

approved by the U.S. Food and Drug Administration (FDA) in 2002 as a Schedule III drug for managing opioid use disorder. Unlike the full agonist methadone, buprenorphine is a partial agonist of mu-opioid receptors with a slow onset and long duration of action. Its partial agonism reduces the risk of unintentional overdose but limits its efficacy to patients who need the equivalent of only 60–70 mg of methadone, and many patients in methadone maintenance require higher doses up to 150 mg daily. Buprenorphine is combined with naloxone at a 4:1 ratio in order to reduce its abuse liability. Because of pediatric exposures and diversion of buprenorphine to illicit use, a new formulation, using mucosal films rather than sublingual pills that were crushed and snorted, is now marketed. A subcutaneous buprenorphine implant that lasts up to 6 months has also been tested and is pending FDA approval as a formulation improvement to prevent pediatric exposures and illicit diversion and enhance compliance.

In the United States, the ability of primary care physicians to prescribe buprenorphine for opioid use disorder represents an important opportunity to improve access and quality of treatment as well as reduce social harm. Europe, Asia, and Australia have found reduced opioid-related deaths and drug-injection-related medical morbidity with buprenorphine available in primary care. Retention in office-based buprenorphine treatment has been high as 70% at 6-month follow-ups.

Opioid Antagonist Medications The rationale for using narcotic antagonist therapy is that blocking the action of self-administered opioids should eventually extinguish the habit, but this therapy is poorly accepted by patients. Naltrexone, a long-acting orally active pure opioid antagonist, can be given three times a week at doses of 100–150 mg. Because it is an antagonist, the patient must first be detoxified from opioid dependence before starting naltrexone. It is safe even when taken chronically for years, is associated with few side effects (headache, nausea, abdominal pain), and can be given to patients infected with hepatitis B or C without producing hepatotoxicity. However, most providers refrain from prescribing naltrexone if liver function tests are three times above normal levels. Naltrexone maintenance

combined with psychosocial therapy is effective in reducing heroin use, but medication adherence is low. Depot injection formulations lasting up to 4 weeks markedly improve adherence, retention, and drug use. Subcutaneous naltrexone implants in Russia, China, and Australia have doubled treatment retention and reduced relapse to half that of oral naltrexone. In the United States, a depot naltrexone formulation is available for monthly use and maintains blood levels equivalent to 25 mg of daily oral use.

Medication-Free Treatment Most opiate addicts enter medication-free treatments in inpatient, residential, or outpatient settings, but 1- to 5-year outcomes are very poor compared to pharmacotherapy except for residential settings lasting 6 to 18 months. The residential programs require full immersion in a regimented system with progressively increasing levels of independence and responsibility within a controlled community of fellow drug abusers. These medication-free programs, as well as the pharmacotherapy programs, also include counseling and behavioral treatments designed to teach interpersonal and cognitive skills for coping with stress and for avoiding situations leading to easy access to drugs or to craving. Relapse is prevented by having the individual very gradually reintroduced to greater responsibilities and to the working environment outside of the protected therapeutic community.

PREVENTION

Preventing opiate abuse represents a critically important challenge for physicians. Opiate prescriptions are the most common source of drugs accessed by adolescents who begin a pattern of illicit drug use. The major sources of these drugs are family members, not drug dealers or the Internet. Pain management involves providing sufficient opiates to relieve the pain over as short a period of time as the pain warrants (**Chap. 18**). The patient then needs to dispose of any remaining opiates, not save them in the medicine cabinet, because this behavior leads to diversion by adolescents. Finally, physicians should never prescribe opiates for themselves.