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20.7 Opioid-Related Disorders

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their psychoactive effects. Continued opioid misuse can result in syndromes of abuse and dependence and cause disturbances in mood, behavior, and cognition that can mimic other psychiatric disorders. In developed countries, the opioid drug most frequently associated with abuse and dependence is heroin; however, there is growing public health concern about prescription opioids, which are widely available, have significant abuse liability, and are used increasingly for purposes. Opioid addiction affects the young and the old, the wealthy and the poor, and the professional and the unemployed. Over the last few

decades there have been significant advances in treatment and understanding of opioid dependence. It is increasingly accepted that opioid dependence is often a chronic, relapsing disorder amenable to medical treatment and intervention. Table 20.7-1 lists various opioids that are used therapeutically in the United States, with the exception of heroin. Table 20.7-1 Opioids Opioid dependence is a cluster of physiological, behavioral, and cognitive symptoms, which together indicate repeated and continuing use of opioid drugs, despite significant problems related to such use. Drug dependence, in general, has been defined by the World Health Organization (WHO) as a syndrome in which the use of a drug or class of drugs takes on a much higher priority for a given person than other behaviors that once had a higher value. These brief definitions each have as their central features an emphasis on the drug-using behavior itself, its maladaptive nature, and how the choice to engage in that behavior shifts and becomes constrained as a result of interaction with the drug over time. Opioid abuse is a term used to designate a pattern of maladaptive use of an opioid drug leading to clinically significant impairment or distress and occurring within a 12-month period, but one in which the symptoms have never met the criteria for opioid dependence. The opioid-induced disorders include such common phenomena as opioid use disorder, opioid intoxication, opioid withdrawal, opioid-induced sleep disorder, and opioidinduced sexual dysfunction. Opioid intoxication delirium is occasionally seen in hospitalized patients. Opioid-induced psychotic disorder, opioid-induced mood disorder, and opioid-induced anxiety disorder, by contrast, are quite uncommon with μ-agonist opioids, but have been seen with certain mixed agonist–antagonist opioids acting at other receptors. The diagnosis of opioid-related disorder not elsewhere classified is used for situations that do not meet the criteria for any of the other opioid-related disorders.

In addition to the morbidity and mortality associated directly with the opioid-related disorders, the association between the transmission of the human immunodeficiency virus (HIV) and intravenous opioid and opiate use is now recognized as a leading national health concern. The words opiate and opioid come from the word opium, the juice of the opium poppy, Papaver somniferum, which contains approximately 20 opium alkaloids, including morphine. Many synthetic opioids have been manufactured, including meperidine (Demerol), methadone (Dolophine), pentazocine (Talwin), and propoxyphene (Darvon). Methadone is the current gold standard in the treatment of opioid dependence. Opioid antagonists have been synthesized to treat opioid overdose and opioid dependence. This class of drugs includes naloxone (Narcan), naltrexone (ReVia), nalorphine, levallorphan, and apomorphine. Compounds with mixed agonist and antagonist activity at opioid receptors have been synthesized and include pentazocine, butorphanol (Stadol), and buprenorphine (Buprenex). Studies have found buprenorphine to be an effective treatment for opioid dependence. EPIDEMIOLOGY The use and dependence rates derived from national surveys do not accurately reflect fluctuations in drug use among opioid-dependent and previously opioid-dependent populations. When the supply of illicit heroin increases in purity or decreases in price,

use among that vulnerable population tends to increase, with subsequent increases in adverse consequences (emergency room visits) and requests for treatment. The number of current heroin users in the United States has been estimated to be between 600,000 and 800,000. The number of people estimated to have used heroin at any time in their lives (lifetime users) is estimated at approximately 3 million. In 2010, an estimated 140,000 persons had used heroin for the first time within the past 12 months. The average age of first use among recent initiates was 21.3 years in 2010. Opioid use in the United States experienced a resurgence in the 1990s, with emergency department visits related to heroin abuse doubling between 1990 and 1995. This increase in heroin use was associated with an increase in heroin purity and a decrease in its street price. In the late 1990s, heroin use increased among people who were 18 to 25 years of age, and a brief upsurge was seen in the use of oxycodone (OxyContin). Methods of administration other than injecting, such as smoking and snorting, increased in popularity. In 2010, the number of new nonmedical users of psychiatry of oxycodone was 598,000, with an average age at first use of 22.8 years. Comparable data on past year oxycodone initiation are not available for prior years, but calendar year estimates of oxycodone initiation show a steady increase in the number of initiates from 1995, the year this drug was first available, through 2003. The male-to-female ratio of persons with heroin dependence is about 3:1. Users of opioids typically started to use substances in their teens and early 20s; currently, most persons with opioid dependence are in their 30s and 40s. The tendency for dependence to remit generally begins after age 40 years and has been called “maturing out.” Many persons,

however, have remained opioid dependent for 50 years or longer. In the United States, persons tend to experience their first opioid-induced experience in their early teens or even as young as 10 years of age. Early induction into the drug culture is likely in communities in which substance abuse is rampant and in families in which the parents are substance abusers. A heroin habit can cost a person hundreds of dollars a day; thus, a person with opioid dependence needs to obtain money through criminal activities and prostitution. The involvement of persons with opioid dependence in prostitution accounts for much of the spread of HIV. The lifetime prevalence for heroin use is about 1 percent, with 0.2 percent having taken the drug during the prior year. NEUROPHARMACOLOGY The primary effects of the opioid drugs are mediated via the opioid receptors, which were discovered in the first half of the 1970s (published in 1973). The μ-opioid receptors are involved in the regulation and mediation of analgesia, respiratory depression, constipation, and drug dependence; the κ-opioid receptors, with analgesia, diuresis, and sedation; and the Δ-opioid receptors, with analgesia. In 1975, the enkephalins, two endogenous pentapeptides with opioid-like actions, were identified. This discovery led to the identification of three classes of endogenous opioids within the brain, including the endorphins, the dynorphins, and the enkephalins. The term “endorphin” (a contraction of “endogenous” and “morphine”) was coined by Dr. Eric Simon, Professor of psychiatry at NYU School of Medicine, one of the scientists who discovered the opioid receptors, to serve as a generic name for all molecules with morphine-like activity found in the brain. Endorphins are involved in neural transmission and pain suppression. They are released naturally in the body when a person is physically hurt or severely stressed and are thought to account for the absence of pain during acute injuries. The endogenous opioids also have significant interactions with other neuronal systems, such as the dopaminergic and noradrenergic neurotransmitter systems. Several types of data indicate that the addictive rewarding properties of opioids are mediated through activation of the ventral tegmental area dopaminergic neurons that project to the cerebral cortex and the limbic system (Fig. 20.7-1).

FIGURE 20.7-1 Scheme illustrating opioid actions in the locus ceruleus (LC). Opioids acutely inhibit LC neurons by increasing the conductance of a K+ channel (light cross-hatch) via coupling with subtypes of Gi and/or Go and by decreasing an Na+-dependent inward current (dark cross-hatch) via coupling with Gi/o and the consequent inhibition of adenylyl cyclase. Reduced levels of cAMP decrease PKA and the phosphorylation of the responsible channel or pump. Inhibition of the cyclic adenosine monophosphate (cAMP) pathway also decreases phosphorylation of numerous other proteins and thereby affects many additional processes in the neuron. For example, it reduces the phosphorylation state of CREB, which may initiate some of the longer-term changes in LC function. Upper bold arrows summarize effects of repeated morphine administration in the LC. Repeated morphine administration increases levels of adenylyl cyclase, PKA, and several phosphoproteins, including CREB. These changes contribute to the altered phenotype of the drug-addicted state. For example, the intrinsic excitability of LC neurons is increased via enhanced activity of the cAMP pathway and Na+-dependent inward current, which contributes to the tolerance, dependence, and withdrawal exhibited by the these neurons. This altered phenotypic state appears to be maintained, in part, by upregulation of CREB expression. (From Nestler EJ. Molecular mechanisms underlying opiate addiction: Implications for medications development. Semin Neurosci. 1997;9:84, with permission.) Heroin, the most commonly abused opioid, is more lipid soluble than morphine. This allows it to cross the blood–brain barrier faster and have a more rapid and pleasurable onset than morphine. Heroin was first introduced as a treatment for morphine addiction, but heroin, in fact, is more dependence producing than morphine. Codeine,

which occurs naturally as about 0.5 percent of the opiate alkaloids in opium, is absorbed easily through the gastrointestinal tract and is subsequently transformed into morphine in the body. Results of at least one study using positron emission tomography (PET) have suggested that one effect of all opioids is decreased cerebral blood flow in selected brain regions in persons with opioid dependence. There is interesting evidence indicating that the endorphins are involved in other addictions, such as alcoholism, cocaine, and cannabinoid addiction. The opioid antagonist, naltrexone, has shown value in mitigating alcohol addiction. The discovery of this new endorphinergic neuromodulatory system has led to the discovery of an endogenous cannabinoid system and has stimulated many outstanding laboratories to do research toward improved pain management and prevention and treatment of narcotic addiction. Tolerance and Dependence Tolerance to all actions of opioid drugs does not develop uniformly. Tolerance to some actions of opioids can be so high that a 100-fold increase in dose is required to produce the original effect. For example, terminally ill cancer patients may need 200 to 300 mg a day of morphine, whereas a dose of 60 mg can easily be fatal to an opioid-naive person. The symptoms of opioid withdrawal do not appear unless a person has been using opioids for a long time or when cessation is particularly abrupt, as occurs functionally when an opioid antagonist is given. The long-term use of opioids results in changes in the number and sensitivity of opioid receptors, which mediate at least some of the effects of tolerance and withdrawal. Although long-term use is associated with increased sensitivity of the dopaminergic, cholinergic, and serotonergic neurons, the effect of opioids on the noradrenergic neurons is probably the primary mediator of the symptoms of opioid withdrawal. Short-term use of opioids apparently decreases the activity of the noradrenergic neurons in the locus ceruleus; long-term use activates a compensatory homeostatic mechanism within the neurons; and opioid withdrawal results in rebound hyperactivity. This hypothesis also provides an explanation for why clonidine (Catapres), an α2-adrenergic receptor agonist that decreases the release of norepinephrine, is useful in the treatment of opioid withdrawal symptoms. COMORBIDITY

About 90 percent of persons with opioid dependence have an additional psychiatric disorder. The most common comorbid psychiatric diagnoses are major depressive disorder, alcohol use disorders, antisocial personality disorder, and anxiety disorders. About 15 percent of persons with opioid dependence attempt to commit suicide at least once. The high prevalence of comorbidity with other psychiatric diagnoses (Table 20.72) highlights the need to develop a broad-based treatment program that also addresses patients' associated psychiatric disorders.

Table 20.7-2 Non–Substance-Related Psychiatric Disorders in Opioid Users ETIOLOGY Psychosocial Factors Opioid dependence is not limited to low socioeconomic status (SES), although the incidence of opioid dependence is greater in these groups than in higher SES groups. Social factors associated with urban poverty probably contribute to opioid dependence. About 50 percent of urban heroin users are children of single parents or divorced parents and are from families in which at least one other member has a substancerelated disorder. Children from such settings are at high risk for opioid dependence, especially if they also evidence behavioral problems in school or other signs of conduct disorder. Some consistent behavior patterns seem to be especially pronounced in adolescents with opioid dependence. These patterns have been called the heroin behavior syndrome: underlying depression, often of an agitated type and frequently accompanied by anxiety symptoms; impulsiveness expressed by a passive-aggressive orientation; fear of failure; use of heroin as an antianxiety agent to mask feelings of low self-esteem, hopelessness, and aggression; limited coping strategies and low frustration tolerance, accompanied by the need for immediate gratification; sensitivity to drug contingencies, with a keen awareness of the relation between good feelings and the act of drug taking; feelings of behavioral impotence counteracted by momentary control over the life situation by means of substances; disturbances in social and interpersonal relationships with peers

maintained by mutual substance experiences. Biological and Genetic Factors Evidence now exists for common and drug-specific, genetically transmitted vulnerability factors that increase the likelihood of developing drug dependence. Individuals who abuse a substance from any category are more likely to abuse substances from other categories. Monozygotic twins are more likely than dizygotic twins to be concordant for opioid dependence. Multivariate modeling techniques have indicated that not only was the genetic contribution high for heroin abuse in this group, but also a higher proportion of the variance because of genetic factors was not shared with the common vulnerability factor—that is, it was specific for opioids. A person with an opioid-related disorder may have had genetically determined hypoactivity of the opiate system. Researchers are investigating the possibility that such hypoactivity may be caused by too few, or less-sensitive, opioid receptors, by release of too little endogenous opioid, or by overly high concentrations of a hypothesized endogenous opioid antagonist. A biological predisposition to an opioid-related disorder may also be associated with abnormal functioning in either the dopaminergic or the noradrenergic neurotransmitter system. Psychodynamic Theory In psychoanalytic literature, the behavior of persons addicted to narcotics has been described in terms of libidinal fixation, with regression to pregenital, oral, or even more archaic levels of psychosexual development. The need to explain the relation of drug abuse, defense mechanisms, impulse control, affective disturbances, and adaptive mechanisms led to the shift from psychosexual formulations to formulations emphasizing ego psychology. Serious ego pathology, often thought to be associated with substance abuse, is considered to indicate profound developmental disturbances. Problems of the relation between the ego and affects emerge as a key area of difficulty. DIAGNOSIS Opioid Use Disorder Opioid use

disorder is a pattern of maladaptive use of an opioid drug, leading to clinically significant impairment or distress and occurring within a 12-month period. A 42-year-old executive in a public relations firm was referred for psychiatric consultation by his surgeon, who discovered him sneaking large quantities of a codeine-containing cough medicine into the hospital. The patient had been a heavy cigarette smoker for 20 years and had a chronic, hacking cough. He had come into the hospital for a hernia repair and found the pain from the incision unbearable when he coughed.

An back operation 5 years previously had led his doctors to prescribe codeine to help relieve the incisional pain at that time. Over the intervening 5 years, however, the patient had continued to use codeine-containing tablets and had increased his intake to 60–90 mg daily. He stated that he often “just took them by the handful—not to feel good, you understand, just to get by.” He spent considerable time and effort developing a circle of physicians and pharmacists to whom he would “make the rounds” at least three times a week to obtain new supplies of pills. He had tried several times to stop using codeine, but had failed. During this period he lost two jobs because of lax work habits and was divorced by his wife of 11 years. Opioid Intoxication Opioid intoxication includes maladaptive behavioral changes and specific physical symptoms of opioid use. In general, altered mood, psychomotor retardation, drowsiness, slurred speech, and impaired memory and attention in the presence of other indicators of recent opioid use strongly suggest a diagnosis of opioid intoxication. Opioid Withdrawal The Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) diagnostic criteria for opioid withdrawal are listed in Table 20.7-3. The general rule about the onset and duration of withdrawal symptoms is that substances with short durations of action tend to produce short, intense withdrawal syndromes and substances with long durations of action produce prolonged, but mild, withdrawal syndromes. An exception to the rule, narcotic antagonist-precipitated withdrawal after long-acting opioid dependence can be severe. Table 20.7-3 DSM-5 Diagnostic Criteria for Opioid Withdrawal

An abstinence syndrome can be precipitated by administration of an opioid antagonist. The symptoms can begin within seconds of such an intravenous injection and peak in about 1 hour. Opioid craving rarely occurs in the context of analgesic administration for pain from physical disorders or surgery. The full withdrawal syndrome, including intense craving for opioids, usually occurs only secondary to abrupt cessation of use in persons with opioid dependence. Morphine and Heroin. The morphine and heroin withdrawal syndrome begins 6 to 8 hours after the last dose, usually after a 1- to 2-week period of continuous use or after the administration of a narcotic antagonist. The withdrawal syndrome reaches its peak intensity during the second or third day and subsides during the next 7 to 10 days, but some symptoms may persist for 6 months or longer. Meperidine. The withdrawal syndrome from meperidine begins quickly, reaches a peak in 8 to 12 hours, and ends in 4 to 5 days. Methadone. Methadone withdrawal usually begins 1 to 3 days after the last dose and ends in 10 to 14 days. Symptoms. Opioid withdrawal consists of severe muscle cramps and bone aches, profuse diarrhea, abdominal cramps, rhinorrhea, lacrimation, piloerection or gooseflesh (from which comes the term cold turkey for the abstinence syndrome), yawning, fever,

pupillary dilation, hypertension, tachycardia, and temperature dysregulation, including hypothermia and hyperthermia. Persons with opioid dependence seldom die from opioid withdrawal, unless they have a severe preexisting physical illness such as cardiac disease. Residual symptoms—such as insomnia, bradycardia, temperature dysregulation, and a craving for

opioids—can persist for months after withdrawal. Associated features of opioid withdrawal include restlessness, irritability, depression, tremor, weakness, nausea, and vomiting. At any time during the abstinence syndrome, a single injection of morphine or heroin eliminates all the symptoms. Opioid Intoxication Delirium Opioid intoxication delirium is most likely to happen when opioids are used in high doses, are mixed with other psychoactive compounds, or are used by a person with preexisting brain damage or a central nervous system (CNS) disorder (e.g., epilepsy). Opioid-Induced Psychotic Disorder Opioid-induced psychotic disorder can begin during opioid intoxication. Clinicians can specify whether hallucinations or delusions are the predominant symptoms. Opioid-Induced Mood Disorder Opioid-induced mood disorder can begin during opioid intoxication. Opioid-induced mood disorder symptoms can have a manic, depressed, or mixed nature, depending on a person's response to opioids. A person coming to psychiatric attention with opioidinduced mood disorder usually has mixed symptoms, combining irritability, expansiveness, and depression. Opioid-Induced Sleep Disorder and Opioid-Induced Sexual Dysfunction Hypersomnia is likely to be more common with opioids than insomnia. The most common sexual dysfunction is likely to be impotence. Unspecified Opioid-Related Disorder The DSM-5 includes diagnoses for other opioid-related disorders with symptoms of delirium, abnormal mood, psychosis, abnormal sleep, and sexual dysfunction. Clinical situations that do not fit into these categories exemplify appropriate cases for the use of the DSM-5 diagnosis of unspecified opioid-related disorder. CLINICAL FEATURES Opioids can be taken orally, snorted intranasally, and injected intravenously or subcutaneously (Fig. 20.7-2). Opioids are subjectively addictive because of the euphoric high (the rush) that users experience, especially those who take the substances

intravenously. The associated symptoms include a feeling of warmth, heaviness of the extremities, dry mouth, itchy face (especially the nose), and facial flushing. The initial euphoria is followed by a period of sedation, known in street parlance as "nodding off." Opioid use can induce dysphoria, nausea, and vomiting in opioid-naive persons. FIGURE 20.7-2 Skin popper. Circular depressed scars, often with underlying chronic abscesses, can result from skin popping. (Courtesy of Michael Baden, M.D.) The physical effects of opioids include respiratory depression, pupillary constriction, smooth muscle contraction (including the ureters and the bile ducts), constipation, and changes in blood pressure, heart rate, and body temperature. The respiratory depressant effects are mediated at the level of the brainstem. Adverse Effects The most common and most serious adverse effect associated with the opioid-related disorders is the potential transmission of hepatitis and HIV through the use of contaminated needles by more than one person. Persons can experience idiosyncratic allergic reactions to opioids, which result in anaphylactic shock, pulmonary edema, and death if they do not receive prompt and adequate treatment. Another serious adverse effect is an idiosyncratic drug interaction between meperidine and monoamine oxidase inhibitors (MAOIs), which can produce gross autonomic instability, severe behavioral agitation, coma, seizures, and death. Opioids and MAOIs should not be given together for this reason. Opioid Overdose Death from an overdose of an opioid is usually attributable to respiratory arrest from the respiratory depressant effect of the drug. The symptoms of overdose include marked unresponsiveness, coma, slow respiration, hypothermia, hypotension, and bradycardia. When presented with the clinical triad of coma, pinpoint pupils, and respiratory depression, clinicians should consider opioid overdose as a primary diagnosis. They can

also inspect the patient's body for needle tracks in the arms, legs, ankles, groin, and even the dorsal vein of the penis. MPTP-Induced Parkinsonism In 1976, after ingesting an opioid

contaminated with methyl-phenyltetrahydropyridine (MPTP), several persons developed a syndrome of irreversible parkinsonism. The mechanism for the neurotoxic effect is as follows: MPTP is converted into 1methyl-4-phenylpyridinium (MPP+) by the enzyme monoamine oxidase and is then taken up by dopaminergic neurons. Because MPP+ binds to melanin in substantia nigra neurons, MPP+ is concentrated in these neurons and eventually kills the cells. PET studies of persons who ingested MPTP but remained asymptomatic have shown a decreased number of dopamine-binding sites in the substantia nigra. This decrease reflects a loss in the number of dopaminergic neurons in that region. TREATMENT AND REHABILITATION Overdose Treatment The first task in overdose treatment is to ensure an adequate airway. Tracheopharyngeal secretions should be aspirated; an airway may be inserted. The patient should be ventilated mechanically until naloxone, a specific opioid antagonist, can be given. Naloxone is administered intravenously at a slow rate—initially about 0.8 mg per 70 kg of body weight. Signs of improvement (increased respiratory rate and pupillary dilation) should occur promptly. In opioid-dependent patients, too much naloxone may produce signs of withdrawal as well as reversal of overdosage. If no response to the initial dosage occurs, naloxone administration may be repeated after intervals of a few minutes. Previously, it was thought that if no response was observed after 4 to 5 mg, the CNS depression was probably not caused solely by opioids. The duration of action of naloxone is short compared with that of many opioids, such as methadone and levomethadyl acetate, and repeated administration may be required to prevent recurrence of opioid toxicity. Medically Supervised Withdrawal and Detoxification Opioid Agents for Treating Opioid Withdrawal METHADONE. Methadone is a synthetic narcotic (an opioid) that substitutes for heroin and can be taken orally. When given to addicts to replace their usual substance of abuse, the drug suppresses withdrawal symptoms. A daily dose of 20 to 80 mg suffices to stabilize a patient, although daily doses of up to 120 mg have been used. The duration of action for methadone exceeds 24 hours; thus, once-daily dosing is adequate. Methadone maintenance is continued until the patient can be withdrawn from methadone, which itself causes dependence. An abstinence syndrome occurs with methadone withdrawal, but patients are detoxified from methadone more easily than from heroin. Clonidine (0.1 to 0.3 mg three to four times a day) is usually given during

the detoxification period. Methadone maintenance has several advantages. First, it frees persons with opioid dependence from using injectable heroin and, thus, reduces the chance of spreading HIV through contaminated needles. Second, methadone produces minimal euphoria and rarely causes drowsiness or depression when taken for a long time. Third, methadone allows patients to engage in gainful employment instead of criminal activity. The major disadvantage of methadone use is that patients remain dependent on a narcotic. Other Opioid Substitutes LEVOMETHADYL (LAAM). LAAM is an opioid agonist that suppresses opioid withdrawal. It is no longer used, however, because some patients developed prolonged QT intervals associated with potentially fatal arrhythmias (torsades de pointes). BUPRENORPHINE. As with methadone and LAAM, buprenorphine is an opioid agonist approved for opioid dependence in 2002. It can be dispensed on an outpatient basis, but prescribing physicians must demonstrate that they have received special training in its use. Buprenorphine in a daily dose of 8 to 10 mg appears to reduce heroin use. Buprenorphine also is effective in thrice-weekly dosing because of its slow dissociation from opioid receptors. After repeated administration, it attenuates or blocks the subjective effects of parenterally administered opioids such as heroin or morphine. A mild opioid withdrawal syndrome occurs if the drug is abruptly discontinued after chronic administrations. Opioid Antagonists. Opioid antagonists block or antagonize the effects of opioids. Unlike methadone, they do not exert narcotic effects and do not

cause dependence. Opioid antagonists include naloxone, which is used in the treatment of opioid overdose because it reverses the effects of narcotics, and naltrexone, the longest-acting (72 hours) antagonist. The theory for using an antagonist for opioid-related disorders is that blocking opioid agonist effects, particularly euphoria, discourages persons with opioid dependence from substance-seeking behavior and, thus, deconditions this behavior. The major weakness of the antagonist treatment model is the lack of any mechanism that compels a person to continue to take the antagonist. Pregnant Women with Opioid Dependence Neonatal addiction is a significant problem. About three fourths of all infants born to addicted mothers experience the withdrawal syndrome. Neonatal Withdrawal. Although opioid withdrawal rarely is fatal for the otherwise healthy adult, it is hazardous to the fetus and can lead to miscarriage or fetal death. Maintaining a pregnant woman with opioid dependence on a low dose of methadone (10 to 40 mg daily) may be the least hazardous course to follow. At this dose, neonatal withdrawal is usually mild and can be managed with low doses of

paregoric. If pregnancy begins while a woman is taking high doses of methadone, the dosage should be reduced slowly (e.g., 1 mg every 3 days), and fetal movements should be monitored. If withdrawal is necessary or desired, it is least hazardous during the second trimester. Fetal AIDS Transmission. Acquired immune deficiency syndrome (AIDS) is the other major risk to the fetus of a woman with opioid dependence. Pregnant women can pass HIV, the causative agent of AIDS, to the fetus through the placental circulation. An HIV-infected mother can also pass HIV to the infant through breast-feeding. The use of zidovudine (Retrovir) alone or in combination with other anti-HIV medication in infected women can decrease the incidence of HIV in newborns. Psychotherapy The entire range of psychotherapeutic modalities is appropriate for treating opioidrelated disorders. Individual psychotherapy, behavioral therapy, cognitive-behavioral therapy, family therapy, support groups (e.g., Narcotics Anonymous [NA]), and social skills training may all prove effective for specific patients. Social skills training should be particularly emphasized for patients with few social skills. Family therapy is usually indicated when the patient lives with family members. Therapeutic Communities Therapeutic communities are residences in which all members have a substance abuse problem. Abstinence is the rule; to be admitted to such a community, a person must show a high level of motivation. The goals are to effect a complete change of lifestyle, including abstinence from substances; to develop personal honesty, responsibility, and useful social skills; and to eliminate antisocial attitudes and criminal behavior. The staff members of most therapeutic communities are persons with former substance dependence who often put prospective candidates through a rigorous screening process to test their motivation. Self-help through the use of confrontational groups and isolation from the outside world and from friends associated with the drug life are emphasized. The prototypical community for persons with substance dependence is Phoenix House, where the residents live for long periods (usually 12 to 18 months) while receiving treatment. They are allowed to return to their old environments only when they have demonstrated their ability to handle increased responsibility within the therapeutic community. Therapeutic communities can be effective but require large staffs and extensive facilities. Moreover, dropout rates are high; up to 75 percent of those who enter therapeutic communities leave within the first month. Education and Needle Exchange. Although the essential treatment of opioid use disorders is encouraging persons to abstain from opioids, education about the transmission of HIV must receive equal attention. Persons with opioid dependence who use intravenous or subcutaneous routes of administration must be taught available safe-

sex practices. Free needle-exchange programs are often subject to intense political and societal pressures but, where allowed, should be made available to persons with opioid dependence. Several studies have indicated that unsafe needle sharing is common when it is difficult to obtain enough clean needles and is also common in persons with legal difficulties, severe substance problems, and psychiatric symptoms. These are just the persons most likely to be involved in transmitting HIV. Narcotic Anonymous Narcotics Anonymous is a self-help group of abstinent drug addicts modeled on the 12step principles of Alcoholics Anonymous (AA). Such groups now exist in most large cities and can provide useful group support. The outcome for patients treated in 12-step programs is generally good, but the anonymity that is at the core of the 12-step model has made detailed evaluation of its efficacy in treating opioid dependence difficult. REFERENCES Barry DT, Beitel M, Cutter CJ, Joshi D, Falcioni J, Schottenfeld RS. Conventional and nonconventional pain treatment utilization among opioid dependent individuals with pain seeking methadone maintenance treatment: A needs assessment study. J Addict Med. 2010;4:81. Bohnert ASB, Valenstein M, Bair MJ, Ganoczy D, McCarthy JF, Ilgen MA, Blow FC. Association between opioid prescribing patterns and opioid overdose-related deaths. JAMA. 2011;305:1315. Comer SD, Sullivan MA, Whittington RA, Vosburg SK, Kowalczyk WJ. Abuse liability of prescription opioids compared to heroin in morphine-maintained heroin abusers. Neuropsychopharmacology. 2008;33(5):1179. Gros DF, Milanak ME, Brady KT, Back SE. Frequency and severity of comorbid mood and anxiety disorders in prescription opioid dependence. Am J Addict. 2013;22(3):261–265. Haller DL, Acosta MC. Characteristics of pain patients with opioid-use disorder. Psychosomatics. 2010;51:257. Howe CQ, Sullivan MD. The missing ‘P’ in pain management: how the current opioid epidemic highlights the need for psychiatric services in chronic pain care. Gen Hosp Psychiatry. 2014;36(1):99–104. Jones HE. Treating opioid use disorders during pregnancy: Historical, current, and future directions. Substance Abuse. 2013;34(2):89–91. Ling W, Casadonte P, Bigelow G, Kampman KM, Patkar A, Bailey GL, Rosenthal RN, Beebe KL. Buprenorphine implants for treatment of opioid dependence. JAMA. 2010;304:1576. Marino EN, Rosen KD, Gutierrez A, Eckmann M, Ramamurthy S, Potter JS. Impulsivity but not sensation seeking is associated with opioid analgesic misuse risk in patients with chronic pain. Addict Beh. 2013;38(5):2154–2157. Martins SS, Keyes KM, Storr CL, Zhu H, Chilcoat HD. Pathways between nonmedical opioid use/dependence and psychiatric disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Drug Alcohol Depend. 2009;103:16. Oviedo-Joekes E, Brissette S, Marsh DC, Lauzon P, Guh D, Anis A, Schechter MT. Diacetylmorphine versus methadone for the treatment of opioid addiction. N Engl J Med. 2009;361:777. Renner JA, Suzuki J. Opiates and prescription drugs. In: Johnson BA, ed. Addiction Medicine: Science and Practice. Vol. 1. New York: Springer, LLC; 2011:463. Rich BA, Webster LR. A review of forensic implications of opioid prescribing with examples from malpractice cases involving opioid-related overdose. Pain Med. 2011;12:S59.

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