ischemia may be worsened by unopposed α-adrenergically mediated coronary arterial vasoconstriction. Patients with a normal electrocardiogram or nonspecific changes can be managed safely with observation.

The immediate treatment of acute cocaine intoxication includes obtaining vascular and airway access, if needed, and careful electrocardiographic monitoring. Benzodiazepines can be given to control CNS agitation; haloperidol or risperidone can be used in the severely agitated patient. A supportive environment is needed, but detoxification is not required, given that few physical signs of true dependence are present.

Most chronic cocaine abusers have psychological dependence and an intense craving for cocaine. Personal and group therapies are important adjuncts to pharmacologic treatment, but relapse is common and is difficult to manage. Although no medication is FDA approved for treatment of cocaine addiction, disulfiram, modafinil, anticonvulsants (e.g., topiramate and tiagabine), serotonin reuptake inhibitors (e.g., citalopram), serotonin receptor antagonists (e.g., ondansetron), and GABA receptor agonists (e.g., baclofen) have shown some promise in promoting cocaine abstinence.

Cannabis

The cannabinoid drugs include marijuana (the dried flowering tops and stems of the hemp plant) and hashish (a resinous extract of the hemp plant). Marijuana is the most commonly used illicit drug in the United States. (It has been recently legalized for recreational use in Alaska, Colorado, Oregon, and Washington.) In

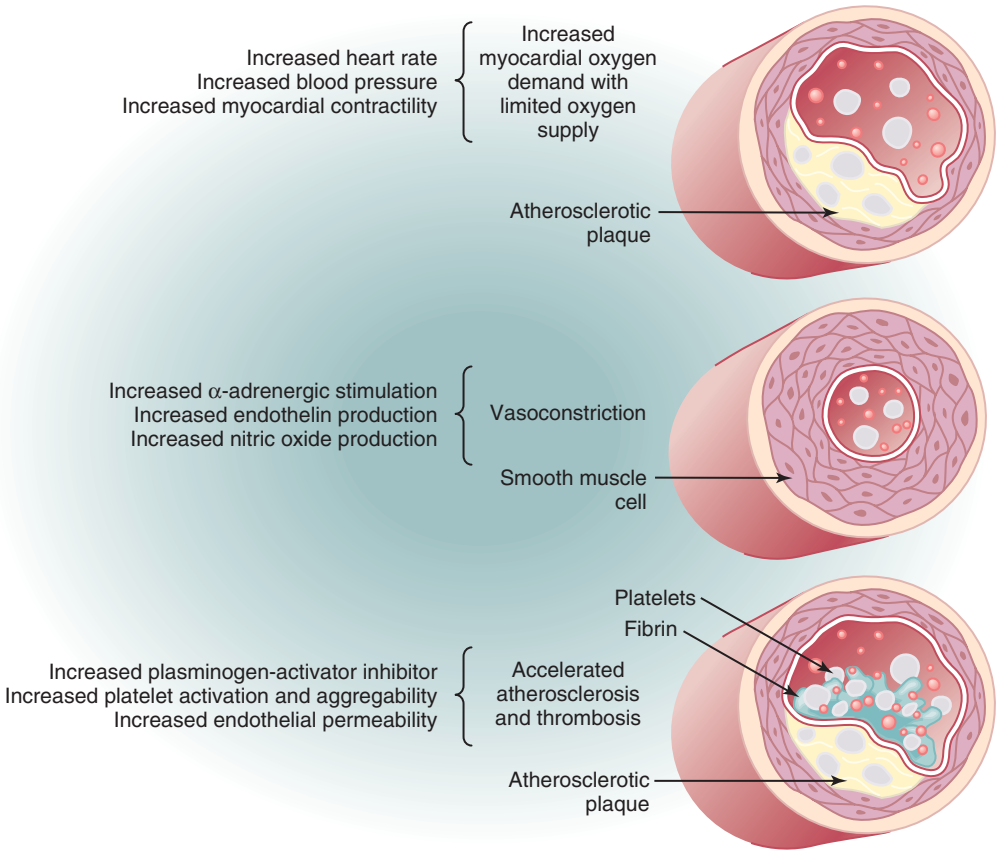

FIGURE 126-5 The mechanisms by which cocaine may induce myocardial ischemia or infarction. Cocaine may cause increases in the determinants of myocardial oxygen demand when oxygen supply is limited *(top)*, when intense vasoconstriction of the coronary arteries occurs *(middle)*, or when accelerated atherosclerosis and thrombosis are present *(bottom)*.