Diagnosis and Pharmacologic Management of Opioid Dependency

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Opioid dependency is a common problem that remains underdiagnosed and undertreated in the United States. The National Survey on Drug Use and Health estimated that in 2002 approximately 2.5 million Americans used pain relievers, mostly opioid agonists (eg, oxycodone, hydrocodone, morphine, methadone), for nonmedical use. Approximately 3.7 million Americans have reported using heroin at some time in their lives, with 314,000 reporting heroin use in the past year.[1] Other sources estimate that the problem of opioid dependency is much larger. The Office of National Drug Control Policy reports that there are between 750,000 and 1 million regular users of heroin in the United States.[2] Worldwide, approximately 16 million individuals (0.4% of the adult population) abuse opiates, but only 7.8% of these individuals receive treatment.[3]

Opioid abuse is a significant problem among hospital patients in the United Statess. In 2004, there were 162,137 emergency department visits due to heroin use and an additional 158,281 visits due to the nonmedical use of opioid pharmaceuticals.[4] In 2003, there were 324,000 admissions for opiate abuse treatment.[1] Still, only 20% of heroin users receive treatment, despite the availability of effective pharmacologic agents.[5] Pharmacologic treatments, such as opioid agonists, are effective at reducing drug use among opioid-dependent patients, but access to these medications is limited. New office-based treatments for opioid dependency are available and provide alternatives for providers and patients. Given their frequent contact with patients who use opioids, hospital physicians and generalists can play an important role in identifying and managing opiate abuse. This article reviews the context of opioid dependence and treatment in the United States, outlines important aspects of assessing opioid dependency, and provides a guide to available treatment options.

TAKE HOME POINTS

- Many patients do not have access to effective treatment for opioid dependency due to inadequate funding, stigma, and lack of recognition of opioid abuse and dependence.
- The Drug Addiction Treatment Act enables physicians with 8 hours of training to obtain a waiver in order to treat opioid-dependent individuals in any setting in which they are licensed to practice.
- Clinical tools, including CAGE-AID, the Structured Clinical Interview for the DSM, and the Clinical Opioid Withdrawal Scale, can help physicians screen for, assess, and diagnose opioid dependence and withdrawal.
- New office-based treatments for opioid dependence, such as buprenorphine, expand the treatment options for patients and physicians.
- Opioid maintenance therapies, including opioid agonists, are more successful than detoxification for treating patients with opioid dependence.

ACCESS TO TREATMENT

Since the 1960s, methadone, an opioid receptor agonist, has been safely and effectively used to treat opioid addiction. However, its use has been restricted to federally licensed opioid treatment programs (OTPs), and this restriction has led to poor access due to lack of public funding and stigma.[6] In 2002, the US Food and Drug Administration approved 2 sublingual formulations of buprenorphine for treatment of opioid addiction. As a Schedule III partial opioid agonist,

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Table 1. Screening Instrument for Drug Abuse: CAGE-AID

1. Have you ever felt the need to **Cut** down on your drinking or drug use?
2. Have people **Annoyed** you by criticizing your drinking or drug use?
3. Have you ever felt bad or **Guilty** about your drinking or drug use?
4. Have you ever needed an **Eye opener** the first thing in the morning to steady your nerves?

Interpretation: 2 or more affirmative answers require further assessment.

Adapted with permission from Brown RL, Rounds LA. Conjoint screening questionnaires for alcohol and other drug abuse: Criterion validity in a primary care practice. Wis Med J 1995;94:136.

buprenorphine can be used for detoxification and maintenance therapy of inpatients and outpatients under the Drug Addiction Treatment Act of 2000.[7] The Drug Addiction Treatment Act enables physicians with 8 hours of training to obtain a waiver so that they may treat opioid-dependent individuals in any setting in which they are licensed to practice. The hope is that the availability of buprenorphine will allow more physicians to provide treatment and attract new patients into treatment. Still, there is a need for increased training of physicians, improved screening practices, and integration of substance abuse treatment in the primary care setting.[8]

In 2005, only 8% (1069) of substance abuse treatment programs offered federally certified opioid dependency treatment with opioid agonist therapy.[9] Some states, such as South Dakota, had no methadone maintenance programs, and others, such as North Dakota, Mississippi, Montana, and Wyoming, had only 1 or 2 programs statewide.[9] A recent evaluation of the buprenorphine waiver program demonstrated that since the beginning of the program in 2002, over 4500 physicians have been trained in buprenorphine treatment; approximately 65% of these physicians are actively prescribing buprenorphine in their practices, the largest portion prescribing in the office-based setting.[10] This suggests that access to treatment has improved due to increasing numbers of trained providers in more locations.

Improved access to opioid dependency treatment is likely to benefit society by reducing medical care needs, increasing productivity, and reducing expenses from criminal behavior. In 2000, it was estimated that heroin dependency cost the United States $21 billion.[11] In terms of reduced HIV transmission, the cost/utility ratio of therapy is estimated to be between $8200 and $10,900 per quality-adjusted life-years.[12] A recent review of cost-benefit studies indicated that a $1 investment in methadone maintenance programs has a return of up to $18 to society.[13]

SCREENING

Although opioid abuse and dependence is a common problem in the United States, research suggests that less than one third of primary care physicians systematically screen for drug abuse.[14] The majority of physicians are not familiar with screening and treatment guidelines, do not feel comfortable diagnosing abuse, do not systematically refer for treatment, and are not optimistic that treatment works.[14–16] It is unclear if screening tools such as CAGE-AID (CAGE-Adapted to Include Drugs; **Table 1**) are more effective for identifying drug abuse than careful history taking. However, CAGE-AID has been found to be 79% sensitive and 77% specific in community practice.[17] The 1996 US Preventive Services Task Force substance abuse screening guidelines suggest there is little evidence that these screening tools are superior to a careful history.[18] Therefore, screening tools such as CAGE-AID may be a useful guide but should not replace a detailed history about type, duration, frequency, and quantity of substances used.

CLINICAL EVALUATION

Careful interviewing regarding substance use, risk taking, and personal and social conflicts will help to identify concerning behavior and/or dependence. The substance abuse portion of the Structured Clinical Interview for the DSM (SCID) is the gold standard for diagnosing drug abuse and/or dependence. This instrument is based on the DSM-IV-TR criteria for drug dependence and abuse, which are outlined in **Table 2**.[19] The clinical evaluation should also include a physical examination and appropriate laboratory and diagnostic tests, including screening for HIV and hepatitis. Opioid users, particularly those who inject heroin, are at increased risk for death due to overdose, violence, infectious disease (eg, HIV, hepatitis B and C) from sharing contaminated injection equipment,[20] psychiatric comorbidities, and polydrug abuse.[21,22] A thorough assessment includes consideration of these conditions (**Table 3**).

An important part of the physical examination is assessment for intoxication, overdose, and withdrawal. Signs of intoxication include slurred speech, nodding off to sleep, sedation, and constricted pupils. Signs of overdose include lack of consciousness, pinpoint pupils, slow and shallow respirations, and low heart rate. The Clinical Opioid Withdrawal Scale (COWS) is a clinician-administered instrument for assessing withdrawal that considers presence and severity of tachycardia, gastrointestinal

symptoms (eg, cramping, nausea, loose stools), sweating, tremor, restlessness, yawning, pupil size, anxiety, runny nose or eyes, joint or bone ache, and gooseflesh. Points are assigned based on the degree of withdrawal symptoms: a total score of 5 to 12 indicates mild withdrawal; 13 to 24 indicates moderate withdrawal; 25 to 36 indicates moderately severe withdrawal; and a score greater than 36 indicates severe withdrawal.[23] Typically, early withdrawal starts 8 to 24 hours after the last use—sooner for shorter-acting opioids such as heroin and later for longer-acting opioids such as methadone. Early withdrawal signs include lacrimation, rhinorrhea, diaphoresis, yawning, insomnia, and restlessness or more severe signs and symptoms, including dilated pupils, piloerection, muscle twitches, myalgias, arthralgias, and abdominal pain. More developed withdrawal is characterized by tachycardia, hypertension, fever, anorexia, nausea and, if more severe, diarrhea and/or vomiting, dehydration, hyperglycemia, and hypotension.[24] Recognition of these signs and symptoms will assist in clinical decision making regarding the need to initiate replacement therapy and the proper dosage.

TREATMENT APPROACHES

Once a clinician has thoroughly assessed opioid abuse and dependency, identifying the patient's interest in changing his/her behavior is crucial to selecting the proper treatment approach. Prochaska and DiClemente's Transtheoretical Model describes 5 stages of change (ie, precontemplation, contemplation, preparation, action, and maintenance) and is a useful tool in evaluating addiction behavior.[25] Clinicians can help patients move through the 5 stages by using motivational interviewing and brief interventions, such as giving feedback, emphasizing the patient's responsibilities, providing advice and a menu of options, being empathic, and supporting self-efficacy.[26] The **Figure** outlines an approach to assessment and treatment that clinicians may find helpful when considering opioid dependency treatment options with their patients.

Detoxification

If a patient is ready to change or requires abstinence from opioids due to hospitalization and/or preoperative care, detoxification is the initial treatment for opioid abuse. Detoxification generally refers to withdrawal from a state of physical dependence.[27] **Table 4** shows commonly available treatments for withdrawal and detoxification.

Nonopioid medications. The primary nonopioid medications used for opioid withdrawal are α_2-adrenergic agonists, such as clonidine and lofexidine.

Table 2. DSM-IV-TR Criteria for Substance Dependence and Abuse

Substance abuse

Not meeting criteria for substance dependence

A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by 1 (or more) of the following, occurring within a 12-month period:

1. Recurrent use resulting in a failure to fulfill role obligations
2. Recurrent use in physically hazardous situations
3. Recurrent substance-related legal problems
4. Continued use despite persistent or recurrent social problems caused or exacerbated by the effects of the substance

Substance dependence

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by 3 (or more) of the following, occurring within a 12-month period:

1. Tolerance: a need for increased amounts of the substance to achieve intoxication or desired effect or a diminished effect with continued use of the same amount
2. Withdrawal: manifestation of the characteristic withdrawal syndrome or the same (or a closely related) substance is taken to relieve or avoid symptoms
3. The substance is often taken in larger amounts or over a longer period than was intended
4. There is a persistent desire or unsuccessful efforts to cut down or control use
5. A great deal of time is spent in activities necessary to obtain, use, or recover from use of the substance
6. Important social, occupational, or recreational activities are given up or reduced because of substance use
7. Substance use is continued despite knowledge of having a persistent or a recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance

Clonidine reduces norepinephrine activity during withdrawal and is more effective at suppressing the autonomic signs and symptoms of withdrawal (eg, tachycardia) than the subjective symptoms (eg, anxiety, irritability). Patients given clonidine should be monitored for hypotension. In studies of clonidine-assisted detoxification in the primary care setting, doses of 0.1 to 0.2 mg every 4 hours up to 1.2 mg daily along with careful monitoring of blood pressure have reduced the severity of withdrawal from opiates.[28,29] Although not approved for use in the United States, lofexidine is a centrally acting α_2-adrenergic agonist commonly used for detoxification in the United Kingdom. Compared with clonidine, it has similar

Table 3. Conditions for Which Drug Users Are at Increased Risk

	Opioid Users	Intravenous Drug Users
Cancer	—	Hepatocellular carcinoma
Cardiovascular	—	Endocarditis, septic thrombophlebitis
Endocrine	Osteopenia, alteration in gonadotropins, decreased sperm motility, menstrual irregularities, amenorrhea	—
Gastrointestinal	Constipation, ileus, intestinal pseudo-obstruction	—
Hematologic	—	Disorders related to liver disease
Hepatic	Granulomatosis	Hepatitis B, C, and delta
Infectious	Aspiration pneumonia	Endocarditis; cellulitis; pneumonia; septic thrombophlebitis; septic arthritis; osteomyelitis; epidural and brain abscess; mycotic aneurysm; abscesses and soft tissue infections; mediastinitis; malaria; tetanus; hepatitis B, C, and delta; HIV; sexually transmitted diseases
Neonatal	Neonatal abstinence syndrome and seizures	—
Neurologic	Seizure, compression neuropathy	—
Pulmonary	Respiratory depression, emphysema, bronchospasm, pulmonary edema	Pulmonary hypertension, talc granulomatosis, septic pulmonary embolism, pneumothorax, emphysema, needle embolization
Renal	Rhabdomyolysis, renal failure, factitious hematuria	Focal glomerular sclerosis, amyloidosis, nephritic syndrome, chronic renal failure, glomerulonephritis
Trauma	Accidents, violence, sexual and physical abuse	—

Adapted from Saitz R. Overview of medical and surgical complications. In: Graham AW, Schultz TK, Mayo-Smith MF, et al, editors. Principles of addiction medicine. 3rd ed. Chevy Chase (MD): American Society of Addiction Medicine; 2003.

effectiveness in reducing withdrawal symptoms with a lower incidence of hypotension.[30] Studies of lofexidine are ongoing in the United States.

Opioid agonists. Opioid-based detoxification is an alternative methodology. Opioid agonists such as methadone and buprenorphine replace the abused opioid and are slowly tapered. Methadone is a long-acting mu-opioid receptor agonist and lacks the euphorigenic effects of opioids such as heroin. With methadone, tolerance and physical dependence develop over a longer period and withdrawal symptoms are milder (although more prolonged) as compared with heroin.[31] For detoxification purposes, 15 to 30 mg of methadone is administered daily, maintained for 2 to 3 days in the acute setting, and then tapered by 10% to 15% per day.[27,32] The initial dose of methadone is based upon the degree of withdrawal. It may be helpful to implement COWS in order to assess the severity of withdrawal using objective measures, such as heart rate, the presence of gooseflesh, increased secretions, and tremor. Any licensed physician may prescribe methadone to hospitalized patients, but outpatients need referrals to federally licensed facilities for ongoing opioid treatment.

In clinical trials, methadone is associated with greater rates of completion of detoxification and fewer withdrawal symptoms during detoxification when compared with placebo.[33] Compared with α_2-adrenergic agonists, methadone-treated patients experienced fewer withdrawal symptoms and side effects, stayed in treatment longer, had lower rates of relapse, and were more likely to complete treatment.[28,34,35]

Methadone can cause QTc interval prolongation; 1 study found QTc prolongation in 16% of patients on chronic high-dose methadone,[36] and another prospective study found modest QTc prolongation positively associated with methadone dose.[37] Although not indicated in all patients taking methadone, screening electrocardiography should be considered in those with certain risk factors (ie, structural heart disease, hypokalemia, use of cytochrome P450 inhibitors, or use of QT-prolonging drugs). Alternatively, clinicians may consider using buprenorphine instead of methadone, which has not been associated with QTc prolongation.[36,37]

Buprenorphine is a partial mu-opioid receptor agonist with a long duration of action due to slow disassociation from mu-opioid receptors, which allows for thrice-weekly dosing.[31] As a partial agonist, buprenorphine produces opioid effects, which alleviate symptoms of withdrawal, and it also blocks opioid receptors from full agonists (eg, heroin). The effects of buprenorphine reach a plateau, contributing to its relative safety for inpatient and outpatient detoxification.[38] Buprenorphine has 60% to 70% bioavailability when absorbed sublingually. The sublingual preparation is available in 2 mg and 8 mg tablets combined with 0.5 mg and

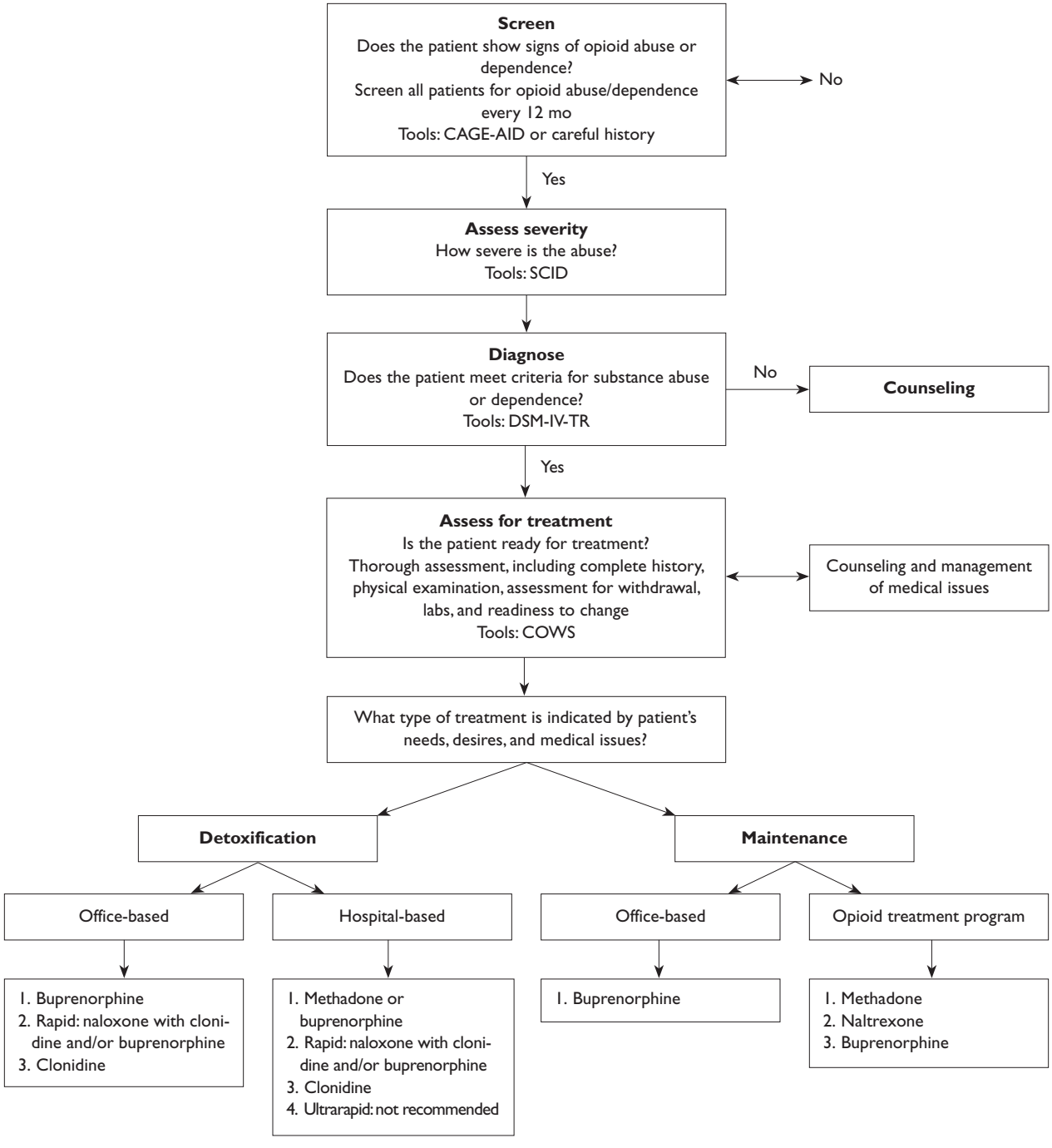

Figure. Algorithm for screening, assessment, and treatment of opioid dependency. CAGE-AID = CAGE-Adapted to Include Drugs; COWS = Clinical Opioid Withdrawal Scale; SCID = Structured Clinical Interview for the DSM.

2 mg of naloxone, respectively. This preparation limits the potential for diversion; naloxone is not absorbed sublingually but will precipitate withdrawal symptoms if administered parenterally.[39] Furthermore, buprenorphine is different from methadone in that it is available by prescription from physicians who have obtained 8 hours of training. Thus, buprenorphine is available for both inpatient and outpatient detoxification.

The guidelines for using buprenorphine for detoxification from short-acting opioids recommend

Table 4. Opioid Detoxification Treatment Options

Treatment	Medication	Availability	Protocol
Opioid detoxification	Methadone	Hospital or opioid treatment program	Initial dose of 15–30 mg daily, maintain for 2–3 days, then taper 10% to 15% daily
	Buprenorphine/naloxone	Hospital or physician office	Initial dose of 4 mg buprenorphine /1 mg naloxone, then increase to 8 mg buprenorphine/2 mg naloxone if withdrawal symptoms are present; stabilize over a period of days to a maximum of 32 mg buprenorphine/4 mg naloxone, and then taper over a period of 3 days (not recommended) to weeks
Nonopioid detoxification	Clonidine	Hospital or physician office	0.1 to 0.2 mg every 4 hr for up to 1.2 mg daily
Rapid detoxification	Naltrexone induction with clonidine	Hospital or physician office	Variable
	Naloxone or naltrexone induction with buprenorphine	Hospital or physician office	Variable
Ultrarapid detoxification	Naloxone induction under general anesthesia or sedation	Not recommended	—

Adapted from Center for Substance Abuse Treatment. Clinical guidelines for the use of buprenorphine in the treatment of opioid addiction. Treatment improvement protocol (TIP) series 40. Available at www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat5.chapter.72248. Accessed 14 Sep 2007; *and* O'Connor PG, Fiellin DA. Pharmacologic treatment of heroin-dependent patients. Ann Intern Med 2000;133:40–54.

initiation of 4 mg buprenorphine/1 mg naloxone once the patient has completely stopped using short-acting opioids and is exhibiting mild signs of withdrawal (the most up-to-date guidelines for detoxification using buprenorphine, including the COWS, can be found at http://buprenorphine.samhsa.gov). This dose can be followed by another equivalent dose in 2 to 4 hours, and the daily dose should then be increased to between 12 mg buprenorphine/3 mg naloxone and 16 mg buprenorphine/4 mg naloxone daily over the next 2 days. Once stabilized, the dose can be tapered using short period (3 days), middle period (10–14 days), or long period (> 14 days) regimens. Unless there are compelling reasons for short or middle period regimens (eg, patients are unlikely to comply with or have access to long-term treatment), the longer period tapering strategies are likely to be more effective.[24]

Buprenorphine has been found to be equivalent to detoxification with methadone in the severity of withdrawal symptoms, although symptoms may be worse earlier in treatment for patients on buprenorphine.[40,41] Clinical trials evaluating buprenorphine and clonidine indicate that withdrawal symptoms are less severe with buprenorphine and that buprenorphine may not be associated with hypotension as observed in clonidine-treated patients.[42] Patients initiating buprenorphine or methadone detoxification and/or maintenance should be warned against a potential interaction with benzodiazepines (eg, respiratory depression, sedation, impaired motor and cognitive function[43]), and patients on prescribed benzodiazepines should be monitored for signs of sedation and respiratory depression. Benzodiazepines have been identified on autopsy in methadone-related deaths, and approximately one third of patients on opioid agonists report recent use of benzodiazepines.[43]

Agents for rapid and ultrarapid detoxification. With rapid and ultrarapid detoxification, patients are given opioid antagonists (naloxone or naltrexone) to precipitate a withdrawal response. The goal is to reduce detoxification time and prevent relapse. Additional pharmacotherapy is administered to help manage acute withdrawal symptoms. A recent review of rapid detoxification studies describing the various methods employed[44] reported that in all except 1 study, patients were given either naloxone or naltrexone and clonidine in addition to medications to help manage withdrawal symptoms (eg, antiemetics, analgesics, sleep inducers). The detoxification period varied from 1 to 12 days.[44] In a study evaluating buprenorphine and clonidine for rapid detoxification, buprenorphine-treated patients experienced less withdrawal and had a higher rapid detoxification completion rate (81%) as compared with clonidine-treated patients (65%).[42] Although the rapid detoxification process was successful in many of these studies, follow-up was limited, and the long-term success of these strategies is unknown.

Ultrarapid detoxification takes place under heavy sedation or anesthesia. Patients are given 2 to 10 mg

Table 5. Maintenance Strategies for Opioid Dependency

Medication	Availability	Dose	Frequency
Methadone	OTP	20–100 mg or more orally	Daily
Buprenorphine	Physician offices	8–24 mg sublingually	Daily to 3 times/wk
Naltrexone	OTP	50–100 mg orally	Daily to 3 times/wk

Adapted with permission from O'Connor PG, Fiellin DA. Pharmacologic treatment of heroin-dependent patients. Ann Intern Med 2000;133:45.

OTP = opioid treatment program.

of naloxone by intravenous bolus or by infusion at a rate of 0.4 to 0.8 mg/hr.[44] Prior to a recent study by Collins et al,[45] studies on ultrarapid detoxification had small sample sizes and limited follow-up. In response to concerns about the safety of these methods as well as the desire for more effective detoxification processes, Collins et al[45] investigated the effectiveness of anesthesia-assisted detoxification with naltrexone induction, buprenorphine-assisted rapid detoxification with naltrexone induction, and detoxification with clonidine-assisted delayed naltrexone induction. They found no differences in the main outcomes (withdrawal severity, completion of inpatient detoxification, retention in treatment, proportion of opioid-positive urine specimens) between the groups, but the anesthesia-assisted strategy was associated with 3 potentially life-threatening events. Researchers concluded that while the effectiveness of anesthesia-assisted or rapid detoxification was similar to that of other treatments, because of safety concerns, tremendous costs, and lack of clear benefit, there is little role for this procedure in the treatment of opioid addiction.[45]

Maintenance

Many patients have long-term success with a maintenance program rather than with detoxification. Although patients may not achieve a drug-free state quickly, improvements in drug use behaviors tend to be longer lasting.[46] Physicians of hospitalized opioid-addicted individuals play a critical role in initiating the maintenance process. However, after discharge, long-term maintenance strategies are managed by primary care physicians and OTPs. Maintenance strategies for opioid dependency are shown in **Table 5**.

Methadone. OTPs are primarily methadone maintenance programs with related counseling and vocational services. These programs have been shown to reduce opioid use, reduce crime, increase employment, and reduce HIV infection due to needle sharing, but there is a large unmet need.[47] For outpatient treatment, methadone detoxification and maintenance is restricted to physicians with a special registration from the US Drug Enforcement Agency. More than 900 programs in the United States incorporate methadone treatment.[32]

The goal of methadone maintenance is to prevent withdrawal as well as to stabilize changes to neurochemistry. Because methadone has a slower onset of action, it is less likely to produce a euphoric effect at steady doses. Also, it acts as a competitive antagonist, thus blocking opioid receptors. When taken orally, methadone has none of the associated risks of injection (eg, infection), and it prevents withdrawal symptoms because of cross-tolerance between heroin and methadone. However, methadone can be abused by injection in individuals who are less opioid-dependent. Long-term side effects of methadone include constipation, weight gain, decreased libido, and menstrual irregularities.[32] Methadone interacts with medications metabolized by the cytochrome P450 system, and as a result, patients concurrently taking alcohol, barbiturates, phenytoin, carbamazepine, isoniazid, rifampin,[48] and some antiretroviral medications, particularly non-nucleoside reverse transcriptase inhibitors (eg, nevirapine, efavirenz), may experience subtherapeutic methadone levels.[49]

Clinical trials have shown that methadone maintenance is effective in retaining heroin users in treatment[50] as well as in reducing the number of opioid-positive urine samples compared with placebo.[51] Data from the Drug Abuse Treatment Outcome Study showed that patients on methadone decreased heroin use in the previous week from 89% to 28% within 1 year of treatment.[52]

Buprenorphine. Clinical trials have demonstrated the safety and effectiveness of buprenorphine treatment for opioid addiction.[53,54] Seventy-five percent of patients on long-term buprenorphine stayed in treatment for 1 year compared with 0% of patients given buprenorphine for 6 days.[55] As a partial agonist, there is decreased risk of overdose compared with methadone; however, like methadone, buprenorphine has occasionally been associated with abnormal liver function in some patients. Thus, liver function tests should

be monitored periodically.[24] A meta-analysis of 6 studies investigating flexible dosing of buprenorphine versus methadone found that methadone was superior to buprenorphine at retaining patients, but heroin and cocaine use was not different between groups.[56] In a large trial comparing buprenorphine with methadone in 405 patients, 50% of patients receiving buprenorphine and 59% of those receiving methadone were retained in treatment for 13 weeks; the difference was not statistically significant.[57] A recent trial comparing 3 levels of counseling with office-based treatment with buprenorphine in 166 patients found that once-weekly counseling and standard medical management was as successful as more intensive counseling and management in terms of the percentage of opioid-free urine samples in patients over 6 months. In the once-weekly counseling group, 44% of urine samples were opioid-free.[58] Because buprenorphine is available through physician offices, new patients may decide to enter treatment based on improved access and the alternative venue of treatment.

Office-based maintenance treatment with buprenorphine initially requires daily visits, but patients are able to transition to weekly visits for dose adjustments once stabilized. Once the patient is stabilized on a consistent dose and experiences no withdrawal symptoms, office visits can be transitioned to every 2 to 4 weeks. During these visits, special attention should be paid to issues such as psychosocial functioning, social support, side effects, employment and financial issues, legal problems, and other drug and alcohol abuse.[24] Although it is a new treatment option, buprenorphine may be suitable and effective for special populations, including patients using opiates and cocaine[59] as well as HIV-positive patients.[60]

Naltrexone. Naltrexone, an orally active naloxone derivative, is a competitive opioid antagonist, which blocks the opioid effects of heroin. It precipitates withdrawal symptoms in patients who have used heroin within the last 7 days. Because abstinence is required, the clinical effectiveness of naltrexone has been limited due to difficulty with induction and early drop out.[32] A systematic review of naltrexone studies found insufficient evidence of success of naltrexone in maintenance therapy for most patients.[61] When compared with placebo, naltrexone was not statistically better than placebo in preventing illicit drug use.[62] However, some studies suggest that naltrexone may be useful in specific populations, such as health professionals, who are highly motivated to stop using opioids.[63] The development of a sustained-release injectable formulation of naltrexone has renewed interest in treating opioid dependence with this method. A recent trial of 60 patients demonstrated a dose response relationship with naltrexone. In this trial, 39% of patients on placebo, 60% of patients on 192 mg naltrexone, and 68% of patients on 384 mg naltrexone were retained in treatment for 8 weeks.[64]

MANAGING PAIN IN PATIENTS WITH OPIOID DEPENDENCE

Patients who need treatment for pain and not dependency should have their pain managed through standard medical practice. Knowing behaviors characteristic of patients with opioid dependence may be helpful to clinicians struggling to differentiate between opioid dependence and pain.[24] As opposed to patients with pain, opioid-dependent patients tend to have compulsive behavior, crave opioids when not in pain, obtain prescriptions from multiple sources, demand specific opioids, supplement with different opioids, procure drugs illegally, have a preferred route of administration, or increase their dose without medical advice. Patients in pain can regulate their dose and can stop when effective alternatives are available.

In cases in which patients are dependent but have pain management needs, physicians should attempt to manage pain with nonopioid medications (eg, nonsteroidal anti-inflammatory drugs).[24] Because patients with opioid dependence may be more sensitive to pain and pain may be unresponsive to nonopioid medications, additional opioid medication may be required.[65] In this case, it is important to take a careful history, reassure the patient that adequate pain control is a goal, and communicate with opioid maintenance providers regarding dosages, if applicable. It may be helpful to administer opioids at shorter durations and to write prescriptions for continuous dosing as opposed to as-needed dosing. For patients on methadone maintenance, the dose can be continued and short-acting analgesics can be added. The same strategy may work for patients on buprenorphine, but alternatives include splitting the buprenorphine dose over shorter intervals (6 or 8 hr), discontinuing buprenorphine and treating exclusively with short-acting opioids, or converting to low-dose methadone (20–40 mg) for opioid maintenance when patients are hospitalized and using short-acting opioids for pain with special attention to signs of overdose.[66] Because of its ceiling effect, buprenorphine is unlikely to provide adequate analgesia for chronic pain.[24]

For patients with chronic pain requiring opioid agonists, some clinicians have implemented the use of opioid contracts under which the patient and physician

agree to certain conditions (eg, urine drug screening, compliance with office visits) in order for the prescription of opioid medications to continue. Although popular, there are few guidelines as to the content of these contracts and scant empirical evidence regarding their effectiveness. This is an area for further investigation.[67]

CONCLUSION

Despite increasingly available and effective treatment options, opioid dependency is not well diagnosed or treated in the United States. Hospital- and office-based physicians will encounter opioid-dependent patients on a regular basis and must be aware of the steps in assessing, diagnosing, and treating such patients. With the expansion of office-based detoxification and maintenance, more physicians can be trained to address opioid dependence in the outpatient setting. **HP**

Test your knowledge and comprehension of this article with the *Clinical Review Quiz* on page 32.

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