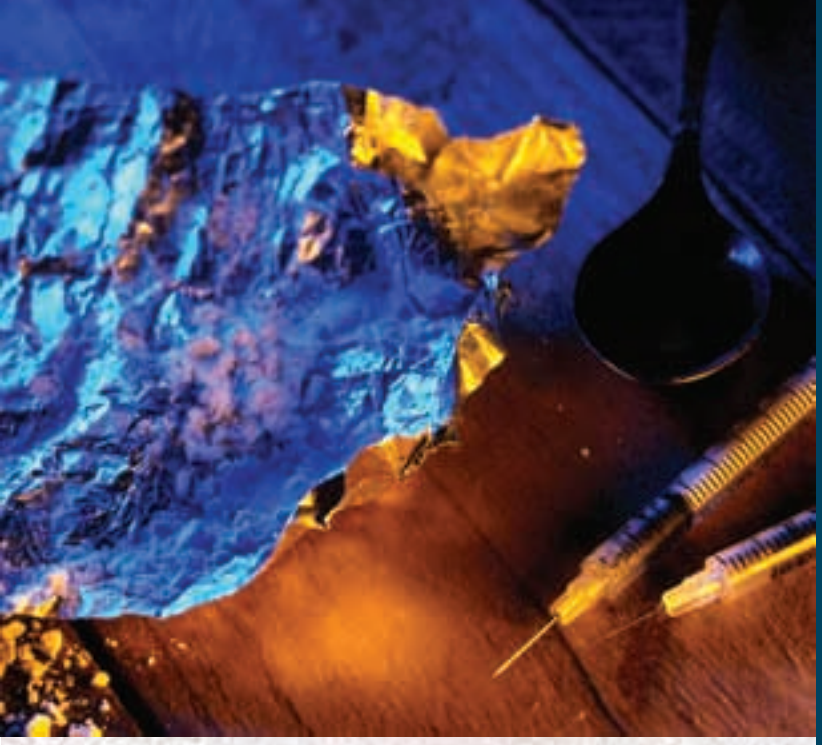

CHAPTER 9

Narcotics (Opioids)

Did You Know?

- The release of natural substances called endorphins activate opioid receptors and can mimic the effects of narcotics such as heroin.
- By the end of the 19th century, almost 1 million Americans were addicted to opiates, primarily due to the use of patent medicines that contained opium products.
- Narcotics are among the most potent analgesics available today.
- In the past decade, treatment for nonmedical use of prescription pain relievers has increased more than four-fold and currently accounts for two-thirds of prescription abuse in the United States.
- Because of concern about abusing prescription narcotic analgesics, many clinicians are hesitant to prescribe sufficient quantities of these drugs to adequately manage severe, long-term pain.
- Addiction to prescription narcotic analgesics rarely happens when these medications are used properly to treat pain.
- There is evidence that acupuncture reduces pain by activating a natural opioid system.
- Many heroin addicts have been exposed to the AIDS virus.
- Heroin supplies today are more potent, cheaper, and more readily available than a decade ago.
- One designer drug, made from the narcotic fentanyl, is 6000 times more potent than heroin.
- Some heroin addicts have to be treated with the narcotic methadone for the rest of their lives to keep them from abusing heroin.
- Dextromethorphan (a common over-the-counter cough medicine chemically related to codeine), when taken in high doses, can cause phencyclidine (PCP)-like hallucinations.

Learning Objectives

On completing this chapter you will be able to:

- Describe the principal pharmacological effects of narcotics, their biological targets, and their main therapeutic uses.
- Identify the major side effects of narcotics, in particular their abuse potential.
- Distinguish between narcotic physical dependence and addiction.
- Identify the abuse patterns for heroin.
- Outline the stages of heroin dependence.
- List the withdrawal symptoms that result from narcotic dependence, list potential treatments, and discuss the significance of tolerance.
- Describe and compare the use of methadone and buprenorphine in treating narcotic addiction.
- Identify the unique features of fentanyl that make it appealing to illicit drug dealers but dangerous to narcotic addicts.
- Describe how "designer" drugs have been associated with narcotics and Parkinson's disease.
- Describe why dextromethorphan in cough medicines is abused.
- Identify the opioid features of tramadol and its potential for abuse.

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Introduction

The proportion of persons admitted for substance abuse treatment whose principal problem was nonmedical use of prescription pain medication (i.e., narcotic analgesics) has gone from 2.2% to almost 10% in the past decade. This startling escalation has made abuse of these drugs the second most prevalent form of illegal drug use in the United States (Bloomberg BusinessWeek 2010). What are these drugs, where do they come from, and how do they work?

The term *narcotic* in general means a central nervous system (CNS) depressant that produces insensibility or stupor. The term has also come to designate those drugs and substances with pharmacological properties related to opium ingredients and their drug derivatives. All opioid narcotics activate opioid receptors and have abuse potential. Narcotics are frequently prescribed for pain relief (**analgesics**), to reduce coughing (**antitussive**), and to reduce diarrhea.

In this chapter, we introduce the opioid narcotics with a brief historical account. The pharmacological properties and therapeutic uses of these drugs are discussed, followed by a description of, and distinction between, their side effects and problems with tolerance, withdrawal, dependence, and addiction. Narcotic abuse, its risks and outcomes, is presented in detail, with special emphasis on heroin. In addition, treatment approaches for narcotic addiction, dependence, and withdrawal are included. This chapter concludes with descriptions of other commonly used opioid narcotics and related drugs.

What Are Narcotics?

The word *narcotic* has been used to label many substances, from opium to marijuana to cocaine. The translation of the Greek word *narkoticos* is "benumbing or deadening." The term *narcotic* is sometimes used to refer to a CNS depressant, producing insensibility or stupor, and at other times to refer to an addicting drug. Most people would not consider marijuana among the narcotics today, although for many years it was included in this category. Although pharmacologically cocaine is not a narcotic either, it is still legally classified as such. Perhaps part of this confusion is due to the fact that cocaine, as a local anesthetic, can cause a numbing effect.

For purposes of the present discussion, the term *narcotic* is used to refer to those naturally occurring substances derived from the opium poppy and their synthetic substitutes. These drugs are referred to as the **opioid** (or opiate) narcotics because of their association with opium. They have similar pharmacological features, including abuse potential, pain-relieving effects (referred to as analgesics), cough suppression, and reduction of intestinal movement, often causing constipation, but useful in reducing severe diarrhea. Some of the most commonly used opioid narcotics are listed in **Table 9.1**.

KEY TERMS

analgesics
drugs that relieve pain without affecting consciousness

antitussive
drugs that block the coughing reflex

opioid
relating to the drugs that are derived from opium

The History of Narcotics

The opium poppy, *Papaver somniferum,* from which opium and its naturally occurring narcotic derivatives are obtained, has been cultivated for millennia. A 6000-year-old Sumerian tablet has an ideograph for the poppy shown as "joy" plus "plant," suggesting that the addicting properties of this substance have been appreciated for millennia. The Egyptians listed opium along with approximately 700 other medicinal compounds in the famous Ebers Papyrus (circa 1500 BC).

The Greek god of sleep, Hypnos, and the Roman god of sleep, Somnus, were portrayed as carrying containers of opium pods, and the Minoan goddess of sleep wore a crown of opium pods. During the so-called Dark Ages that followed the collapse of the Roman Empire, Arab traders actively engaged in traveling the overland caravan routes to China and to India, where they introduced opium. Eventually, both China and India grew their own poppies.

Opium in China

The opium poppy had a dramatic impact in China, causing widespread addiction (Karch 1996). Initially, the seeds were used medically, as was opium later. However, by the late 1690s, opium was being smoked and used for diversion. The Chinese government, fearful of the weakening of national vital-

Table 9.1 Commonly Used Opioid Narcotic Drugs and Products

NARCOTIC DRUGS	COMMON NAMES	MOST COMMON USES
Heroin	Horse, smack, junk (street names)	Abuse
Morphine	Several	Analgesia
Methadone	Dolophine	Treat narcotic dependence
Meperidine	Demerol	Analgesia
Oxycodone	Percodan, OxyContin	Analgesia
Propoxyphene	Darvon	Analgesia
Codeine	Several	Analgesia, antitussive
Loperamide	Imodium A-D	Antidiarrheal
Diphenoxylate	Lomotil	Antidiarrheal
Opium tincture	Paregoric	Antidiarrheal
Buprenorphine	Suboxone	Treat narcotic dependence

ity by the potent opiate narcotic, outlawed the sale of opium in 1729. The penalty for disobedience was death by strangulation or decapitation. Despite these laws and threats, the habit of opium smoking became so widespread that the Chinese government went a step further and forbade its importation from India, where most of the opium poppy was grown. In contrast, the British East India Company (and later the British government in India) encouraged cultivation of opium. British companies were the principal shippers to the Chinese port of Canton, which was the only port open to Western merchants. During the next 120 years, a complex network of opium smuggling routes developed in China with the help of local merchants, who received substantial profits, and local officials, who pocketed bribes to ignore the smugglers.

Everyone involved in the opium trade, but particularly the British, continued to profit until the Chinese government ordered the strict enforcement of the edict against importation. Such actions by the Chinese caused conflict with the British government and helped trigger the Opium War of 1839 to 1842. Great Britain sent in an army, and by 1842, 10,000 British soldiers had won a victory over 350 million Chinese. Because of the war, the island of Hong Kong was ceded to the British, and an indemnity of $6 million was imposed on China to cover the value of the destroyed opium and the cost of the war. In 1856, a second Opium War broke out. Peking was occupied by British and French troops, and China was compelled to make further concessions to Britain. The importation of opium continued to increase until 1908, when Britain and China made an agreement to limit the importation of opium from India (Austin 1978).

American Opium Use

Meanwhile, in 1803, a young German named Frederick Serturner extracted and partially purified the active ingredients in opium. The result was 10 times more potent than opium itself and was named

Famous cartoon, showing a British sailor shoving opium down the throat of a Chinese man, which dates back to the Opium War of 1839–1842.

morphine after Morpheus, the Greek god of dreams. This discovery increased worldwide interest in opium. By 1832, a second compound had been purified and named *codeine,* after the Greek word for "poppy capsule" (Maurer and Vogel 1967).

The opium problem was aggravated further in 1853, when Alexander Wood perfected the hypodermic syringe and introduced it first in Europe and then in America. Christopher Wren and others had worked with the idea of injecting drugs directly into the body by means of hollow quills and straws, but the approach was never successful or well received. Wood perfected the syringe technique with the intent of preventing morphine addiction by injecting the drug directly into the veins rather than by oral administration (Golding 1993). Unfortunately, just the opposite happened; injection of morphine increased the potency and the likelihood of dependence (Maurer and Vogel 1967).

The hypodermic syringe was used extensively during the Civil War to administer morphine to treat pain, dysentery, and fatigue (Kosten and Hollister 1998). A large percentage of the soldiers who returned home from the war were addicted to morphine. Opiate addiction became known as the "soldier's disease" or "army disease."

By 1900, an estimated 1 million Americans were dependent on opiates (Abel 1980). This drug problem was made worse because of (1) Chinese laborers, who brought with them to the United States opium to smoke (it was legal to smoke opium in the United States at that time); (2) the availability of purified morphine and the hypodermic syringe; and (3) the lack of controls on the large number of patent medicines that contained opium derivatives (Karch 1996). Until 1914, when the Harrison Narcotic Act was passed (regulating opium, coca leaves, and their products), the average opiate addict was a middle-aged, Southern, white woman who functioned well and was adjusted to her role as a wife and mother. She bought opium or morphine legally by mail order from Sears and Roebuck or at the local store, used it orally, and caused very few problems. A number of physicians were addicted as well. One of the best-known morphine addicts was William Holsted, a founder of Johns Hopkins Medical School. Holsted was a very productive surgeon and innovator, although secretly an addict for most of his career. He became dependent on morphine as a substitute for his cocaine dependence (Brecher 1972).

Looking for better medicines, chemists found that modification of the morphine molecule resulted in a more potent compound. In 1898, diacetylmorphine was placed on the market as a cough suppressant by Bayer. It was to be a "heroic" drug, without the addictive potential of morphine—it thus received the name *heroin.*

Heroin was first used in the United States as a cough suppressant and to combat addiction to other substances (Hubbard 1998). However, its inherent abuse potential was quickly discovered. When injected, heroin is more addictive than most of the other narcotics because of its ability to enter the brain rapidly and cause a euphoric surge (DiChiara and North 1992). Heroin was banned from U.S. medical practice in 1924, although it is still prescribed legally as an analgesic in other countries (Bammer 2005).

The Vietnam War was an important landmark for heroin use in the United States (Hubbard 1998). It has been estimated that as many as 40% of the

With the development of the hypodermic needle and its use during the Civil War, heroin addiction became more likely and more severe.

Chinese laborers often smoked heroin at the turn of the 20th century.

Heroin use by soldiers fighting in Afghanistan is a great concern.

U.S. soldiers serving in Southeast Asia at this time used heroin to combat the frustrations and stress associated with this unpopular military action. Although only 7% of the soldiers continued to use heroin after returning home, those who were addicted to this potent narcotic became a major component of the heroin-abusing population in this country (Golding 1993).

Heroin smoking became popular in the mid-1980s in response to the AIDS epidemic. This was due to a fear of HIV infection when using infected needles to administer the drug intravenously (Hubbard 1998). The effect resulting from inhalation is as intense as that caused by injection, although a very pure drug is required for smoking. Smoking continues to be a favorite form of heroin administration today.

As experience has shown, problems with the opiate drugs such as heroin are closely linked with war and its associated miseries and pains. As our country again finds itself in the middle of an extended and increasingly less popular military engagement in the Middle East, problems with heroin are becoming more and more apparent (Edwards 2010). As during previous wars, soldiers turn to drugs like heroin to cope and even to survive emotionally in a war zone. This is reflected in comments such as: "Life is unbearable. You don't know whether you're going to be alive in 10 minutes' time or not." "Life has few pleasures; you're uncomfortable . . . the food is pretty awful, the ever-present smell of death and you see some of your closest buddies die before your very eyes." "So life is really unbearable and heroin is cheap" (Edwards 2010).

Pharmacological Effects

Even though opioid narcotics have a history of being abused, they continue to be important therapeutic agents.

Narcotic Analgesics

The most common clinical use of the opioid narcotics is as analgesics to relieve pain. These drugs are effective against most varieties of pain, including *visceral* (associated with internal organs of the body) and *somatic* (associated with skeletal muscles, bones, skin, and teeth) types. Used in sufficiently high doses, narcotics can even relieve the intense pain associated with some types of cancer (Gutstein and Akil 2006).

The opioid narcotics relieve pain by activating the same group of receptors that are controlled by the endogenous substances called *endorphins* (Trigo et al. 2010). As discussed in Chapter 4, the endorphins are a family of peptides (small proteins) that are released in the brain, in the spinal cord, and from the adrenal glands in response to stress and painful experiences. When released, the endorphins serve as transmitters and stimulate receptors designated as opioid types. Activation of opioid receptors by either the naturally released endorphins or administration of the narcotic analgesic drugs blocks the transmission of pain through the spinal cord or brain stem and alters the perception of pain in the "pain center" of the brain. Because the narcotics work at multiple levels of pain transmission, they are potent analgesics against almost all types of pain.

Interestingly, the endorphin system appears to be influenced by psychological factors as well. Thus, natural activation of opioid receptors also contributes to the regulation of emotional behaviors such as stress, learning, and memory as well as the regulation of the brain's reward circuits (Trigo et al. 2010). It is possible that pain relief caused by administration of placebos or nonmedicinal manipulation such as acupuncture is due in part to the natural release of endorphins (Eshkevari and Heath 2005). This relationship suggests that physiological, psychological, and pharmacological factors are intertwined in pain management through the opioid system, which makes it impossible to deal with one without considering the others.

Although the narcotics are very effective analgesics, they do cause some side effects that are particularly alarming; thus, their clinical use usually is limited to the treatment of moderate to severe pain (*Drug Facts and Comparisons* 2010). Other, safer drugs, such as the aspirin-type analgesics (see Chapter 15), are preferred for pain management when possible. Often, the amount of narcotic required for pain relief can be reduced by combining a narcotic, such as codeine, with aspirin or acetaminophen (the active ingredient in Tylenol). Such

combinations reduce the chance of significant narcotic side effects while providing adequate pain relief (*Drug Facts and Comparisons* 2010).

Morphine is a particularly potent pain reliever and often is used as the analgesic standard by which other narcotics are compared (Gutstein and Akil 2006). With continual use, tolerance develops to the analgesic effects of morphine and other narcotics, sometimes requiring a dramatic escalation of doses to maintain adequate pain control (*Drug Facts and Comparisons* 2010).

Because pain is expressed in different forms with many different diseases, narcotic treatment can vary considerably. Usually, the convenience of oral narcotic therapy is preferred but often is inadequate for severe pain. For short-term relief from intense pain, narcotics are effective when injected subcutaneously or intramuscularly. Narcotics can also be given intravenously for persistent and potent analgesia or administered by transdermal patches for sustained chronic pain (*Drug Facts and Comparisons* 2010). Despite the fact that most pain can be relieved if enough narcotic analgesic is properly administered, physicians frequently underprescribe narcotics or are not well trained in proper pain management or how to use the opioid narcotics responsibly (Meier 2010; Young 2007). Because of fear of causing narcotic addiction or creating legal problems with federal agencies such as the Drug Enforcement Administration (DEA) (see "Here and Now: Are Restrictions on Pain Pills Too Painful?"), many patients in the United States are often inadequately treated for their pain (Jointogether.org 2010). An important rule of narcotic use is that adequate pain relief should not be denied because of concern about the abuse potential of these drugs (Hall and Sykes 2004). Indeed, addiction to narcotics is rare in patients receiving these drugs for therapy unless they have a history of drug abuse or have an underlying psychiatric disorder (Gutstein and Akil 2006; O'Brien 2006).

Occasionally, there are outbreaks of abuse of commonly prescribed narcotic products such as OxyContin (Brady 2010; "'Oxy' Kids Crisis" 2007). This product includes the opiate oxycodone, which has the approximate narcotic potency of morphine and can be obtained with relative ease. Authorities claim that the illegal pills come from doctors' offices, from dealers who fake illness to get legal prescriptions or who are writing phony orders, and from others who steal the supplies from pharmacies. OxyContin has been called *oxys, O.C.,* and *killers* on the street and is popular with narcotic abusers because of its rapid and potent effect. However, many, if not most, of those who use prescriptions drugs for nonmedical purposes obtain their painkillers from the medicine cabinets of a family member or a friend (*Alcoholism and Drug Abuse Weekly* 2010a). On the street, the drug can cost 10 times its prescription price. Because of its potent ability to suppress respiration, OxyContin appears to have been involved in overdose deaths throughout the country, although there is some evidence that other drugs were also involved in many of these cases. Critics claim that part of the abuse problem with OxyContin stems from overuse in situations that should be managed by a less potent and less addicting opioid analgesic.

Here and Now

Are Restrictions on Pain Pills Too Painful?

Because of a spiraling increase in the abuse of prescription "painkillers," the DEA has warned doctors who specialize in pain management that they risk special investigation if they do not comply with DEA guidelines. For example, the DEA recommends avoiding the use of opioid analgesics for the treatment of pain in patients who have a history of abusing these drugs. In addition, the DEA frowns upon the practice of doctors writing prescriptions for these pain drugs that can be filled on a future date. These and other restrictive DEA policies are viewed by some pain doctors as overregulation. Some are concerned that physicians will hesitate to prescribe even needed pain medication for fear of being investigated and charged with breaking the law. They worry that the DEA's actions are sending a chilling message that could result in withholding opioid narcotics from millions of patients who cannot be adequately treated by other drugs.

Sources: Kaufman, M. "New DEA Statement Has Pain Doctors More Fearful." *Washington Post* (30 November 2004): A-17; and Borigini, M. "Prescribing Narcotics: A Doctor's Point of View." Health Central, Chronic Pain Connection. 27 October 2008. Available at: http://www.healthcentral.com/chronic-pain/c/91/46424/prescribing-view. Accessed March 14, 2011.

Other Therapeutic Uses

Opioid narcotics are also used to treat conditions not related to pain. For example, these drugs suppress the coughing center of the brain, so they are effective antitussives. Codeine, a natural opioid narcotic, is commonly included in cough medicine. In addition, opioid narcotics slow the movement of materials through the intestines, a property that can be used to relieve diarrhea or can cause the side effect of constipation (*Drug Facts and Comparisons* 2010). Paregoric contains an opioid narcotic substance and is commonly used to treat severe diarrhea.

When used carefully by the clinician, opioid narcotics are very effective therapeutic tools. Guidelines for avoiding unnecessary problems with these drugs include the following (Rolfs 2008):

- Opioid pain relievers should only be used for pain when severity warrants and after consideration of other nonopioid pain medications such as aspirin or ibuprofen.
- Doses and duration of use should be limited as much as possible while permitting adequate therapeutic care.
- The patient should be counseled to store the medications securely, not share with others, and dispose of drugs properly when the pain has subsided and the medication is no longer needed.
- Long-duration opioid drugs should not be used to treat acute pain, except in situations where adequate monitoring can be conducted.
- The use of opioids should be reevaluated if pain persists beyond the anticipated time period for acute pain management.
- A comprehensive evaluation should be conducted before initiating opioid treatment.
- The provider should consider conducting a screen for risk of abuse or addiction before initiating opioid treatment.
- A treatment plan should be established between the doctor and patient that includes measurable goals for reduction of pain and improvement of function.
- The patient, and if appropriate, family members, should be informed of the risks and benefits of the opioid treatment. Sometimes a written contract identifying these elements should be prepared and signed.
- Opioid treatment should be discontinued if the terms of the contract are not being met by the patient.
- If significant abuse is suspected, the clinician should discuss the concerns with the patient and help the patient find appropriate treatment.

Abuse of Prescription Opioid Painkillers

As already mentioned, the abuse of prescription opioid painkillers has become a major problem in the United States and has been described by the American Drug Czar (i.e., director of the Office of National Drug Control Policy [ONDCP]), R. Gil Kerlikowske, as the "nation's fastest-growing drug problem" (*USA Today* 2010). An example of what has become all too common is the tragic narcotic overdose death of Leslie Cooper near Portsmouth, Ohio. She was never known to wander the streets or dark alleys to get her opioid narcotics. She received her drugs "legally" from multiple doctors and "pain-management clinics." Her problem with these prescription analgesics started when doctors prescribed potent painkillers to deal with the severe discomfort after a difficult surgery. More surgeries were necessary, which meant continual demand for, and access to, the opioid pain relievers. Something went terribly wrong and Leslie paid the price with her life. In her system was found a deadly combination of depressant drugs prescribed for muscle relaxation and depression, and two very potent narcotic analgesics. Leslie fell asleep and did not wake up. This is an example of why the misuse of these pain killers has led to a doubling of emergency room visits since 2004 (*USA Today* 2010), and also has caused some critics to question whether many doctors who prescribe such drugs are sufficiently trained in either proper pain or substance abuse management (Meier 2010).

Abuse problems with these drugs are partially due to the facts that these narcotic analgesics are very popular and account for about 7% of all prescribed drugs and that the number of patients who are taking the long-lasting versions of the agents (e.g., OxyContin) has increased 30% during the past decade (Meier 2010). This means that these drugs are more readily available and their use more widely accepted than ever before. However, it is important to appreciate that when used properly (i.e., as prescribed), the likelihood of becoming addicted to these narcotics for most people is very small (likely less than 1%; O'Brien 2006). But there are risk factors that make some patients more likely to have problems with these drugs; for those with these

Prescription for Addiction: What Makes People Vulnerable?

For most patients, the responsible use of prescription opioid analgesics is very helpful in the management of moderate to severe pain; however, a relatively small population has factors that can increase the danger of becoming addicted to these drugs as much as 25-fold. The risks that lead to this vulnerability include:

- Family history of substance abuse problems, which suggests the likelihood of genetic vulnerability (Levran et al. 2009)
- Dependence on nicotine, alcohol, or sleeping pills
- Depression
- Use of psychiatric medications
- Younger than 65 years of age

The value of identifying these risks is they may help warn which patients require special consideration and caution when prescribing narcotics to treat their pain.

Sources: Sify News. "Risk Factors for Painkiller Addiction Identified." 28 August 2010. Available at: http://sify.com/news/risk-factors-for-painkiller-addiction-identified-news-scitech-ki3pEjahbic.html. Accessed March 14, 2011; Reuters. "Do Smokers Use More Prescription Painkillers?" 17 June 2010. Available at: http://www.reuters.com/article/idUSTRE65G5RQ20100617. Accessed March 14, 2011; Medical News Today. "Study Identifies Risk Factors for Painkiller Addiction and Links the Addiction to Genetics." 28 August 2010. Available at: http://www.medicalnewstoday.com/articles/199263.php. Accessed March 14, 2011; and American Academy of Pain Medicine. "Psychiatric Factors Linked to Increased Risk for Misuse of Opioid Medications." 23rd Annual Meeting. Abstract 151. 7 February 2007.

risk factors the rate of addiction jumps to 25% (see "Prescription for Addiction: What Makes People Vulnerable?") (Sify News 2010).

Abuse of prescription opioid narcotics such as OxyContin and illicit narcotics such as heroin might seem to some people very different because one comes from a doctor and the other from drug dealers in the street. But in reality, because both types of drugs are opiates, they both can cause similar addiction, overdoses, and even death. In fact, a surprising rise in heroin abuse is occurring across the United States, which is likely in part the result of people who become addicted to the prescription opioid painkillers and switch to heroin because it is more accessible and easier to obtain. Heroin also can cost as little as one-fifth the price of prescription medications. All too often cases of heroin overdose deaths appear to have their origins from the victim first being exposed to the opioid narcotics during a chronic treatment for pain often associated with sports-related injuries (Valenzuela 2010; Willis 2008).

Mechanisms of Action

As mentioned earlier, the opioid receptors are the site of action of the naturally occurring endorphin peptide transmitters and are found throughout the nervous system, intestines, and other internal organs. Because narcotic drugs such as morphine and heroin enhance the endorphin system by directly stimulating opioid receptors, these drugs have widespread influences throughout the body.

For example, the opioid receptors are present in high concentration within the limbic structures of the brain. Stimulation of these receptors by narcotics causes release of the transmitter dopamine in limbic brain regions. This effect contributes to the rewarding actions of these drugs and leads to dependence and abuse (see "Signs & Symptoms: Narcotics") (Trigo et al. 2010; Zocchi et al. 2003).

Side Effects

One of the most common side effects of the opioid narcotics is constipation. Other side effects include

Signs & Symptoms Narcotics

POSSIBLE SIGNS OF USE	POSSIBLE SIGNS OF OVERDOSE
Euphoria	Low and shallow breathing
Drowsiness	Clammy skin
Respiratory depression	Convulsions
Constricted pupils	Coma
Nausea	Possible death

drowsiness, mental clouding, respiratory depression (suppressed breathing is usually the cause of death from overdose), nausea and vomiting, itching, inability to urinate, a drop in blood pressure, and constricted pupils (*Drug Facts and Comparisons* 2010). This array of seemingly unrelated side effects is due to widespread distribution of the opioid receptors throughout the body and their involvement in many physiological functions (Gourlay 2004; Trigo et al. 2010). With continual use, tolerance usually develops to some of these undesirable narcotic responses.

Drugs that selectively antagonize the opioid receptors can block the effects of natural opioid systems in the body and reverse the effects of narcotic opiate drugs (*Drug Facts and Comparisons* 2010). When an opioid antagonist such as the drug naloxone is administered alone, it has little noticeable effect. The antiopioid actions of naloxone become more apparent when the antagonist is injected into someone who has taken a narcotic opioid drug. For example, naloxone will cause (1) a recurrence of pain in the patient using a narcotic for pain relief, (2) the restoration of consciousness and normal breathing in the addict who has overdosed on heroin, and (3) severe withdrawal effects in the opioid abuser who has become dependent on narcotics (*Drug Facts and Comparisons* 2010; Szalavitz 2005). Because of the ability of these antagonists to block the effects of opioid drugs, they are also used as treatment for some opioid-dependent patient (Laino 2010).

An interesting recent use of opioid antagonists is to treat alcohol dependence. The Food and Drug Administration (FDA) has approved the use of naltrexone (a narcotic antagonist) in a regular and extended-release formulation to relieve the craving of alcoholics for excessive alcohol consumption (*Drug Facts and Comparisons* 2010; Laino 2010).

Abuse, Tolerance, Dependence, and Withdrawal

All the opioid narcotic agents that activate opioid receptors have abuse potential and are classified as scheduled drugs (see **Table 9.2**). Their patterns of abuse are determined by the ability of these drugs to cause tolerance, dependence, withdrawal effects, and eventually addiction. However, it is important to recognize that because a patient treated by these drugs for pain develops physical dependence and experiences significant withdrawal when the drug is abruptly removed, they are not necessarily addicted (Hitti 2010). In fact, relatively few patients properly receiving the opioid narcotics for pain relief will go on to become truly addicted, even though they may develop physical dependence and are temporarily uncomfortable when the narcotic treatment is discontinued. This distinction between physical dependence and the compulsive need to use the opioid narcotics despite very negative consequences (e.g., addiction) is very important and needs to be appreciated in order to provide proper pain management, especially for severe long-term pain conditions (Get the Facts 2010).

The process of tolerance literally begins with the first dose of a narcotic, but tolerance does not become clinically evident until after 2 to 3 weeks of frequent use (either therapeutic- or abuse-related). Tolerance occurs most rapidly with high doses given in short intervals and is a common result of the extended clinical use of prescription opioid painkillers. It also is caused by abuse of these narcotics in addicted persons. The result of tolerance is that doses of these drugs must be increased (sometimes

Table 9.2 Schedule Classification of Some Common Narcotics

NARCOTIC	SCHEDULE
Heroin	I
Morphine	II, III
Methadone	II
Fentanyl	II
Hydromorphone	II
Meperidine	II
Codeine	II, III, V
Buprenorphine	III
Pentazocine	IV
Tramadol	Unscheduled
Narcotics combined with nonsteroidal anti-inflammatory drugs	III

Source: Drug Enforcement Administration (DEA). Controlled Substances Act. 1 February 2010. Available at: http://uscode.house.gov/download/pls/21C13.txt. Accessed March 16, 2011.

several-fold) to retain or regain the therapeutic or nonmedicinal narcotic effects. Physical dependence invariably accompanies severe tolerance (Reisine and Pasternak 1995). Psychological dependence can also develop with continual narcotic use because these drugs can cause euphoria and relieve stress. Such psychological dependence leads to compulsive use (Gutstein and Akil 2006; O'Brien 2006). Because all narcotics affect the same opioid systems in the body, developing tolerance to one narcotic drug means the person has cross-tolerance to all drugs in this group.

The development of psychological and physical dependence makes stopping the drug uncomfortable due to resulting unpleasant withdrawals. Someone who has used potent narcotics for a long time, like a major long-term addict, will experience severe withdrawal effects such as exaggerated pain responses, agitation, anxiety, stomach cramps and vomiting, joint and muscle aches, runny nose, and an overall flu-like feeling. Although these withdrawal symptoms are not fatal, they are extremely aversive and encourage continuation of the narcotic habit (McEvoy 2003). Overall, the narcotics have similar actions; there are differences, however, in their potencies, severity of side effects, likelihood of being abused, and clinical usefulness.

Heroin Abuse

> "My parents had no idea. My mom thought I was smoking a lot of weed and taking diet pills, because who would've thought that such a bad drug (heroin) could be so easily accessible to me. Growing up, everything is pushed on you. You're trying to be the smartest, trying to compete with everyone. Heroin was an escape."
>
> "It hits you hard, but it's so smooth and enticing at the same time. It hits you like a train of false love."
>
> "Believe it or not, as a high school teenager, it is easier for us to get than alcohol." *(Quotes from three young people in rehabilitation in New York; Buckley 2009)*

These quotes from three young people illustrate the powerful attraction of heroin and help explain why it is so frequently abused. They also illustrate that the use of heroin, especially by teenagers and young adults, appears to be increasing. The likely explanations for this recent rise in popularity include the facts that high-grade heroin has become very cheap and readily available (Schneider 2009). In addition, it appears that elevated heroin use is an indirect consequence of the increase in the abuse of prescription opioid painkillers. Thus, as more people abuse the prescribed narcotics they increase their consumption because they develop tolerance. This makes their habit more expensive and makes it more difficult to obtain enough of the prescription drugs to satisfy their nonmedical (addiction) needs. Consequently, these people frequently switch to street heroin, which is a fraction of the cost while being reasonably pure and potent (Cole 2010; Schneider 2009). Of course, this switch to heroin increases the risk of getting a bad batch of drug that is much more potent than expected or contains other drugs that are more dangerous. The unintended outcomes can be, at the least, very dangerous and result in a trip to the emergency room, or in the extreme, can cause an accidental overdose fatality (Bernstein 2010; Caldwell and Salter 2010).

Heroin is currently classified as a Schedule I drug by the DEA (see Table 9.2). It is not approved for any clinical use in the United States, is one of the most widely abused illegal drugs in the world, and is reported to account for more than $120 billion in global sales each year (Chossudovsky 2006; GlobalSecurity.org 2010). It is also thought to be associated with some of the highest mortality rates and most emergency room visits of any of the illegal drugs of abuse in the United States (National Institute on Drug Abuse [NIDA] 2005). Heroin was illicitly used more than any other drug of abuse in the United States (except for marijuana) until 20 years ago, when it was unseated by cocaine (DiChiara and North 1992). In 2009, 0.7% of high school seniors reported having used heroin during the previous year, and 1.2% indicated that they had used this drug sometime during their life (Johnston 2010).

From 1970 through 1976, most of the heroin reaching the United States originated from the Golden Triangle region of Southeast Asia, which includes parts of Burma, Thailand, and Laos. During that period, the United States and other nations purchased much of the legal opium crop from Turkey in an effort to stop opium from being converted into heroin. From 1975 until 1980, the major heroin supply came from opium poppies grown in Mexico. The U.S. government furnished the Mexi-

can government with helicopters, herbicide sprays, and financial assistance to destroy the poppy crop. Changes in political climates have shifted the source of supply back to the Golden Triangle and Latin American countries (e.g., Colombia; Seper 2003) and more recently to Afghanistan where 92% of the world's heroin is currently produced (Christensen 2010), accounting for approximately $3 billion in revenue for local farmers (AFP 2010). Heroin produced in Afghanistan has taken a heavy toll on the Afghan people (Christenson 2010) (see "Here and Now: Afghans' Drug War"). It has been speculated that heroin trafficked from Afghanistan has killed more than a million people worldwide in the past decade (AFP 2010), and as previously discussed, is a substantial problem for U.S. and NATO soldiers fighting in the Afghanistan war (Edwards 2010). Despite these disturbing effects, the United States has stopped its previous policy of crop eradication because it alienated the poorest Afghan populations who rely on this crop to survive and support their families and tended to turn them against the efforts by the American/European-supported government to eliminate insurgent groups such as the Taliban. More recently, the U.S. government and military have been trying to convince farmers to replace their opium poppies with other profitable crops (AFP 2010; Starikov 2010). Despite these efforts to be more "compassionate and understanding," many experts question the effectiveness of these strategies (Starikov 2010).

Heroin Combinations

Heroin is typically smuggled into the United States from one of four foreign sources: Mexico, South America, Southeast Asia (e.g., Burma), or Southwest Asia (e.g., Afghanistan). It is carried into the United States hidden in commercial and private vehicles driven from Mexico or Canada or carried by couriers traveling on commercial flights. Pure heroin is a white powder. Other colors, such as brown Mexican heroin, result from unsatisfactory

Here and Now

Afghans' Drug War

How goes the "war" in Afghanistan? The answer may be quite different depending on whether you are referring to the military war being fought against the Taliban with guns, explosives, and military maneuvers or the drug war being fought against poor opium farmers trying to survive on meager earnings that come from the few acres they are able to cultivate. Opium crops are particularly well suited to this land and historically brought good prices. Consequently, it is difficult to convince the poor farmers that crops that allow them to feed their families are evil and should be stopped. Despite the fact that efforts by both the Afghan and U.S. governments to educate opium farmers and help them develop profitable alternative crops reduced poppy cultivation by 22% in 2009, production of Afghan opium has risen dramatically during the Afghan War and currently is thought to provide 92% of the world's heroin. Just because they produce the opium, the Afghan people are not immune to its problems. It is speculated that 1 in 25 Afghans is an addict, and there are very few resources to provide adequate treatment or initiate effective prevention programs. Statistics such as these are powerful evidence that the Afghans' drug war goes very badly indeed.

Sources: Constable, P. "A Poor Yield for Afghans' 'War on Drugs.' " *Washington Post* (19 September 2006): 14A; and Christenson, S. "Heroin Addiction Takes Brutal Toll on Afghanistan." *San Antonio Express-News.* 24 May 2010. Available at: http://www.mysanantonio.com/news/local_news/in_kabul_regrets_rehab_and_redemption_94714589.html?showFullArticle=y. Accessed March 14, 2011.

processing of morphine or from adulterants. Heroin is usually "cut" (diluted) with lactose (milk sugar) to give it bulk and thus increase profits. When heroin first enters the United States, it can be up to 95% pure; by the time it is sold to users, its purity can be as low as 3% or (recently) as high as 70% (Epstein and Gfroerer 1998; Schneider 2009; Stockman 2003). If users are unaware of the variance in purity and do not adjust doses accordingly, the results can be extremely dangerous and occasionally fatal (Bernstein 2010; NIDA 2005).

Heroin has a bitter taste, so sometimes it is cut with quinine, a bitter substance, to disguise the fact that the heroin content has been reduced. Quinine can be a deadly adulterant. Part of the "flash," or immediate rush, from direct injection of heroin may be caused by this contaminant. Quinine is an irritant, and it causes vascular damage, acute and potentially lethal disturbances in heartbeat, depressed respiration, coma, and death from respiratory arrest. Opiate poisoning causes acute pulmonary edema as well as respiratory depression. To counteract the constipation caused by heroin, sometimes mannitol is added for its laxative effect.

Another potentially lethal combination emerges when heroin is laced with the much more potent artificial narcotic fentanyl. This adulterated heroin can be extremely dangerous due to its unexpected potency (NIDA 2004).

Frequently, heroin is deliberately combined with other drugs when self-administered by addicts (Hickman et al. 2007). According to the National Institute on Drug Abuse (NIDA)–sponsored Drug Abuse Warning Network (DAWN) survey of emergency rooms in the United States, 41% of the reported heroin abuse cases involved other drugs of abuse in combination with this narcotic. Heroin is most frequently used with alcohol, but it is often combined with CNS stimulants, such as cocaine (Hickman et al. 2007). Some crack cocaine smokers turn to heroin to ease the jitters caused by the CNS stimulant (Leland 1996). It also has been reported that heroin addicts use cocaine to withdraw or detoxify themselves from heroin by gradually decreasing amounts of heroin while increasing amounts of cocaine. This drug combination is called **speedballing**, and addicts claim the cocaine provides relief from the unpleasant withdrawal effects that accompany heroin abstinence in a dependent user (Rowlett et al. 2010).

Crude heroin is dark and sometimes referred to as black tar heroin, whereas purified heroin is a white powder.

Profile of Heroin Addicts

An estimated 600,000 to 1 million active heroin addicts live in the United States, a figure that has remained relatively stable despite changes in the number of infrequent and moderate users. Heroin addicts often search for a better and purer drug; however, if they do find an unusually potent batch of heroin, there is a good chance they will get more than they bargained for. Addicts are sometimes found dead with the needle still in the vein after injecting a particularly potent batch of heroin (Caldwell and Salter 2010). More than 3000 deaths occur annually in the United States from heroin overdoses (Caldwell 2010). Death associated with heroin injection is usually due to concurrent use of alcohol or barbiturates—not the heroin alone—and frequently occurs after an addict has gone weeks or months without the drug and injects the same amount of heroin he or she used before, not realizing that tolerance has worn off (Rombey 2003b).

Hard-core addicts often share a common place where they can stash supplies and equipment for their heroin encounters. These locations, called *shooting galleries,* serve as gathering places for addicts (Cowan and Carvel 2006). Shooting galleries can be set up in homes, but are usually located in less established locations such as abandoned cars, cardboard lean-tos, and weed-infested vacant lots. An entrance charge often is required of the pa-

KEY TERMS

speedballing
combining heroin and cocaine

trons. Conditions in shooting galleries are notoriously filthy, and these places are frequented by intravenous heroin users with bloodborne infections that can cause AIDS or hepatitis. Because of needle sharing and other unsanitary practices, shooting galleries have become a place where serious communicative diseases are spread to a wide range of people of different ages, races, genders, and socioeconomic statuses (Bearak 1992; Nakamura 2008). In some countries such as the United Kingdom, there are controversial efforts to develop government-regulated shooting galleries in order to assure sanitary conditions and clean needles for the heroin addicts to prevent their exposure to the dangers of contracting devastating and potentially deadly diseases (Leach 2009).

The heroin in shooting galleries is typically prepared by adding several drops of water to the white powder in an improvised container (such as a metal bottle cap), and lightly shaking the container while heating it over a small flame to dissolve the powder. The fluid is then drawn through a tiny wad of cotton to filter out the gross contaminants into an all-too-often used syringe where it is ready for injection (Bearak 1992).

Some addicts become fixated on the drug's paraphernalia, especially the needle. They can get a psychological "high" from playing with the needle and syringe. The injection process and syringe plunger action appear to have sexual overtones for them. As one reformed user explained, "I think what I miss more than heroin sometimes is just the ritual of shooting up." A current user concurred, explaining, "You get addicted to the needle . . . Just the process of sticking something into your vein, having such a direct involvement with your body . . ." ("Mary" 1996, p. 42; Winkler et al. 2010).

Heroin paraphernalia is usually simple and crude but effective: a spoon on which to dissolve the narcotic and a makeshift syringe with which to inject it.

Heroin and Crime

In 1971, the Select Committee on Crime in the United States released a report on methods used to combat the heroin crisis that arose in the 1950s and 1960s. This report was a turning point in setting up treatment programs for narcotic addicts. The report stated that drug arrests for heroin use had increased 700% since 1961, and that the cost of heroin-related crimes to U.S. society was estimated to exceed $3 billion per year. Other studies since that time have linked heroin addiction with crime (McMurran 2007).

Although many young heroin addicts come from affluent or middle-class families (Weiss 1995), research shows heavy users (usually addicts who inject their heroin) are frequently poorly educated with minimal social integration and live in neighborhoods surrounded by poverty (Nandi et al. 2010). Because of these disadvantages, these heroin addicts often have a low level of employment, exist in unstable living conditions, and socialize with other illicit drug users. Clearly, such undesirable living conditions encourage criminal activity. However, three other factors also likely contribute to the association between heroin use and crime:

1. The use of heroin and its pharmacological effects encourage antisocial behavior that is crime related. Depressants such as heroin diminish inhibition and cause people to engage in activities they normally would not. The effects of heroin and its withdrawal make addicts self-centered, demanding, impulsive, and governed by their "need" for the drug.
2. Because heroin addiction is expensive, the user is forced to resort to crime to support the drug habit (McMurran 2007).
3. A similar personality is driven to engage in both criminal behavior and heroin use. Often, heroin addicts start heroin use about the same time they begin to become actively involved in criminal activity. In most cases, the heroin user has been taking other illicit drugs, especially marijuana, years before trying heroin (Reid, Elifson, and Sterk 2007).

These findings suggest that for many heroin addicts, the antisocial behavior causes the criminal behavior rather than the criminal behavior resulting from the heroin use. Thus, the more a drug such as heroin is perceived as being illegal, desirable, and addictive, the more likely it will be used by deviant criminal populations. However, typically heroin users are not violent, although they may participate in criminal activity to fund their drug habit. Violence is more likely associated with heroin trafficking and distribution because of the criminal groups involved in this activity.

Patterns of Heroin Abuse

It has become apparent that problems with narcotics are no longer confined to the inner cities, but have infiltrated suburban areas and small towns and afflict both rich and poor (see "Here and Now: Heroin Use in a Small Town"). The following are recent heroin trends (see **Table 9.3**):

- Heroin use among adolescents and young adults, after holding steady through much of the first decade in 2000, is thought to be rising due to a decrease in cost, and increases in purity and availability (Cole 2010; Schneider 2009).
- Heroin has become purer (60–70% purity) and cheaper ($10/bag [~100 mg]) (Schneider 2009).
- Thanks to the greater purity, new users are able to administer heroin in less efficient ways, such as smoking and snorting, and avoid the dangers of intravenous use (Cole 2010). Many youths believe that heroin can be used safely if it is not injected.
- Because of its association with popular fashions and entertainment, heroin has been viewed as glamorous and chic, especially by many young people, despite its highly publicized lethal consequences. The look of being "wasted" and unkempt has been referred to as "heroin chic" (Urban Dictionary 2005). However, this "druggy look" and malnourished appearance has fallen out of fashion within the glamour business because of its very negative implications and health consequences (Quinion 2005).
- Approximately 190,000 emergency room visits each year are due to heroin overdoses (My Addiction.com 2010).

Stages of Dependence

Initially, the early effects of heroin are often unpleasant, especially after the first injection (Gutstein and Akil 2006). It is not uncommon to experience nausea and vomiting after administration; gradually, however, the euphoria overwhelms the aversive effects (Quinion 2005). There are two major stages in the development of a psychological dependence on heroin or other opioid narcotics:

1. In the rewarding stage, euphoria and positive effects occur in at least 50% of users. These positive feelings and sensations increase with continued administration and encourage use.
2. Eventually, the heroin or narcotic user must take the drug to avoid withdrawal symptoms that start about 6 to 12 hours after the last dose. At this stage, it is said that "the monkey is on his

Here and Now

Heroin Use in a Small Town

Heroin is supposed to be a "big town" drug, but is gaining popularity in smaller towns. This is very disturbing to those who have chosen to live the rural life with the belief that such an environment will somehow protect them from the ugliness, fear, and pain of typical metropolitan drug problems. They are finding out that drugs such as heroin can be anywhere and used by anybody. Stories like that of Sandi Daost are tragic: her 19-year-old son Robby died from a heroin overdose after months of going in and out of rehab centers trying to stay clean. He grew up in the typical small town—Springville, Utah. The family believed that Robby finally had kicked the habit. He had been clean for 7 months and laughed and joked with the family again. He had a job and a cute girlfriend and was attending church with his family. One Sunday, he told his mother he was going to play golf with a friend. Robby didn't go golfing, but made his last trip to meet his heroin connection. He was found in his bed the next morning, dead from a heroin overdose. The citizens of Springville were bewildered and shocked because within a relatively short time, five other heroin overdose deaths occurred to young men also in their late teens or early 20s. We expect this type of thing in Los Angeles or New York, but no one seems to have an answer to "why in Springville?"

Sources: Rombey, D. "Heroin Is Silent Scourge of Sheltered Springville." *Deseret News* (9 June 2003): A-1; Rombey, D. "Heroin Takes Toll on Families." *Deseret News* (10 June 2003): A-1; and Van Hollen, J. "Heroin Abuse Now a Rural Threat Too." *The Cap Times.* 3 October 2010. Available at: http://host.madison.com/ct/news/opinion/mailbag/article_c47ae879-6bf7-5bf3-a2e5-87c2bebf92a0.html. Accessed March 14, 2011.

Table 9.3 Prevalence of Heroin and Other Opioid Abuse Among High School Seniors

	ANNUAL USE		LIFETIME USE	
YEAR	HEROIN	OTHER OPIOIDS	HEROIN	OTHER OPIOIDS
1989	0.6%	4.4%	1.3%	8.3%
1995	1.1%	4.7%	1.6%	7.2%
1999	1.1%	6.7%	2.0%	10.2%
2002	1.0%	9.4%*	1.7%	13.5%*
2007	0.9%	9.2%	1.5%	13.1%
2009	0.7%	9.2%	1.2%	13.2%

* In 2002, the question text was changed in half of the questionnaire forms. The list of examples of narcotics other than heroin was updated: Talwin, laudanum, and paregoric—all of which had negligible rates of use by 2001—were replaced with Vicodin, OxyContin, and Percocet. The 2002 data presented here are based on the changed forms only; *N* is one half of *N* indicated. In 2003, the remaining forms were changed to the new wording. Data based on all forms beginning in 2003.

Sources: Johnston, L. D., P. M. O'Malley, J. G. Bachman, and J. E. Schulenberg. *Monitoring the Future*. "Trends in Lifetime Prevalence of Use of Various Drugs in Grades 8, 10, and 12 (Table 1)." Ann Arbor, MI: University of Michigan, 2010. Available at http://monitoringthe future.org/data/10data/pr10t1.pdf. Accessed April 22, 2011; and Johnston, L. D., P. M. O'Malley, J. G. Bachman, and J. E. Schulenberg. *Monitoring the Future*. "Trends in Annual Prevalence of Use of Various Drugs in Grades 8, 10, and 12 (Table 2)." Ann Arbor, MI: University of Michigan, 2010. Available at http://monitoringthe future.org/data/10data/pr10t2.pdf. Accessed April 22, 2011.

back." This stage is psychological dependence. If 1 grain of heroin (about 65 milligrams) is taken over a 2-week period on a daily basis, the user becomes physically dependent on the drug.

Methods of Administration

Many heroin users start by sniffing the powder or injecting it into a muscle (intramuscular) or under the skin ("skin popping"). Because of the increased purity and decreased cost, many of today's heroin users are administering their drug by smoking and snorting (Caldwell and Salter 2010; Schneider 2010).

Most established heroin addicts still prefer to **mainline** the drug (intravenous injection) (Community Epidemiology Work Group [CEWG] 2002). The injection device can be made from an eyedropper bulb, part of a syringe, and a hypodermic needle. Mainlining drugs causes the thin-walled veins to become scarred and, if done frequently, the veins will collapse. Once a vein is collapsed, it can no longer be used to introduce the drug into the blood. Addicts become expert in locating new veins to use: in the feet, the legs, the neck, even the temples. When addicts do not want "needle tracks" (scars) to show, they inject under the tongue or in the groin ("Opioids" 1996).

Heroin Addicts and AIDS

As noted previously, because needle sharing is common among heavy heroin users, the transmission of deadly communicable diseases such as AIDS is a major problem (see Chapter 17). The Centers for Disease Control and Prevention (CDC) reports that more than 250,000 AIDS patients in the United States contracted the HIV virus through drug injection; most were heroin users (DrugWarFacts 2010). Fear of contracting this deadly disease has contributed to the increase of administering this drug by smoking and snorting (Healthtree 2010); however, many heroin users who start by smoking and snorting eventually progress to intravenous administration due to its more intense effects (Leland 1996).

Heroin and Pregnancy

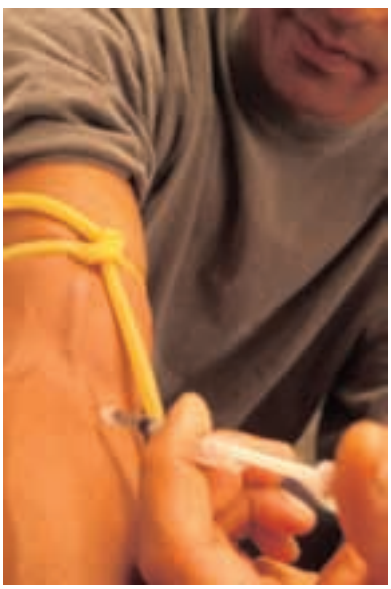
Devin acts like any normal two-year-old. He particularly enjoys the fast-food Chick-fil-A restaurant and playing with the barbecue sauce containers. Looking at Devin gives no clue that his mother had become addicted to prescription painkillers when she discovered her pregnancy. She was urged by her sister to seek professional help immediately. Devin was born on time and was undersized at 5 pounds and 5 ounces. Devin was able to avoid the worst withdrawal symptoms after birth because he was immediately placed on methadone and gradually weaned to allow his small body to adjust to not having the painkillers that his mother had been using throughout her pregnancy. Devin was lucky: other babies under

KEY TERMS

mainline
to inject a drug of abuse intravenously

> similar circumstances who do not receive proper medical care suffer through severe feeding problems, vomiting, diarrhea, muscle stiffness, and severe tremors. These babies cry constantly as they experience severe narcotic withdrawal and in extreme cases they may even suffer seizures. (Colon 2011)

Many women use heroin during their pregnancy. In the United States, as many as 7000 infants are born each year to women who chronically used either heroin or other opioid drugs during their pregnancies (Bhuveneswar et al. 2008). There is no evidence that prenatal exposure to opioid drugs causes overt structural damage, although incidents of smaller birth weights or even reduced head size have been reported in infants born to mothers using opioid drugs (Wang 2010). The most devastating consequence of heroin or opioid use during pregnancy appears to be physical dependence in the newborn, resulting in withdrawal symptoms usually immediately after birth. These symptoms are characterized by high-pitched crying, inconsolability, tightened muscle tone, tremors, vomiting, and even seizures. Elements of this withdrawal persist for weeks (Wang 2010). Treatment for such withdrawal problems generally includes low doses of a long-lasting opioid narcotic to reduce the intensity of the symptoms and then a gradual tapering of the dose to eventually wean the infant from the drug. For heroin, this typically takes up to 2 weeks (Pain and Central Nervous System 2005; Wang 2010). In addition, there is some evidence that the use of heroin during pregnancy increases the likelihood of sudden infant death syndrome (SIDS) in offspring (American SIDS Institute 2005).



A heroin addict "mainlining" his drug.

Withdrawal Symptoms

After the effects of heroin wear off, the addict usually has only a few hours in which to find the next dose before severe withdrawal symptoms begin. A single "shot" of heroin lasts only 4 to 6 hours. It is enough to help addicts "get straight" or relieve the severe withdrawal symptoms called dope sickness but is not enough to give a desired "high" (Bearak 1992). Withdrawal symptoms start with a runny nose, tears, and minor stomach cramps. The addict may feel as if he or she is coming down with a bad cold (Galanter and Kleber 2008). Between 12 and 48 hours after the last dose, the addict loses all of his or her appetite, vomits, has diarrhea and abdominal cramps, feels alternating chills and fever, and develops goose pimples all over (going "cold turkey"). Between 2 and 4 days later, the addict continues to experience some of the symptoms just described, as well as aching bones and muscles and powerful muscle spasms that cause violent kicking motions ("kicking the habit"). After 4 to 5 days, symptoms start to subside, and the person may get his or her appetite back. However, attempts to move on in life will be challenging because compulsion to keep using the drug remains strong.

The severity of the withdrawal varies according to the purity and strength of the drug used and the personality of the user. The symptoms of withdrawal from heroin, morphine, and methadone are summarized in **Table 9.4**. Withdrawal symptoms from opioids such as morphine, codeine, meperidine, and others are similar, although the time frame and intensity vary (Galanter and Kleber 2008; Gutstein and Akil 2006).

Treatment of Heroin and Other Narcotic Dependence

The ideal result of treatment for dependency on heroin or other narcotics is to help the addict live a normal, productive, and satisfying life without drugs (Galanter and Kleber 2008). Unfortunately, the minority of heroin addicts receive adequate treatment for their addiction. Of those who are treated, relatively few heroin users become absolutely "clean" from drug use; thus, therapeutic compromise often is necessary (see **Figure 9.1**). In the real world, treatment of heroin dependency is considered successful if the addict does the following:

Table 9.4 Symptoms of Withdrawal from Heroin, Morphine, and Methadone

SYMPTOMS	TIME IN HOURS HEROIN	MORPHINE	METHADONE
Craving for drugs; anxiety	4	6	24–48
Yawning, perspiration, runny nose, tears	8	14	34–48
Pupil dilation, goose bumps, muscle twitches, aching bones and muscles, hot and cold flashes, loss of appetite	12	16	48–72
Increased intensity of preceding symptoms, insomnia, raised blood pressure, fever, faster pulse, nausea	18–24	24–36	≥72
Increased intensity of preceding symptoms, curled-up position, vomiting, diarrhea, increased blood sugar, foot kicking ("kicking the habit")	26–36	36–48	—

1. Stops using heroin
2. No longer associates with dealers or users of heroin
3. Avoids dangerous activities often associated with heroin use (such as needle sharing, injecting unknown drugs, and frequenting shooting galleries) (Tur 2010)
4. Improves employment status
5. Refrains from criminal activity
6. Is able to enjoy normal family and social relationships

For more than 30 years, many heroin addicts have achieved these goals by substituting a long-lasting synthetic narcotic, such as methadone, for the short-acting heroin (Galanter and Kleber 2008; O'Brien 2006; Zickler 1999). The maintenance ("substitute") narcotic is made available to heroin-dependent people through drug treatment centers under the direction of trained medical personnel. The dispensing of the substitute narcotic is tightly regulated by governmental agencies. The rationale for the substitution is that a long-acting drug such as methadone can conveniently be taken once a day (Galanter and Kleber 2008; O'Brien 2006) to prevent the unpleasant withdrawal symptoms that occur within 4 hours after each heroin use (see Table 9.4). Although the substitute narcotic may also have abuse potential and be scheduled by the DEA (see Table 9.2), it is given to the addict in its oral form; thus, its onset of action is too slow to cause a rush like that associated with heroin use, which means that its abuse potential is substantially less (Galanter and Kleber 2008). In addition, the cost to society is dramatically reduced. According to one study, an untreated heroin addict costs the community $21,000 for 6 months, but the cost of methadone maintenance for a person dependent on heroin is only about $1000 for the same period (Hubbard 1998; Substance Abuse and Mental Health Services Administration [SAMHSA] 2008).

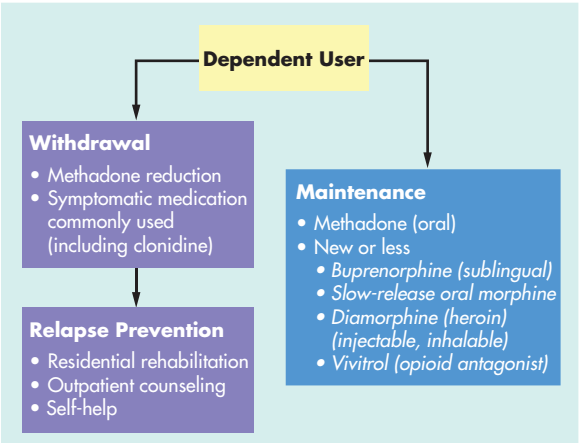


FIGURE 9.1

The principal aspects of treating heroin addiction include minimizing the very aversive withdrawal effect (usually with drug adjuncts); preventing relapse (usually with behavioral modification); and, if necessary, providing maintenance support with other opioid-like drugs that have longer action than heroin.

Currently, methadone is approved by the FDA for "opiate maintenance therapy" in the treatment of heroin (or other narcotic) dependency (Galanter and Kleber 2008). It has been used in heroin treatment for more than 30 years. Although it is not the best treatment for every person dependent on an opiate drug, it is an effective tool for managing many heroin addicts (Benfield 2010). Proper use

of methadone has been shown to effectively decrease illicit use of narcotics and other undesirable behavior related to drug dependence (Galanter and Kleber 2008). Although methadone does not tend to make users high, it helps heroin addicts by reducing their drug craving (Benfield 2010). Often methadone-assisted therapy will be long-term and even for the rest of the addict's life (Miller 2010). The methadone is typically well tolerated, although if misused it can be problematic and has been associated with a startling number of overdose deaths across the country (Colberg 2010; Miller 2010).

A second narcotic, buprenorphine, which is used as an analgesic, also has been approved for treatment of narcotic dependence (Hanson 2003). Because buprenorphine is both an opioid agonist and antagonist, it has minimal potential for dependence and is easy to manage, which makes this drug a desirable substitute for heroin (*Drug Facts and Comparisons* 2010). Efforts are being made to provide education and training to primary care physicians so they will be able to use buprenorphine to treat patients addicted to narcotics in their own offices (SAMHSA 2010). This novel strategy opens the door to physicians heretofore not involved in the treatment of drug addiction to become familiar with substance abuse management and hopefully increase the opportunities to diagnose and treat these patients. There is considerable discussion as to how buprenorphine products compare to methadone in treatment of dependence on, and addiction to, opioids in general and heroin in particular. Although the issues clearly require further study, there is some evidence that buprenorphine is usually the better and safer strategy for detoxification (i.e., treatment of withdrawal) and treatment for infants of opiate-addicted mothers (Boughton 2010; Meader 2010; ACOG 2010). However, such claims are disputed by some experts in the field (Bates 2010; More 2008).

A third, and very different drug approved in 2010 by the FDA to treat heroin and other opioid addictions is Vivitrol, an extended-release form of naltrexone, an opioid antagonist (National Center for Biotechnology Information [NCBI] 2010; Rubin 2010). In 2006, Vivitrol was originally approved as a treatment for alcoholism because of its ability to reduce alcohol craving and its consumption (Drugs.com 2010a; Rubin 2010). Vivitrol has been found to also reduce craving for narcotic drugs such as heroin. Its administration consists of a monthly deep muscle injection. Some of the potential side effects of using Vivitrol include: (1) interference with thinking or reactions, (2) wheezing, (3) enhanced pain, and (4) mood changes (Drugs.com 2010a).

Table 9.5 compares the opioids that have been used for maintenance therapy. Other drugs used less frequently for similar maintenance therapy of heroin addicts include slow-release oral morphine and even heroin itself for addicts who do not respond to the other maintenance opioid drugs (Bammer et al. 1999).

Some people, including some professionals involved in drug abuse therapy, view heroin or narcotic addiction as a "failure of the will" and see methadone treatment as substituting one addiction for another. However, evidence has demonstrated that this approach is very effective in preventing the spread of infectious diseases such as AIDS and he-

Table 9.5 Comparison of Narcotic Substitutes Used in Opiate Maintenance Therapy

PROPERTIES	METHADONE	BUPRENORPHINE
Administration	Oral	Oral or sublingual
Frequency of doses	Daily	Daily
Other uses	Analgesic	Analgesic
Physical dependence	Yes	Little
Causes positive subjective effects	Yes	Yes
Abuse potential	Yes	Limited

Source: Swan, N. "Two NIDA-Tested Heroin Treatment Medications Move Toward FDA Approval." *NIDA Notes* (March/April 1993): 45.

patitis and helps the heroin addict to return to a normal productive life (McClure 2009). Unrealistic treatment expectations are sometimes imposed on heroin addicts, leading to high failure rates. For example, some methadone treatment programs distribute inadequate methadone doses to maintain heroin or narcotic abstinence (Recovery Helpdesk 2010); alternatively, narcotic-dependent patients may be told their methadone will be terminated within 6 months regardless of their progress in the program. Such ill-advised policies often drive clients back to their heroin habits and demonstrate that many professionals who treat heroin and narcotic dependency do not understand that methadone is not a cure for heroin addiction but is a means to achieve a healthier, more normal lifestyle (McClure 2009).

It also is essential to understand that even proper treatment does not guarantee resolution of heroin or narcotic addiction (see "Case in Point: Heroin Addiction"). To maximize the possibility of successful treatment, clients must also participate in regular counseling sessions to help modify the drug-seeking behavior and receive on-site care from professionals, including job training, career development, education, general medical care, and family counseling. These supplemental services dramatically improve the success rate of narcotic dependence treatment (Grinspoon 1995; Heroin Detox 2010; McLellan et al. 1993).

Other Narcotics

A large number of nonheroin narcotics are used for medical purposes. However, many are also distributed in the streets, such as morphine, methadone, codeine, hydromorphone (Dilaudid), meperidine (Demerol), and other synthetics (hydrocodone [Vicodin] and oxycodone [OxyContin]). A few of the most commonly abused opioids are discussed briefly in the following sections. Except where noted, they are all Schedule II or III drugs.

Morphine

As noted earlier, morphine is the standard by which other narcotic analgesic agents are measured (Way, Fields, and Way 1998). It has been used to relieve pain since it was first isolated in 1803. Morphine has about half the analgesic potency of heroin but 12 times the potency of codeine. It is commonly used to relieve moderate to intense pain that cannot be controlled by less potent and less dangerous narcotics. Because of its potential for serious side effects, morphine is generally used in a hospital setting where emergency care can be rendered, if necessary. Most pain can be relieved by morphine if high enough doses are used (Reisine and Pasternak 1995; Way et al. 1998); however, morphine is most effective against continuous dull pain.

Case in Point: Heroin Addiction: Not a Funny Matter

Artie Lange, a regular "funnyman" on "The Howard Stern Show," was discovered by his mother bleeding on his Hoboken apartment floor. According to paramedics, Lange had been stabbed nine times with a kitchen knife. Police investigators concluded the wounds were self-inflicted and called it a suicide attempt. Lange had experienced multiple bouts of serious depression associated with a heroin addiction. Despite treatment, Lange manifested self-destructive tendencies that apparently led to this attempt to take his own life. His behavior had been compared to other self-destructive comics such as Chris Farley and John Belushi, who both experienced untimely deaths apparently by accidental causes linked to their drug/heroin use.

Source: Relative, S. "Artie Lange Stabbed Himself Nine Times, Attempted Suicide Confirmed." Associated Content, Arts and Entertainment. 8 January 2010. Available at: http://www.associatedcontent.com/article/2568063/artie_lange_stabbed_himself_nine_times.html. Accessed February 16, 2011.

The side effects that occur when using therapeutic doses of morphine include drowsiness, changes in mood, and inability to think straight. In addition, therapeutic doses depress respiratory activity; thus, morphine decreases the rate and depth of breathing and produces irregular breathing patterns. Like the other narcotics, it can create an array of seemingly unrelated effects throughout the body, including nausea and vomiting, constipation, blurred vision, constricted pupils, and flushed skin (*Drug Facts and Comparisons* 2010; Way et al. 1998).

The initial response to morphine is varied. In normal people who are not suffering pain, the first exposure can be unpleasant, with nausea and vomiting being the prominent reactions. However, continual use often leads to a euphoric response and encourages dependence. When injected subcutaneously, the effects of heroin and morphine are almost identical; this situation occurs because heroin is rapidly metabolized in the body into morphine. After intravenous administration, the onset of heroin's effects is more rapid and more intense than that of morphine because heroin is more lipid-soluble and enters the brain faster. Because heroin is easier to manufacture and is more potent, it is more popular in illicit trade than morphine. Even so, morphine also has substantial abuse potential and is classified as a Schedule II substance (McEvoy 2003).

Tolerance to the effects of morphine can develop very quickly if the drug is used continuously. For example, an addict who is repeatedly administering the morphine to get a "kick" or maintain a "high" must constantly increase the dose. Such users can build up to incredible doses. One addict reported using 5 grams of morphine daily; the normal analgesic dose of morphine is 50 to 80 milligrams per day (Jaffe and Martin 1990). Such high doses are lethal in a person without tolerance to narcotics.

Methadone

Methadone was first synthesized in Germany in 1943, when natural opiate analgesics were not available because opium could not be obtained from the Far East during World War II. Methadone was first called *Dolophine,* after Adolf Hitler; one company still uses that trade name. (On the street, methadone pills have been called dollies.) As previously described, methadone is often substituted for heroin in the treatment of narcotic-dependent people (*Drug Facts and Comparisons* 2010). It is an effective analgesic, equal to morphine if injected and more potent if taken orally (*Drug Facts and Comparisons* 2010; Way et al. 1998).

The physiological effects of methadone are the same as those of morphine and heroin. As a narcotic, methadone produces psychological dependence, tolerance, and then physical dependence and addiction if repeated doses are taken (Belluck 2003; *Drug Facts and Comparisons* 2010). It is effective for about 24 to 36 hours; therefore, the addict must take methadone daily to avoid narcotic withdrawal. It is often considered as addictive as heroin if injected; consequently, because methadone is soluble in water, it is formulated with insoluble, inert ingredients to prevent it from being injected by narcotic addicts.

Among methadone's most useful properties are cross-tolerance with other narcotic drugs and a less intense withdrawal response (Recovery Helpdesk 2010). If it reaches a sufficiently high level in the blood, methadone blocks heroin euphoria. In addition, withdrawal symptoms of patients physically dependent on heroin or morphine and the postaddiction craving can be suppressed by oral administration of methadone (Meader 2010). The effective dose for methadone maintenance is 50 to 100 milligrams per day to treat severe withdrawal symptoms (*Drug Facts and Comparisons* 2010; Way et al. 1998; Zickler 1999).

The value of substituting methadone for heroin lies in its longer action. Because addicts no longer need heroin to prevent withdrawal, they often can be persuaded to leave their undesirable associates, drug sources, and dangerous lifestyles. The potential side effects from methadone are the same as those from morphine and heroin, including constipation and sedation; yet if properly used, methadone is a safe drug (*Drug Facts and Comparisons* 2010).

When injecting methadone, some people feel the same kind of euphoria that can be obtained from heroin. Methadone addicts receiving maintenance treatment sometimes become euphoric if the dose is increased too rapidly. There are cases of people who injected crushed methadone pills and developed serious lung conditions from particles that lodged in the tissue, creating a condition somewhat like emphysema. The number of deaths from methadone overdose have increased substantially. Data from the CDC demonstrate methadone-related deaths in the United States increased more than five-fold

in the past decade. The reasons for this startling increase include the following (Zielinski 2010):

- Large quantities of methadone are being stolen from legitimate businesses such as hospitals and pharmacies for personal use or to sell.
- Excessive amounts of methadone are being accumulated and abused by doctor-shopping, prescription fraud, or illegal Internet pharmacy web sites.
- It is being misused by patients who received their methadone by legitimate prescriptions for pain.
- Because of increases in pain management clinics, it has become easier to obtain methadone.

Like heroin, methadone overdoses can be reversed by the antagonist naloxone if the person is treated in time.

Fentanyls

The fentanyls belong to a family of very potent narcotic analgesics (more than 200 times the potency of morphine) that are often administered intravenously for general anesthesia. These synthetic opioid narcotics include drugs such as sufentanil and alfentanil (Gutstein and Akil 2007). Fentanyls are also used in transdermal systems (patches on the skin) and as lollipops in the treatment of chronic pain (Adams 2010). Occasionally, reports surface of individuals abusing a fentanyl patch by licking, swallowing, or even smoking it (Hull et al. 2007).

It is estimated that some 100 different active forms of fentanyl could be synthesized; up to now, about 10 derivatives have appeared on the street. They are considered to be "designer" drugs (see Chapter 1). Because of their great potency, ease of production, and low costs, the fentanyls have sometimes been used to replace heroin (Fodale 2006). Fentanyl-type drugs can appear in the same forms and colors as heroin, so there is nothing to alert users that they have been sold a heroin substitute (NIDA 2007). Due to their powerful effects, these drugs are especially dangerous, and incredibly small doses can cause fatal respiratory depression in an unsuspecting heroin user (Adams 2010; Fodale 2006). It is likely that hundreds have died from overdosing with heroin laced with fentanyl. Because of an enhanced "high," addicts are tempted to use these lethal combinations (Boddigger 2006). Because these drugs are sometimes very difficult to detect in the blood owing to the small quantities used, there is no reliable information regarding the extent of fentanyl abuse. Fentanyl is so potent that abusing the patch has caused overdoses and even death (AboutLawsuits 2010; Douglas 2006).

Hydromorphone

Hydromorphone (Dilaudid) is prepared from morphine and used as an analgesic and cough suppressant. It is a stronger analgesic than morphine and is used to treat moderate to severe pain. Nausea, vomiting, constipation, and euphoria may be less marked with hydromorphone than with morphine (Karch 1996; Way et al. 1998). It is becoming more popular with opiate addicts due to its potency; however, combination with other CNS depressants can be fatal (Marsh 2009). On the street, it is taken in tablet form or injected.

Oxycodone

Oxycodone (OxyContin) is a moderate narcotic analgesic that in the past decade has been increasingly abused as the proprietary product OxyContin and has created considerable controversy (see "Here and Now: OxyContin Controversy Rages"). OxyContin is a long-lasting version of oxycodone and is considered to be an important and effective therapy for the treatment of severe pain from cancer or other lingering diseases (DrugLib 2010; *Drug Facts and Comparisons* 2010). A dramatic rise in the abuse of OxyContin has been a considerable cause for alarm by officials. Street names for OxyContin include *OC, kicker, OxyCotton,* and *hillbilly heroin* (CBS News 2007). This drug is easily abused by simply crushing the tablet, which the abuser can then ingest, inject, inhale, or place rectally. The drug can have particularly serious side effects when injected because it has a prolonged extended action (AddictionSearch 2010).

The problems with OxyContin are underscored by the report that in 2009, 4.9% and 5.1% of high school seniors and 10th graders, respectively, abused this drug (Johnston 2010). Interestingly, the abuse rate by this population for the less potent Vicodin was almost double that for OxyContin, likely due to easier access (Johnston 2010). Concern has been further heightened with reports of drug rings, including physicians illegally distributing OxyContin (McCartney and Risling 2010). Deaths and trips to the emergency room caused by OxyContin

Here and Now

OxyContin Controversy Rages

Controversy surrounds the drug OxyContin, with some hailing its painkilling abilities even as others emphasize its potentially deadly effects. At a 3-day conference on drug abuse prevention, protesters held up signs referring to friends and family members who they claimed had died as a result of OxyContin overdose, in the hopes of raising awareness about the potential problems associated with the drug. One protester described a young man who had gone through withdrawal and depression after being prescribed the drug as a painkiller, and who eventually died from an accidental overdose. Others recognized the beneficial effects of the drug, noting that OxyContin had relieved pain that other drugs could not alleviate in their loved ones. Most individuals attending the conference felt that the problem was not OxyContin or prescriptions, but rather persuading communities to work together to create solutions to the abuse of this drug.

Source: Bloodsworth, D. "Crowd Protests." 20 November 2003. Available at: http://www.oxyabusekills.com/crowdprotests.html. Accessed February 16, 2011.

are becoming more and more common and are concerning to both medical and law enforcement organizations (DEA 2010). However, these reports of adverse events associated with OxyContin use must be put into perspective by the knowledge that the vast majority of these emergency events are associated with drug abuse or physical causes (e.g., cancer) in addition to the effects of OxyContin (*Biotech Week* 2003). As a result, the FDA and DEA control OxyContin at the same level as morphine.

Meperidine

Meperidine (Demerol) is a synthetic drug that frequently is used as an analgesic for treatment of moderate pain; it can be taken in tablet form or injected. Meperidine is about one-tenth as powerful as morphine, and its use can lead to dependence (Gutstein and Akil 2006). This drug is sometimes given too freely by some physicians because tolerance develops, requiring larger doses to maintain its therapeutic action. With continual use, it causes physical dependence. Meperidine addicts may use large daily doses (3–4 grams per day). Repeated use of high doses of meperidine can cause seizures (Gutstein and Akil 2006; *Drug Facts and Comparisons* 2010).

Buprenorphine

Buprenorphine, a mild-to-moderate narcotic analgesic, was available as a Schedule V pain reliever for years. As discussed earlier, after extensive research, this drug was approved in 2002 as an effective medication for the treatment of narcotic abuse and dependence (Hanson 2003). Buprenorphine has been shown to be effective in relieving the cravings for narcotic pain relievers with minimal tendency to cause addiction itself (Bates 2010a). Although buprenorphine has been reported to have a minimal high (Leinweind 2006) when used properly, there have been isolated reports of occasional deaths, especially when combined with other CNS depressant drugs (Williams 2009). Despite buprenorphine's significant safety record and its minimal propensity for abuse, its new FDA-approved indication would cause it to be dispensed to patients with drug abuse histories, so the DEA revised it classification to a Schedule III drug. Of particular importance is the fact that buprenorphine (in the form of Subutex and Suboxone, a combination of buprenorphine and the opioid antagonist, naloxone) has been approved for the treatment of opiate dependence in an office setting. Trained physicians are allowed to treat up to 100 narcotic-dependent patients with buprenorphine in their medical offices

(Curley 2007). This means opioid addictions and dependence can now be treated with a prescribed medication by trained primary care physicians, in the offices of private doctors. This is an important step in what may become a revolution in addiction treatment, allowing patients to discreetly receive help from a family doctor for their substance abuse problem (Bates 2010a). Since buprenorphine was approved in 2002 as the first office-based treatment for opiate addiction, only about 300,000 patients have received prescriptions for this drug (Bates 2010a). Currently, almost 20,000 physicians are certified to prescribe it for treatment of opioid drug dependence (Kuehn 2010). With time, it is hoped that use of buprenorphine by primary care physicians will become rather routine (Anderson 2007).

MPTP: A "Designer" Tragedy

Attempts to synthesize illicit designer versions of meperidine by street chemists have proved tragic for some unsuspecting drug addicts. In 1976, a young drug addict with elementary laboratory skills attempted to make a meperidine-like drug by using shortcuts in the chemical synthesis. Three days after self-administering his untested drug product, the drug user developed a severe case of tremors and motor problems identical to Parkinson's disease, a neurological disorder generally occurring in the elderly. Even more surprising to attending neurologists was that this young drug addict improved dramatically after treatment with levodopa, a drug that is very effective in treating the symptoms of traditional Parkinson's disease. After 18 months of treatment, the despondent addict committed suicide. An autopsy revealed he had severe brain damage that was almost identical to that occurring in classical Parkinson's patients. It was concluded that a by-product resulting from the sloppy synthesis of the meperidine-like designer narcotic was responsible for the irreversible brain damage.

This hypothesis was confirmed by a separate and independent event on the West Coast in 1981, when a cluster of relatively young heroin addicts (ages 22–42) in the San Francisco area also developed symptoms of Parkinson's disease. All of these patients had consumed a new "synthetic heroin" obtained on the streets, which was produced by attempting to synthesize meperidine-like drugs (Aminoff 1998; Langston et al. 1983). Common to both incidents was the presence of the compound MPTP, which was a contaminant resulting from the careless synthesis. MPTP is metabolized to a very reactive molecule in the brain that selectively destroys neurons containing the transmitter dopamine in the motor regions of the basal ganglia (see Chapter 4). Similar neuronal damage occurs in classical Parkinson's disease over the course of 50 to 70 years, whereas ingestion of MPTP dramatically accelerates the degeneration to a matter of days (Goldstein 1994). As tragic as the MPTP incident was, it was heralded as an important scientific breakthrough—MPTP is now used by researchers as a tool to study why Parkinson's disease occurs and how to treat it effectively (Lane and Dunnett 2008).

Codeine

Codeine is a naturally occurring constituent of opium and the most frequently prescribed of the narcotic analgesics. It is used principally as a treatment for minor to moderate pain and as a cough suppressant. Maximum pain relief from codeine occurs with 30 to 50 milligrams. Usually, when prescribed for pain, codeine is combined with either a salicylate (such as aspirin) or acetaminophen (Tylenol). Aspirin-like drugs and opioid narcotics interact in a synergistic fashion to give an analgesic equivalence greater than what can be achieved by aspirin or codeine alone.

Although not especially powerful, codeine may still be abused. Codeine-containing cough syrup is currently classified as a Schedule V drug. Because the abuse potential is considered minor, the FDA has ruled that codeine cough products can be sold without a prescription; however, the pharmacist is required to keep them behind the counter and must be asked in order to provide codeine-containing cough medications. Despite the FDA ruling, many states have more restrictive regulations and require that codeine-containing cough products be available only by prescription (Way et al. 1998).

Although codeine dependence is possible, it is not very common; most people who abuse codeine developed narcotic dependence previously with one of the more potent opioids. In general, large quantities of codeine are needed to satisfy a narcotic addiction; therefore, it is not commonly marketed on the street.

Pentazocine

Pentazocine (Talwin) was first developed in the 1960s in an effort to create an effective analgesic with low abuse potential. When taken orally, its analgesic effect is slightly greater than that of codeine.

Its effects on respiration and sedation are similar to those of the other opioids, but it does not prevent withdrawal symptoms in a narcotic addict. In fact, pentazocine will precipitate withdrawal symptoms if given to a person on methadone maintenance (Gutstein and Akil 2006). Pentazocine is not commonly abused because its effects can be unpleasant, resulting in dysphoria. It is classified as a Schedule IV drug.

Propoxyphene

Propoxyphene (Darvon, Dolene) is structurally related to methadone, but it is a much weaker analgesic, about half as potent as codeine (Gutstein and Akil 2006). Like codeine, propoxyphene is frequently given in combination with aspirin or acetaminophen. Although it was once an extremely popular analgesic, the use of propoxyphene declined as its potency was questioned. Research suggested that this narcotic was no more effective in relieving pain than aspirin (Gutstein and Akil 2006). To a large extent, new, more effective nonnarcotic analgesics replaced propoxyphene. In very high doses, it caused delusions, hallucinations, and convulsions and even fatal heart problems. Alone, propoxyphene caused little respiratory depression; however, when combined with alcohol or other CNS depressants, this drug could depress respiration. Due to these negative properties, the FDA requested the removal of this controversial painkiller, and it was removed from the market in 2010 (Stein 2010).

Tramadol

Tramadol (Ultram) was first introduced into the U.S. market in 1994 as a synthetic, moderately effective analgesic sometimes used as a substitute for opioid painkillers (Smith 2010). Although tramadol itself causes some activation of opioid receptors in the brain, it appears that its analgesic properties are related to more than just its opioid actions. For example, tramadol alters GABA, noradrenaline, and serotonin transmitter systems as well, in a manner that might contribute to its atypical analgesic properties. For this reason, tramadol may have some antidepressant effects that augment its analgesic abilities (Medic8 2010).

Tramadol is frequently prescribed for patients who either do not respond well or have difficulty with the opioid painkillers. Despite the fact that opioid action likely is not the sole basis of its analgesia, it is significant enough to cause some dependence issues. For example, there is an illegal street market for this substance, where it is known by names such as *chill pills* or *ultra*. There are clinicians who claim that for some patients tramadol can cause a serious opioid-like dependence (Smith 2010). Such conclusions are based on findings such as: (1) from 1998 to 2006 there was a six-fold increase in admissions for treatment of tramadol-related dependence; (2) for teens, tramadol is easier to get than alcohol and easy to sell on the streets; (3) emergency room visits nationwide that included tramadol as a significant component went from about 5000 in 2004 to about 13,500 in 2008; and (4) there is evidence that regular daily use of tramadol can cause physical dependence and causes withdrawals when discontinued abruptly (Lanier et al. 2010). These increases in tramadol-related problems correspond to an explosion in its popularity, resulting in about 26 million prescriptions being dispensed by retailers in 2008 (Smith 2010). Tramadol is available as both regular and extended-release tablets (Drugs.com 2010b).

Even though tramadol is marketed as an opioid drug with low risk of dependence and most health authorities consider it to have a relatively low dependence liability, it is clear that some patients can become addicted to this analgesic (Breakthrough Addiction Recovery 2010). Currently, tramadol is available only by prescription, but is not scheduled by the DEA even though the prescribing information typically warns that tramadol "may induce psychological and physical dependence of the morphine-type." In some countries, tramadol is actually available OTC (Breakthrough Addiction Recovery 2010). Because of many clinical complaints across the country, the DEA is reviewing the status of tramadol products in order to determine if scheduling of these drugs would be appropriate.

Narcotic-Related Drugs

Although not classified as narcotics, the following drugs are either structurally similar to narcotics (dextromethorphan) or are used to treat narcotic withdrawal (clonidine) or overdose (naloxone).

Dextromethorphan

Dextromethorphan is a synthetic used in cough remedies since the 1960s and can be purchased without prescription. Although its molecular structure resembles that of codeine, this drug does not have analgesic action nor does it cause typical narcotic dependence (Encyclopedia Britannica 2010).

Although dextromethorphan is not traditionally considered a major drug abuse problem, recent studies are cause for concern. They reveal that more than 3 million young people have used OTC products containing dextromethorphan to get high (Buddy 2008). Overdose of dextromethorphan-containing cough medicines has been reported in the United States and other countries, sometimes resulting in deadly consequences (see "Here and Now: Dextromethorphan"). From 1998–2008, 72 cases of dextromethorphan-related deaths were identified. The majority of these cases were suicides, often involving multiple substances (Traynor 2010). Abuse of dextromethorphan typically occurs among adolescents and young adults (Traynor 2010). The relatively few cases of addiction reveal a pattern of high-dose use for months to even years. The principal symptoms of abuse include altered perceptions, sense of floating, hallucinations, visual distortions, and even paranoia and psychotic reactions. Its effects have been described to be similar to those of phencyclidine (PCP) and the general anesthetic ketamine (Morgan, Porritt, and Poling 2006). There is some suggestion that both physical and psychological dependence can occur with dextromethorphan, resulting in withdrawal when its use is discontinued (Mutschler et al. 2010). Dextromethorphan is sometimes mixed with drugs such as alcohol, amphetamines, and cocaine to give unusual psychoactive interactions. As of 2010, the DEA had taken no steps to restrict the use of dextromethorphan in over-the-counter (OTC) products; in fact, advisers to the FDA voted against placing this drug in a schedule of controlled substances, which likely will preclude the DEA from making a change in its category (Traynor 2010).

Young people are becoming aware of dextromethorphan's abuse potential from web sites on the Internet. A growing number of these sites have promoted dextromethorphan as a powerful OTC mind-altering drug. Included on these sites are personal experiences of users as well as directions on how to use the drug, predictions about what to expect, warning signs of adverse reactions, and instructions as to how to extract dextromethorphan from OTC cough medicines (Vaults of Erowid 2007).

Clonidine

Clonidine (Catapres) was created in the late 1970s. It is not a narcotic analgesic and has no direct effect

Here and Now

Dextromethorphan: No Coughing Matter

Dextromethorphan, a key active ingredient in cough suppressants, is the reason why many young people are using OTC cough medicines to get high. The substance—also known as robo, skittles, dxm, dex, and tussin—is found in at least 80 OTC products. Dextromethorphan usually produces a disassociative feeling (roboing, robo rolling, robo tripping) or a feeling of intoxication, but its abuse can also lead to psychotic behavior. When large amounts of dextromethorphan are taken, the drug attaches to receptors in the central nervous system—the same receptors to which PCP attaches. In the long term, this effect can cause depression, memory problems, and suicidal tendencies. Dextromethorphan abuse also can result in death: in 2005, five teenage boys from three different states died after ingesting dextromethorphan powder from an online source that illegally sold the drug in bulk. The company was closed down the next year.

Sources: Magnus, E. "Addicted to Cough Medicine?" MSNBC News. 27 March 2004. Available at: http://www.msnbc.msn.com/id/4608341. Accessed March 14, 2011; and Traynor, K. "Advisers Vote Against Declaring Dextromethorphan a Controlled Substance." American Society of Health Pharmacists. 2010. Available at: http://www.ashp.org/import/news/HealthSystemPharmacyNews/newsarticle. aspx?id=3418. Accessed March 14, 2011.

on the opioid receptors; instead, it stimulates receptors for noradrenaline. Its principal use is as an oral antihypertensive (*Drug Facts and Comparisons* 2010; O'Shea, Law, and Melichar 2010). Clonidine is mentioned here because it is a nonaddictive, noneuphorigenic prescription medication with demonstrated efficacy in relieving some of the physical effects of opiate withdrawal (such as vomiting and diarrhea). However, clonidine does not alter narcotic craving or the generalized aches associated with withdrawal (O'Brien 2006; O'Shea et al. 2010). The dosing regimen is typically a 7- to 14-day inpatient treatment for opiate withdrawal. Length of treatment can be reduced to 7 days for withdrawal from heroin and short-acting opiates; the 14-day treatment is needed for the longer-acting methadone-type opiates. Because tolerance to clonidine may develop, opiates are discontinued abruptly at the start of treatment. In this way, the peak intensity of withdrawal will occur while clonidine is still maximally effective (McEvoy 2003).

One of the most important advantages of clonidine over other treatments for opiate withdrawal detoxification is that it shortens the time for withdrawal to 14 days compared with several weeks or months using standard procedures, such as methadone treatment (O'Shea et al. 2010). The potential disadvantage of taking clonidine is that it can cause serious side effects of its own, the most serious being significantly lowered blood pressure, which can cause fainting and blacking out (*Drug Facts and Comparisons* 2010; O'Shea et al. 2010). Overall, its lack of abuse potential makes clonidine particularly useful in rapid treatment of narcotic dependence; however, the long-term benefit is controversial (Gowing et al. 2003).

Naloxone/Naltrexone

Naloxone and the related drug naltrexone are relatively pure narcotic antagonists. These drugs attach to opiate receptors in the brain and throughout the body. They do not activate the receptors, but rather prevent narcotic drugs, such as heroin and morphine, from having an effect. By themselves, these antagonists do not cause much change, but potently block or reverse the effects of all narcotics. Because of its antagonistic properties, naloxone is a useful antidote in the treatment of narcotic overdoses; its administration rapidly reverses life-threatening, narcotic-induced effects on breathing and the cardiovascular system (*Alcoholism and Drug Abuse Weekly* 2010b; O'Brien 2006). However, if not used carefully, this antagonist will also block the analgesic action of the narcotics and initiate severe withdrawals in narcotic-dependent people (Way et al. 1998). Its use has been proposed to prevent addicts from experiencing the effects of heroin (Mathias 2003); in fact, as discussed earlier in this chapter, an extended form of naloxone (its effect persists for 1 month) called Vivitrol was recently approved by the FDA for the treatment of heroin addiction (Rubin 2010). However, many individuals dependent on heroin are not interested in using this drug because it can precipitate withdrawal symptoms. But a recent study found that of those heroin addicts who received six monthly injections, 70% did not go back to heroin use (this was twice the success rate of heroin addicts given placebo), and they claimed that the Vivitrol reduced their cravings for the opiate drug (Rubin 2010).

An interesting use of naloxone has been to combine it with buprenorphine in small quantities (Suboxone). As long as this product is taken as prescribed, the quantity of naloxone is too small to have an antagonistic effect; however, if Suboxone is consumed in high doses, such as would occur if it were being abused, there would be sufficient naloxone to block the opioid effect (Center for Substance Abuse Research [CESAR] 2003). The FDA also has approved Suboxone to reduce the craving for alcohol in the treatment of chronic alcoholism (*Drug Facts and Comparisons* 2010). There are additional reports suggesting that opioid receptors may contribute to other drug addictions such as those caused by nicotine and psychostimulants. At this time it is not clear if an opioid antagonist like naloxone would be effective in treating these other addictions.

Natural Narcotic Substances

Although many herbal preparations can cause drowsiness or have some analgesic properties, few of these actually contain opioid narcotic drugs. The naturally occurring opioid drugs include morphine, codeine, heroin, papaverine, and thebaine and are found only in the opium poppy, *Papaver somniferum*. Although several varieties of opium-yielding poppies exist, they are typically winter crops in the Southern Hemisphere and do best in climates that have warm days and cool nights. All of the plants thrive in sandy soil. Most of the active drugs are found in the seepage from the seed heads located beneath the flower petals of the poppy flowers, although small amounts of these active ingredients are found in other parts of the plant such as the stem and leaves. Although

Opium poppy containing natural narcotics such as morphine, codeine, and heroin.

this species of plant can survive in the United States if the environment is rigidly controlled, the vast majority of the supplies of the naturally occurring narcotic drugs are brought into the country, either legally and sold as legitimate pharmaceuticals or smuggled across borders and sold as illicit narcotics.

Discussion Questions

1. Why do narcotics have high abuse potential?
2. What are the principal clinical uses of the opioid narcotics?
3. What is the relationship between endorphin systems and the opioid narcotics?
4. Why do the opioid pain relievers account for two-thirds of prescription drug abuse?
5. What effect has the rising abuse of prescription narcotic analgesics had on legitimately prescribing these drug for pain management?
6. What is the difference between opioid addiction and opioid physical dependence?
7. Why was there a substantial increase in heroin abuse in the United States throughout the 1990s?
8. Why does heroin addiction contribute to criminal activity?
9. What are the principal withdrawal effects when heroin use is stopped in addicts?
10. How does methadone maintenance work for the treatment of narcotic dependence? Explain a possible drawback to this approach.
11. How does buprenorphine compare to methadone as treatment for narcotic addictions?
12. How does naloxone (e.g., Vivitrol) compare to methadone maintenance treatment for heroin/opioid addiction?
13. What is considered to be successful treatment for heroin addiction?
14. How does morphine compare with heroin?
15. How does tramadol compare to other opioid analgesics?
16. Why is dextromethorphan potentially addicting, and what should the federal government do to stop its abuse?
17. What does the fact that naloxone is effective in the treatment of alcoholism suggest about the role of endogenous opioid systems in alcohol dependence?

Summary

1 The term *narcotic* refers to naturally occurring substances derived from the opium poppy and their synthetic substitutes. These drugs are referred to as the opioid (or opiate) narcotics because of their association with opium. For the most part, the opioid narcotics possess abuse potential, but they also have important clinical value and are used to relieve all kinds of pain (they are analgesic), suppress coughing (they are antitussive), and stop diarrhea.

2 The principal side effects of the opioid narcotics, besides their abuse potential, include drowsiness, respiratory depression, nausea and vomiting, constipation, inability to urinate, and sometimes a drop in blood pressure. These side effects can be annoying or even life-threatening, so caution is required when using these drugs.

3 Heroin is the most likely of the opioid narcotics to be severely abused; it is easily prepared from opium and has a rapid, intense effect.

4 When narcotics such as heroin are first used by people not experiencing pain, the drugs can cause unpleasant, dysphoric sensations. However,

euphoria gradually overcomes the aversive effects. The positive feelings increase with narcotic use, leading to psychological dependence. After psychological dependence, physical dependence occurs with frequent daily use, which reinforces the narcotic abuse. If the user stops taking the drug after physical dependence has occurred, severe withdrawal symptoms result.

5 Tolerance to narcotics can occur rapidly with intense use of these drugs. This tolerance can result in the use of incredibly large doses of narcotics that would be fatal to a nontolerant person.

6 Methadone and buprenorphine are frequently used to help narcotic addicts stop using heroin or one of the other highly addicting drugs. Oral methadone relieves the withdrawal symptoms that would result from discontinuing narcotics. Methadone can also cause psychological and physical dependence, but it is less addicting than heroin and easier to control. Buprenorphine is distinct from methadone in that it has been approved for use in primary care settings and may be safer for treating women who use opioid narcotics during pregnancy.

7 Fentanyls are very potent synthetic opioid narcotics. They can be easily synthesized and converted into drugs that are as much as 3000 to 6000 times more potent than heroin itself. Detection and regulation of these fentanyl derivatives by law enforcement agencies are very difficult. The fentanyl-type drugs are used as heroin substitutes and have killed narcotic addicts because of their unexpected potency.

8 Attempts to create designer narcotics have led to the synthesis of very potent fentanyl-like drugs that are responsible for a number of overdose deaths. In addition, attempts to synthesize a meperidine (Demerol) designer drug resulted in the inadvertent creation of MPTP, a very reactive compound that causes a dramatic onset of Parkinson's disease in its users.

9 Tramadol is an atypical opioid-like analgesic that has some antidepressant actions that might contribute to its effectiveness as a moderately potent pain killer. It likely has less addicting properties than most of the other opioid narcotics, but its dramatic rise in popularity has revealed a potential for causing dependence and withdrawal in some patients. Although not currently scheduled, the DEA is considering its addition to the list of controlled substances.

10 Dextromethorphan is a codeine-related drug used as an antitussive in OTC cough medicines. In very high doses, dextromethorphan can cause PCP-like hallucinations and sensory distortions. The abuse of this drug has not been substantial enough to result in its removal or special control by federal agencies.

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