

## **In This Chapter...**

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# **4 Physical Detoxification Services for Withdrawal From Specific Substances**

This chapter highlights specific treatment regimens for specific substances and provides guidance on the medical, nursing, and social services aspects of these treatments. It also includes considerations for specific populations. Although it is written principally for healthcare professionals, some professionals without medical training may find it of use. To accommodate a broad audience, the chapter includes definitions for technical terms that may be unfamiliar to some readers—for example, “the patient was afebrile (without fever).”

## **Psychosocial and Biomedical Screening and Assessment**

This section covers more complex psychosocial and biomedical assessments that may occur after initial contact as an individual undergoes detoxification. Psychosocial and biomedical screening and services are closely associated: neither is likely to succeed without the other, as the case study below illustrates.

Although the medical issues in this case indicate that the patient could successfully be managed as an outpatient, careful assessment of psychosocial and biomedical aspects of the patient’s condition, including lack of transportation, the risk of violence, and his inability to carry out routine medical instructions, strongly indicated that the patient remain in a 24-hour supervised setting such as a residential detoxification or treatment program. For an illustration of some of the fundamental

## Case Study

A 44-year-old Caucasian male with a fifth-grade education presented to an emergency clinic in mild alcohol withdrawal with no alcohol for 9 hours. The patient was mildly tremulous with some nausea and insomnia; blood pressure was 142/94; pulse was 96. The patient was afebrile [i.e., without fever], and Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) (see below) score = 12, indicating mild withdrawal. A treatment plan was recommended that called for an outpatient 3-day fixed-dose taper of lorazepam (a benzodiazepine medication) plus multivitamins and oral thiamine. The patient was instructed to return daily for brief assessment by nursing personnel. The social worker assigned to this client pointed out that there was no reliable transportation to the clinic, there had been domestic violence on the parts of both spouses, and the patient's ability to carry out routine medical instructions was questionable.

aspects of the patient's health and psychosocial status that should be covered in screening and assessment, see Figure 3-1, p. 25.

Figure 4-1 lists several instruments useful in characterizing the intensity of specific withdrawal states (see appendix C for more information on these instruments and how to obtain them).

### Biochemical Markers and Their Use

This section focuses on biochemical laboratory tests that detect the presence or absence of alcohol or another substance of abuse, may be able to quantify the level of present use, or may be able to quantify cumulative use over the past few weeks. Tests in all of these areas are reasonably well developed and validated for alcohol. *This is not the case for most other substances of abuse.* Biochemical markers are not adequate screening or assessment instruments alone, but rather are used to support a more comprehensive clinical assessment. Common uses of these biochemical markers are:

1. In the initial screening setting to support or refute other information that leads to proper diagnosis, assessment, and management.
2. For forensic purposes (e.g., evaluating a driver after an automobile accident).
3. In detecting occult (secretive or hidden) use of alcohol and other substances in therapeutic settings where abstinence,

rehabilitation, and treatment are being promoted.

Clinicians also can use the presentation of information from biochemical markers to patients as an effective tool in motivational enhancement. For example, information regarding liver transaminases (specific kinds of enzymes that perform chemical reactions within the liver) helps provide the patient with objective information on the level of recent alcohol use and potential acute hepatic damage. This may help the patient move from contemplating treatment to actually beginning treatment. For a more detailed discussion of biological markers in substance abuse, see Javors and colleagues (1997).

### Blood alcohol content

Blood alcohol content (BAC) can be determined by highly sensitive laboratory procedures that generally are available in most emergency departments, hospitals, and clinical chemistry laboratories. Alcohol elimination undergoes, for the most part, zero-order kinetics (decreasing a set amount per unit of time rather than a set percentage), so the concept of half-life is not really accurate. However, first-order kinetics and half-life do occur when BAC is low (i.e., below 10mg percent), and the half-life is on the order of about 15 minutes at that point. Though disappearance rates of 15mg percent per hour are probably average for moderate drinkers, higher values were seen in a group of Swedish drivers apprehended for driving while intoxicated (19mg/dL/hr) (Jones and Andersson

**Figure 4-1**  
**Assessment Instruments for Dependence and Withdrawal From Alcohol and Specific Illicit Drugs**

Drug of Dependence	Instrument	Reference	Notes
Alcohol	CIWA-Ar	Sullivan et al. 1989	10 items that take 2 to 5 minutes to complete; scores 0–67, with 10 or greater as clinically significant; requires training to administer
Cocaine	Cocaine Selective Severity Assessment (CSSA)	Kampman et al. 1998	18 items that take 10 minutes to complete; high scores correlated with poor outcome
Opioids	Subjective Opiate Withdrawal Scale (SOWS)	Handelsman et al. 1987	16-item questionnaire; using a scale of 0–4, respondents rate to what extent they are currently experiencing each of 16 characteristics; higher scores indicate more severe withdrawal
	Objective Opiate Withdrawal Scale (OOWS)	Handelsman et al. 1987	Rater observes patient for about 10 minutes and indicates if any of 13 manifestations of withdrawal are present; scores can range from 0 to 13, with higher scores indicating more severe withdrawal; staff must be familiar with withdrawal signs

1996). The rate of metabolism of alcohol increases with dependence—some alcoholics can metabolize 20–25mg/dL/hr (Jones and Andersson 1996), and Jones and Sternebring (1992) have found that alcohol-dependent patients may metabolize 22mg/dL/hr during detoxification.

When knowledge of BAC is combined with clinical information, the healthcare provider can make some predictions regarding the acuteness of withdrawal. For example, in an individual whose blood alcohol level is 200mg percent but who is already showing tremulousness (shakiness of the hands), brisk reflexes, tachycardia (rapid heart rate), diaphoresis (excessive sweating), and perhaps a CIWA-Ar score in the moderate or high

range (about 15 or higher), the clinician can reasonably predict that the withdrawal will be relatively severe. As noted, however, the rate of metabolism of alcohol increases with dependence. The diagnosis of alcohol intoxication is a clinical diagnosis and not based simply on a BAC. A person with a BAC of 200mg percent could be in withdrawal, intoxicated (showing related signs and symptoms), or showing no signs and symptoms of either intoxication or withdrawal. A BAC above 100mg percent does not necessarily indicate clinical intoxication. Like all laboratory procedures, the blood alcohol levels test has limitations. Usually, patient permission must be obtained prior to testing, the testing itself can be expensive, and forensic testing may be subject to specific legal procedures.

## **Reading Blood Alcohol Concentrations**

Blood alcohol concentrations are measured in milligrams (mg) of alcohol per deciliter (dL) of blood. This figure is converted to a percentage. One hundred mg/dL equals 100mg percent or 0.1 percent. Thus, a BAC of .1mg percent is equivalent to a concentration of 100mg of alcohol per deciliter of blood.

*Source:* Center for Substance Abuse Treatment (CSAT) 1995a.

### **Breath alcohol levels**

Although the initial cost of small breath alcohol instruments may be relatively high, the recurring costs (of disposable mouthpieces and periodic recalibration) are low. The technique is less invasive than blood testing and health providers can follow breath alcohol levels repeatedly at low expense during the course of assessment and detoxification. The detection of rapidly rising, high levels of alcohol over a short period of time may indicate alcohol poisoning overdose. Breath alcohol levels provide useful guidance in determining whether to hospitalize these patients.

Limitations on breath alcohol determinations are that patient cooperation is required and that some patients with lung diseases are not able to muster a sufficient tidal volume (forceful breath) to give an accurate reading to the machine. On occasion, patients whose breath alcohol levels indicate recent alcohol use will assert that they have recently gargled with mouthwash that contained alcohol. Having the patient rinse his mouth with water several times and then making another breath alcohol determination in 15 to 30 minutes usually will resolve whether the patient's assertion is valid.

### **Urine drug screens**

Urine drug screens vary widely in their methods of detection, sensitivity and specificity, expense, and availability. The healthcare provider assessing patients for detoxification should be familiar with the type of assay (test measurement) being used; some examples are enzyme multiple assay techniques, thin layer chromatography, high performance liquid

chromatography, urine alcohol concentration, and gas chromatography-mass spectrometry.

Informed clinicians also should be aware of which drugs are screened for by the laboratory they use, the relative time window of detection (a substance's metabolic half-life, or approximately how long a drug can be detected once ingested), and whether cross-reactivity with other interfering substances may alter outcomes. Many laboratories perform more specific confirmation testing on positive screening tests, which can largely eliminate false-positives. It is important to clarify which type of test result is being reported. Interfering and cross-reactive substances leading to false-positive tests frequently are discussed in bulletins and publications periodically published by the National Institute on Drug Abuse (NIDA) and the Centers for Disease Control and Prevention (CDC). Usually, the senior laboratory supervisor has up-to-date information in this area and often can be consulted via e-mail or telephone in an emergency. Limitations of urine drug screening include consent and privacy issues, expense, the inability to screen for some drugs of abuse, and the inability of urine drug screens to provide information on the current level of intoxication.

Urine testing should at a minimum test for the presence of

- Benzodiazepines
- Barbiturates
- Cocaine
- Amphetamines
- Opioids
- PCP

It also should be noted that current testing for opioids primarily refers to “organic” drugs that are derived from opium (i.e., heroin, codeine, and morphine). Synthetic opioids like hydrocodone and methadone are not detected by the usual tests; this is true of oxycodone as well. If the use of these drugs is suspected, special tests can be ordered. Most important, each program should tailor its urine screening tests to reflect the substance use patterns prevalent in the community.

### ***Gamma-glutamyltransferase (GGT)***

GGT has been measured in serum (the portion of the blood that has neither red nor white blood cells) for many years as a marker for liver damage. More recently, GGT has been advocated as a measure of cumulative alcohol use (Dackis 2001). Sensitivity of the test is in the 60 to 70 percent range and specificity (its ability not to misidentify or confuse alcohol use with other disorders) is in the 40 to 50 percent range. In general, both sensitivity and specificity are lower in females than males. GGT does correlate with alcohol intake but often requires heavy drinking (more than six drinks per day) to elevate it, and only about half of individuals will show elevations. The half-life of elevated serum GGT after the onset of abstinence is said to be 2 to 3 weeks with alcoholic liver disease. Chlorpromazine, phenobarbital, and acetaminophen can all raise serum GGT levels.

GGT is limited by its expense and its relatively low specificity, which sometimes leads to false-positive evaluations. GGT is helpful as a motivational enhancer in patients with a high degree of denial during detoxification. Evidence of liver damage, as measured by the GGT, provides patients with objective feedback concerning the consequences of their alcohol use and thus plays a very important role in enhancing motivation.

Hepatitis is a general term that refers to inflammation of the liver with damage to liver cells (hepatocytes). Hepatitis may be due to viruses (such as in hepatitis A, B, C) or

insults to the liver from toxins (such as chemicals, alcohol, prescribed or over-the-counter medications). In any form of hepatitis, GGT may be elevated, indicating damage to liver cells. Therefore, GGT elevation does not automatically mean liver damage from alcohol use, although this is certainly one of the most common reasons for elevated GGT levels in patients hospitalized in North America. The use of GGT levels along with carbohydrate-deficient transferrin (CDT) levels is a relatively sensitive and specific indicator of alcohol use. The CDT test is discussed below.

### ***Carbohydrate-deficient transferrin***

CDT has been developed over the past 20 years as a marker of cumulative alcohol consumption but is just now becoming widely available as a clinical tool. Sensitivities appear to be in the 70 to 80 percent range, and specificities of greater than 90 percent have been found. Sensitivity and specificity are somewhat lower among females than males. Most therapeutic drugs or drugs of abuse do not appear to affect CDT levels. When CDT and GGT levels are combined, sensitivity and specificity rise to more than 90 percent (Anton 2001). CDT testing is limited by its relatively high cost, lack of clinical availability in some laboratories, and false-positive results in abstaining individuals who have endstage liver disease from causes other than alcohol use (DiMartini et al. 2001).

### ***Mean corpuscular volume (MCV)***

Erythrocyte (red blood cell) size is measured in a Coulter counter and often is part of a complete blood count; therefore, it is widely available to clinicians. Sensitivity and specificity are in the 30 to 50 percent range. Hence, caution should be exercised when interpreting an elevated MCV in relation to drinking behavior. This lab test should be considered complementary to other biological markers that are more specific and sensitive, such as GGT or CDT. Advanced age, nutritional status, cigarette

smoking, and co-occurring disease states without the presence of alcoholism may make test results abnormal.

## Alcohol Intoxication and Withdrawal

### Intoxication Signs and Symptoms

The clinical presentation of intoxication from alcohol varies widely depending in part on blood alcohol level and level of previously developed tolerance. At alcohol concentrations between 20mg percent and 80mg percent, loss of muscular coordination, changes in mood, personality alteration, and [increases in motor activity] begin. At levels from 80 to 200mg percent, more progressive neurologic impairment occurs with ataxia (inability to coordinate muscular activity) and slurring of speech being prominent. A variety of cognitive functions also are impaired. At blood alcohol levels between 200 and 300mg percent nausea and vomiting may occur, which along with sedation may place patients at grave risk for aspiration of stomach contents. At levels greater than 300mg percent, hypothermia (low body temperature) with impairment of level of consciousness is likely except in all but the most tolerant individuals. Coma begins to be seen at levels of 400 to 600mg percent, but this is variable, again depending on tolerance. Although exceptions are found, BACs between 600 and 800mg percent are fatal. At this point, respiratory, cardiovascular, and body temperature controls fail. See Figure 4-2 for more symptoms of alcohol intoxication.

Since the elimination rate of alcohol from the body generally is 10 to 30mg percent per hour, the goals for the treatment of alcohol intoxication are to preserve respiration and cardiovascular function until alcohol levels fall into a safe range. Patients who are severely intoxicated and comatose as the result of alcohol use should be managed in the same manner as all comatose patients, with particular care taken

in monitoring vital functions, protecting respiration, and observing aspiration, hypoglycemia, and thiamin deficiency. Screening for other drugs that may contribute to the coma, as well as other sources of coma induction, should be done. Agitation is best managed with interpersonal and nursing approaches rather than additional medications, which may only complicate and delay the elimination of the alcohol.

### Withdrawal Signs and Symptoms

Hippocrates, writing around 400 B.C., gave us our first written clinical picture of alcohol withdrawal when he wrote that if the patient is “in the prime of life and if from drinking he has trembling hands,” it may well be the case that the patient is showing withdrawal signs and symptoms. To this day, alcohol withdrawal remains underrecognized and undertreated. The signs and symptoms of acute alcohol withdrawal generally start 6 to 24 hours after the patient takes his last drink. Alcohol withdrawal may begin when the patient still has significant blood alcohol concentrations. The signs and symptoms may include the following:

- Restlessness, irritability, anxiety, agitation
- Anorexia (lack of appetite), nausea, vomiting
- Tremor (shakiness), elevated heart rate, increased blood pressure
- Insomnia, intense dreaming, nightmares
- Poor concentration, impaired memory and judgment
- Increased sensitivity to sound, light, and tactile sensations
- Hallucinations (auditory, visual, or tactile)
- Delusions, usually of paranoid or persecutory varieties
- Grand mal seizures (grand mal seizures represent a severe, generalized, abnormal electrical discharge of the major portions of the brain, resulting in loss of consciousness, brief cessation of breathing, and muscle rigidity followed by muscle jerking; a brief period of

**Figure 4-2**  
**Symptoms of Alcohol Intoxication\***

Blood Alcohol Level	Clinical Picture
20–100mg percent	<ul style="list-style-type: none"> <li>• Mood and behavioral changes</li> <li>• Reduced coordination</li> <li>• Impairment of ability to drive a car or operate machinery</li> </ul>
101–200mg percent	<ul style="list-style-type: none"> <li>• Reduced coordination of most activities</li> <li>• Speech impairment</li> <li>• Trouble walking</li> <li>• General impairment of thinking and judgment</li> </ul>
201–300mg percent	<ul style="list-style-type: none"> <li>• Marked impairment of thinking, memory, and coordination</li> <li>• Marked reduction in level of alertness</li> <li>• Memory blackouts</li> <li>• Nausea and vomiting</li> </ul>
301–400mg percent	<ul style="list-style-type: none"> <li>• Worsening of above symptoms with reduction of body temperature and blood pressure</li> <li>• Excessive sleepiness</li> <li>• Amnesia</li> </ul>
401–800mg percent	<ul style="list-style-type: none"> <li>• Difficulty waking the patient (coma)</li> <li>• Serious decreases in pulse, temperature, blood pressure, and rate of breathing</li> <li>• Urinary and bowel incontinence</li> <li>• Death</li> </ul>
*Varies greatly with level of tolerance (chronic users of alcohol may show less effect at any given blood alcohol level).	
<i>Source:</i> Consensus Panelist Robert Malcolm, M.D.	

sleep, awakening later with some mild to even severe confusion, generally occurs)

- Hyperthermia (high fever)
- Delirium with disorientation with regard to time, place, person, and situation; fluctuation in level of consciousness

For a discussion of seizures and delirium, including delirium tremens, see below under

the heading Management of Delirium and Seizures (p. 63).

Mild alcohol withdrawal generally consists of anxiety, irritability, difficulty sleeping, and decreased appetite. Severe alcohol withdrawal usually is characterized by obvious trembling of the hands and arms, sweating, elevation of pulse (above 100) and blood pressure (greater

than 140/90), nausea (sometimes with vomiting), and hypersensitivity to noises (which seem louder than usual) and light (which appears brighter than usual). Brief periods of hearing and seeing things that are not present (auditory and visual hallucinations) also may occur. A fever greater than 101° F also may be seen, though care should be taken to determine whether the fever is the result of an infection. Seizures and true delirium tremens, as discussed elsewhere, represent the most extreme forms of severe alcohol withdrawal. Moderate alcohol withdrawal is defined more vaguely, but represents some features of both mild and severe withdrawal.

The course of these symptoms is extremely variable. An individual may progress partially through some of the symptoms noted above and then have a slow improvement. Other individuals may have mild to moderate symptoms with almost abrupt resolution. Yet another group may present with a grand mal seizure or with hallucinations. Some people with alcohol dependence, regardless of their pattern of drinking or the extent of drinking, appear to develop minor symptoms or show no symptoms of withdrawal. Infrequent binge drinkers seem less likely to have withdrawal symptoms than individuals who are heavy regular users of alcohol who then abruptly cease their alcohol use, but this is not well substantiated. As previously discussed in the assessment section, the use of a standardized clinical rating instrument for withdrawal such as the CIWA-Ar is valuable because it guides the clinician through multiple domains of alcohol withdrawal and allows for semi-quantitative assessment of nausea, tremor, autonomic hyperactivity, anxiety, agitation, perceptual disturbances, headache, and disorientation. Age, general health, nutritional factors, and possible co-occurring medical or psychiatric conditions all appear to play a role in increasing the severity of the symptoms of alcohol withdrawal.

The most useful clinical factors to assess the likelihood and the extent of a current withdrawal is the patient's last withdrawal and

the number of previous withdrawals (treated or untreated) experienced, with three or four being a particularly significant number for the appearance of severe withdrawal reactions unless adequate medical care is provided. This assumption that this phenomenon will manifest itself, which has been referred to as the "kindling hypothesis," is well-established in the research literature (Booth and Blow 1993; Wojnar et al. 1999).

Uncomplicated or mild to moderate withdrawal is characterized by restlessness, irritability, anorexia (lack of appetite), tremor (shakiness), insomnia, impaired cognitive functions, and mild perceptual changes.

Complicated or severe medical withdrawal has one or more elements of delirium, hallucinations, delusions, seizures, and disturbances of body temperature, pulse, and blood pressure.

## **Medical Complications of Alcohol Withdrawal: Possible Fatal Outcomes**

Seizures; delirium tremens (severe delirium with trembling); and dysregulation of body temperature, pulse, and blood pressure are outcomes in severe alcohol dependence that can lead to fatal consequences. Other medical complications of alcohol withdrawal include infections, hypoglycemia, gastrointestinal (GI) bleeding, undetected trauma, hepatic failure, cardiomyopathy (dilation of the heart with ineffective pumping), pancreatitis (inflammation of the pancreas), and encephalopathy (generalized impaired brain functioning). The suspicion of impending complications or their appearance will require hospitalization of the client and possible intensive care unit level of management. Consultation with internists specializing in infectious disease, pulmonary care, and hepatology; surgeons; neurologists; psychiatrists; anesthesiologists; and other specialists also may be warranted, depending on the nature of the complications.

## Management of Withdrawal Without Medication

The management of an individual in alcohol withdrawal without medication is a difficult matter because the indications for this have not been established firmly through scientific studies or any evidence-based methods.

Furthermore, the course of alcohol withdrawal is unpredictable and currently available techniques of screening and assessment do not allow us to predict with confidence who will or will not experience life-threatening complications. Severe alcohol withdrawal may be associated with seizures due to relative impairment of gamma-aminobutyric acid (GABA) and relative over-activity of N-methyl-D-aspartate systems (a subtype of the excitatory glutamate receptor system) (Moak and Anton 1996). The failure to treat incipient convulsions is a deviation from the established general standard of care.

Positive aspects of the nonmedication approach are that it is highly cost-effective and provides inexpensive access to detoxification for individuals seeking aid. Observation is generally better than no treatment, but people in moderate to severe withdrawal will be best served at a higher level of care. Young individuals in good health, with no history of previous withdrawal reactions, may be well served by management of withdrawal without medication. However, personnel supervising in this setting should possess assessment abilities and be able to summon help through the emergency medical system. Methods of withdrawal management without medication include frequent interpersonal support, provision of adequate fluids and food, attention to hygiene, adequate sleep, and the maintenance of a no-alcohol/no-drug environment.

## Social Detoxification

Social detoxification programs are defined as short-term, nonmedical treatment services for individuals with substance use disorders. A social detoxification program offers room, board, and interpersonal support to intoxicated individuals and individuals in substance use

withdrawal. The consensus panel has found that in actual practice, social detoxification programs vary greatly in their approach and scope. Some programs offer some medical and nursing onsite supervision, while others provide access to medical and nursing evaluation through clinics, urgent care programs, and emergency departments.

Some social detoxification programs only offer basic room and board for a “cold turkey” detoxification, while other programs offer supervised use of medications. Sometimes medications are prescribed at the onset of withdrawal by health-care professionals in an outpatient setting, while the staff in the social detoxification program supervises the administration of these medications.

Whatever the particular situation might be, there should always be medical surveillance, including monitoring of vital signs, as part of every social detoxification program.

The consensus panel agrees that for alcohol, sedative-hypnotic, and opioid withdrawal syndromes, hospitalization (or some form of 24-hour medical care) is generally the preferred setting for detoxification, based on principles of safety and humanitarian concerns. When hospitalization cannot be provided, a setting that provides a high level of nursing and medical backup 24 hours a day, 7 days a week is desirable. The panel readily acknowledges that social detoxification programs are, for some

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communities, the only available resources for uninsured, homeless individuals. Social detoxification is preferable to detoxification in unsupervised settings such as the street, shelters, or jails. The panel also notes that in some large urban areas, social detoxification programs have longstanding, excellent reputations of providing high-quality supervision and nurturance

for their clients.

Social detoxification programs are organized and funded by a variety of sources, including faith-based organizations, community charities, and municipal and other local governments.

The genesis of social detoxification is complex. Often, these programs grew out of community needs when no other alternatives were available. Early reports (Whitfield et al. 1978) indicated that many individuals in alcohol withdrawal could be managed successfully

without medications in a social detoxification setting. Subsequent reviews that have revisited the topic (Lapham et al. 1996) have reached similar conclusions. Critical analysis of these reports by the consensus panel indicates that some of the scientific issues were oversimplified and misleading. A number of these studies, in fact, excluded many seriously ill clients from their surveys prior to referral to social detoxification. Some of these surveys had a very high staff-to-client ratio during social detoxification, thus providing an unusually high level of psychological support. This level of staffing is not frequently found today in social detoxification programs.

The consensus panel acknowledges that, for a substantial group of individuals, substance use withdrawal syndromes do not lead to fatal outcomes or even significant morbidity.

Determining which individuals will have benign outcomes often is difficult, and in fact this determination prior to social detoxification referral frequently is not made. Some incorrect beliefs have sprung up in the context of social detoxification: Individuals undergoing opioid withdrawal often are considered to require hospitalization to alleviate suffering, while individuals undergoing alcohol withdrawal sometimes are, for a variety of reasons, denied hospital-level treatment for detoxification, even though alcohol withdrawal produces suffering and may have fatal consequences.

The consensus panel agreed on several guidelines for social detoxification programs:

- Such programs should follow local governmental regulations regarding their licensing and inspection.
- It is highly desirable that individuals entering social detoxification be assessed by primary care practitioners (physicians, physician assistants, nurse practitioners) with some experience in substance abuse treatment.
- Such an assessment should determine whether the patient currently is intoxicated and the degree of intoxication, the type of withdrawal syndrome, severity of the withdrawal, information regarding past withdrawals, and the presence of co-occurring psychiatric, medical, and surgical conditions that might well require specialized care (see chapter 3, Figure 3-1, p. 25).
- Particular attention should be paid to those individuals who have undergone multiple withdrawals in the past and for whom each withdrawal appears to be worse than previous ones—this is the so-called “kindling effect” (Ballenger and Post 1978; Booth and Blow 1993; Malcolm et al. 2000; Shaw et al. 1998; Wojnar et al. 1999; Worner 1996). Subjects with a history of severe withdrawals, multiple withdrawals, delirium

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tremens, or seizures are not good candidates for social detoxification programs.

- All social detoxification programs should have an alcohol- and drug-free environment, have personnel who are familiar with the features of substance use withdrawal syndromes, have training in basic life support, and have access to an emergency medical system that can provide transportation to emergency departments and other sites of clinical care.

## Management of Withdrawal With Medications

Over the last 15 years several reviews and position papers (Fuller and Gordis 1994; Lejoyeux et al. 1998; Mayo-Smith 1997; Nutt et al. 1989; Shaw 1995) have asserted that only a minority of patients with alcoholism will in fact go into significant alcohol withdrawal requiring medications. Identifying that significant minority sometimes is problematic, but there are signs and symptoms of impending problems that can alert the caretaker to seek medical attention.

Deciding on whether to use medical management for the treatment of alcohol withdrawal requires that patients be separated into three groups. The first and most obvious group comprises those clients who have had a previous history of the most extreme forms of withdrawal, that of seizures and/or delirium. This group is discussed in more detail below, but in general, the medication treatment of this group in early abstinence, whether or not they have had the initiation of withdrawal symptoms, should proceed as quickly as possible.

The second group of patients requiring immediate medication treatment includes those patients who are already in withdrawal and demonstrating moderate symptoms of withdrawal.

The third group of patients includes those who may still be intoxicated and therefore have not had time to develop withdrawal symptoms or who have, at the time of admis-

sion, been abstinent for a few hours and have not developed signs or symptoms of withdrawal. A decision regarding medication for this group should be in part based on age, number of years of alcohol dependence, and the number of previously treated or untreated severe withdrawals (three or four appears to be a significant threshold in predicting future serious withdrawal) (Shaw 1995). If there is an opportunity to observe the patient in the emergency department of the clinic or similar setting over the next 6 to 8 hours, then it is possible to delay a decision regarding treatment and periodically reevaluate a client of this category. If this is not possible, then the return of the patient to a setting in which there is some supervision by family, significant others, or in a social detoxification program is desirable.

The decision as to whether to give the patient a single medication dose prior to discharge and perhaps provide one or two additional medication doses to be administered in the referral setting rests on adequacy of supervision, the probability of whether the patient will drink while undergoing treatment, and whether the patient can or will return for assessments the following day. In some circumstances, no treatment may be safer than treatment with medication. Mayo-Smith (1997) has shown that benzodiazepines confer protection against alcohol withdrawal seizures and thus patients with previous seizures should be treated early. The same applies to delirium. Both of these topics will be explored in greater detail in the next section.

Extremely heavy drinking in the weeks prior to complete cessation also predicts more severe withdrawal (Lejoyeux et al. 1998), but confirming such a history often is difficult.

A less accepted and more controversial position on the indications for medication treatment for alcohol withdrawal springs from studies that attempt to measure oxidative stress, which is the formation of oxidative free radicals (chemicals that damage proteins), and stress hormones during alcohol withdrawal (Dupont et al. 2000; Tsai et al.

1998). These studies have asserted that individuals who are undergoing mild withdrawal without treatment still have the formation of toxic oxidative products which have the hypothetical potential of producing neuronal damage and perhaps some cell death. Lending support to this argument is the fact that alcohol withdrawal appears to be progressive in that it worsens with each successive episode (Malcolm et al. 2000) and that some patients dependent on alcohol develop evidence of dementia over time. On the other hand, age, nutritional status, trauma, co-occurring conditions, and other unspecified events also probably contribute to this process.

The decision to treat a patient in alcohol withdrawal or at potential risk for alcohol withdrawal will in great part rest on the clinical judgment of the practitioner, relying on the factors noted above in addition to the issue of whether treatment may in fact actually do more harm than good. This topic is discussed below under the heading Limitations of Benzodiazepines in Outpatient Treatment (p. 60). For more information about medication-assisted treatment, see TIP 43, *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs* (CSAT 2005d).

## ***Benzodiazepine treatment of alcohol withdrawal***

Depending upon the clinical setting and the patient circumstances, there are several acceptable regimens for treating alcohol withdrawal that make use of benzodiazepines. These drugs remain the medication class of choice for treating alcohol withdrawal. The early recognition of alcohol withdrawal and prompt administration of a suitable benzodiazepine usually will prevent the withdrawal reaction from proceeding to serious consequences. Patients suspected of alcohol withdrawal should be seen promptly by a primary care provider (physician, nurse practitioner, physician assistant) who has experience in diagnosing and managing alcohol withdrawal. Practitioners are reminded that

benzodiazepines have side effects and limitations. These limitations are far more prominent when treating alcohol withdrawal in an outpatient setting.

### ***Loading dose of a benzodiazepine***

Medical or nursing administration of a slowly metabolized benzodiazepine, frequently intravenously, but sometimes orally, may be carried out every 1 to 2 hours until significant clinical improvement occurs (such as reducing the CIWA-Ar score to 10 or less) or the patient becomes sedated (Sellers and Naranjo 1985). Patients at grave risk for the most severe complications of alcohol withdrawal or who are already experiencing severe withdrawal should be hospitalized and can be treated with this regimen. In general, patients with severe withdrawal may receive 20mg of diazepam or 100mg of chlordiazepoxide every 2 to 3 hours until improvement or sedation prevails. Oversedation, ataxia (lack of muscular coordination), and confusion, particularly in elderly patients, may occur with this protocol. The treatment staff should closely monitor hemodynamic (blood pressure and pulse) and respiratory features. They should particularly be prepared to detect and rapidly treat apnea (no breathing) with assisted ventilation. Having experienced staff with adequate time to frequently monitor the patient and provide intravenous medication is necessary.

### ***Symptom-triggered therapy***

Using the CIWA-Ar or similar alcohol withdrawal rating scales, medical personnel can be trained to recognize signs and symptoms of alcohol withdrawal, make a rating, and based on that rating administer benzodiazepines to their patients only when signs and symptoms reach a particular threshold score. Studies have demonstrated that appropriate training of nurses in the application of the CIWA-Ar dramatically reduces the number of patients who need to receive symptom-triggered medication (Saitz et al. 1994; Wartenberg et al. 1990). This regimen has been used successfully with short, intermediate, and long half-life benzodiazepines.

The training of staff in a standardized procedure of administering rating scales is important and periodic retraining to ensure continued reliability among raters is essential. A typical routine of administration of symptom-triggered therapy is as follows: Administer 50mg of chlordiazepoxide (Librium) for CIWA-Ar > 9 and reassess in 1 hour. Continue administering 50mg chlordiazepoxide every hour until CIWA-Ar is < 10. Dosage amount and frequency can be modified depending on the individual clinical situation as determined by the medical provider. Patients with a history of withdrawal seizures should receive scheduled doses of a long-acting benzodiazepine (e.g., diazepam [Valium], 20mg every 6 hours for 3 days) regardless of CIWA-Ar score, and should receive additional doses if indicated by elevated CIWA-Ar score. It must be noted here that symptom-triggered therapy is not recommended for outpatient detoxification. Symptom-triggered therapy requires monitoring and decision-making by a healthcare professional.

### *Gradual, tapering doses*

Before beginning any tapering regimen, the patient must be fully stabilized; that is, all signs and symptoms of withdrawal must be improved. Without proper stabilization, no tapering scheme will succeed. Once the patient has been stabilized, oral benzodiazepines can be administered on a predetermined dosing schedule for several days and gradually tapered over time. This is a commonly used regimen.

Dosing protocols vary widely among treatment facilities based on the needs of the patient population. One example is that patients might receive 50mg of chlordiazepoxide or 10mg of diazepam every 6 hours during the first day of treatment and 25mg of chlordiazepoxide or 5mg of diazepam every 6 hours on the second and third days. This approach to dosing, that is, every 6 hours, is not as accurate in tailoring medications to counter symptoms; a more precise dosing regimen is titrating (adjusting dosage in light of

drug response) according to severity of symptoms. An alternative regimen might be the administration of 1 to 2mg lorazepam two or three times a day the first day, followed by gradual reduction over the next 3 to 5 days. The general approach to tapering is to establish an acute dose in the first 24 hours, then to reduce it over the next three days: for example, 400 chlordiazepoxide total on day 1, then 300, 200, 100, and off on day 5. This has to be extended if lorazepam is used. Doses of withdrawal medication are omitted if the patient is sleeping soundly, showing signs of oversedation, or exhibiting marked ataxia.

The use of gradual, tapering doses is appealing in settings where trained nursing or medical observations cannot be made frequently; however, this in itself is a pitfall.

Under- or overmedication with this regimen can occur depending on benzodiazepine tolerance; the presence of chronic cigarette smoking, which induces benzodiazepine metabolism; liver function; age; and the presence of co-occurring medical or psychiatric conditions. The use of this regimen may be problematic in the outpatient settings in which it frequently is applied. Supplying the patient with 4 to 5 days of a benzodiazepine and facing the probability that the patient may drink and take the benzodiazepine is a hazard. It is important to enforce strict limitations on driving automobiles, climbing, or operating hazardous machinery.

**Benzodiazepines**  
remain the  
medication class  
of choice for  
treating alcohol  
withdrawal.

### *Single daily dosing protocol*

Jauhar and Anderson (2000) compared single daily dosing of diazepam to multiple daily dosing of chlordiazepoxide in inpatients being treated for alcohol withdrawal. Patients in the diazepam single daily dose group did as well as the chlordiazepoxide multiple dosing group. The authors suggest that this regimen might be attractive in community or social detoxification settings, particularly if patients could be monitored between administered doses. Further study with a larger group of patients is needed.

The choice of the specific benzodiazepine for any particular regimen depends on a number of factors, but the most significant factor is that the clinician administer one that she has the most experience using. Despite 30 years of research, no single benzodiazepine has emerged as the number one drug of choice in treating alcohol withdrawal. All benzodiazepines studied have worked better than placebo but have been roughly equivalent with each other. Many clinicians prefer long half-life benzodiazepines such as chlordiazepoxide and diazepam, desiring less frequent daily dosing, relatively steady serum levels, and the ability of these drugs to self-taper based on their long half-lives.

### *Diazepam and chlordiazepoxide*

Both diazepam and chlordiazepoxide have excellent rapid oral absorption and are available for intravenous (IV) use. Intramuscular use of these drugs is to be discouraged since muscle absorption is erratic. One study suggests that if chlordiazepoxide (Librium) is taken in overdose with alcohol, it is less likely to be fatal than diazepam (Valium) (Serfaty and Masterton 1993). Detractors of the use of these two drugs point out that they have long half-lives (although some clinicians see this as an advantage because it prevents the emergence of withdrawal symptoms between doses), have multiple active metabolites, and go through many oxidative metabolic steps in the liver. Older patients or patients with liver disease are likely to accumulate these medications quickly without being able to metabolize them. Possible consequences include oversedation or

ataxia, and on rare occasions, confusion may ensue.

### *Lorazepam*

Lorazepam (Ativan) has an intermediate half-life of about 8–15 hours, and although it usually is administered in multiple doses each day, it can be given approximately twice per day. Lorazepam, with its shorter half-life and lack of storage in adipose (fatty) tissue, actually has to be given more frequently than the long-acting preparations, not less. It is absorbed easily orally, intramuscularly, and intravenously. Older patients and patients with severe liver disease tolerate it well and it is an effective anticonvulsant in blocking a second alcohol withdrawal seizure (D’Onofrio et al. 1999). However, it has been suggested that seizures may occur late in detoxification with short-acting benzodiazepines such as lorazepam and oxazepam (Shaw 1995).

### *Oxazepam*

Oxazepam (Serax) often is favored by internists and hepatologists treating alcohol withdrawal in patients with severe liver failure. It has a relatively short half-life of 6 to 8 hours. Its metabolism is very simple and it has no metabolites. The agent is relatively limited in that its oral absorption is quite slow compared to other benzodiazepines, it must be given three to four times a day, and is only available in the United States in an oral form.

Ultimately, the experience of the treating clinician, characteristics of the patient, and the setting in which he will be treated will determine the choice of drug. Although all benzodiazepines are now generic in the United States, costs vary and this too may be a factor in choice.

### *Limitations of benzodiazepines in outpatient treatment*

Although benzodiazepines remain the mainstay of treatment for alcohol withdrawal, they have limitations that are particularly pronounced when treating outpatients. Benzodiazepines’ potential interactions with alcohol can lead to coma and respiratory suppression, motor inco-

ordination (leading to falls and automobile accidents), and abuse of the medications. Abuse usually is in the context of the concurrent use of alcohol, opioids, or stimulants.

There are two other limitations of benzodiazepines that may be relevant in some clinical settings for some patients. First, although benzodiazepines have been studied for more than 30 years and are effective for suppressing alcohol withdrawal symptoms at any one episode, their ability to halt the progressive worsening of each successive alcohol withdrawal reaction is in question. There are now at least nine studies that have found that an ever-increasing number of previous alcohol withdrawals increases the severity of withdrawal, particularly seizures and delirium tremens, and decreases responsiveness to benzodiazepines (Ballenger and Post 1978; Booth and Blow 1993; Brown et al. 1988; Gross et al. 1972; Lechtenberg and Worner 1990, 1992; Malcolm et al. 2000; Shaw et al. 1998; Worner 1996). A tenth study (Wojnar et al. 1999) found that increasing severity of alcohol withdrawal symptoms was observed only in a minority (22 percent) of 418 repeatedly treated clients. However, within this group of one in five individuals, seizures were three times more common than in the larger, nonprogressive group and premature age of death was 7 years younger than for the nonprogressive group. In

the majority of these studies, patients were treated with benzodiazepines, although in a few, phenobarbital was used.

A second, and at present more hypothetical, concern about benzodiazepine use to treat outpatients in alcohol withdrawal is that they may “prime” or reinstate alcohol use during their administration. Two preclinical studies support this premise (Deutsch and Walton 1977; Hedlund and Wahlstrom 1998). A recent randomized, blinded, clinical trial comparing carbamazepine to lorazepam for the outpatient treatment of alcohol withdrawal found that the outpatients on lorazepam were three times as likely to drink as those on carbamazepine. The lorazepam group drank about twice as much alcohol in the immediate post-detoxification period than the carbamazepine group (Malcolm et al. 2002).

For a list of potential contraindications to using benzodiazepines to treat alcohol withdrawal in certain patients, see Figure 4-3.

## ***Other medications***

### ***Barbiturates***

Barbiturates have been used for nearly a century for the treatment of alcohol withdrawal. Most barbiturates, other than phenobarbital, have fallen into disfavor because of severe

### ***Figure 4-3 Potential Contraindications To Using Benzodiazepines To Treat Alcohol Withdrawal***

- Previous allergic reaction
- Previous paradoxical disinhibition (e.g., violence, agitation, self-harm)
- Previous serious adverse outcomes that could have medico-legal consequences if they re-occur (e.g., fractured hip, status epilepticus [continuous seizures of several minutes])
- Severe alterations in mental status with low dose of benzodiazepines (e.g., confusion, delirium)
- An outpatient setting where benzodiazepine use with alcohol has occurred previously with extreme intoxication leading to injuries, coma, or apnea

*Source:* Consensus Panelist Robert Malcolm, M.D.

Delirium and seizures are the two most pathological responses seen in alcohol withdrawal.

lethal interactions with alcohol, death from overdose of the agents alone, rapid tolerance, and high abuse potential. Barbiturates are highly addictive. In clinical practice, the medication is effective both for the treatment of alcohol withdrawal and sedative-hypnotic withdrawal although few controlled trials have been conducted with it (Wilbur

and Kulik 1981). Phenobarbital has a long half-life and may rapidly accumulate. Overdoses with phenobarbital also can be fatal. Members of the consensus panel recommend its use only in highly supervised settings.

### *Anticonvulsants*

Anticonvulsants have been used in Europe for a quarter of a century for the treatment of alcohol withdrawal. Carbamazepine (Atretol, Tegretol) has been shown in at least three trials to be as effective as various benzodiazepines in mild to moderate alcohol withdrawal (Malcolm et al. 2001). Although less well studied, valproic acid also has been shown to be effective (Reoux et al. 2001). Older, first-generation anticonvulsants have limitations in that they only have been studied in mild to moderate withdrawal, can on rare occasions have serious hepatic and bone marrow toxicities, interact with several other classes of medication, and are only available in oral forms. They are not, however, controlled substances, are not abused, and as previously noted, carbamazepine may have the propensity to reduce some of the indices of drinking behavior immediately in the post-withdrawal treatment of outpatients. Newer drugs such as tiagabine, oxcarbazepine, and gabapentin do not appear to have these liabilities, but sufficient studies have not been done to confirm their effectiveness and safety.

### *Other agents*

Beta blockers and alpha adrenergic agonists such as clonidine have been used in the treatment of alcohol withdrawal. They do not prevent seizures in delirium and have only modest benefits for ameliorating symptoms of withdrawal. However, some patients will have tachycardia (rapid heartbeat) and hypertension (high blood pressure) that will not be controlled by benzodiazepines, and beta blockers and alpha adrenergic agonists can be of use in these patients. Calcium channel antagonists will also ameliorate some symptoms of alcohol withdrawal. As with beta blockers and clonidine, calcium channel antagonists should be considered adjunctive therapy primarily to manage extreme hypertension during withdrawal.

### *Antipsychotics*

Antipsychotics have long been used to control extreme agitation, hallucinations, delusions, and delirium during alcohol withdrawal. Older, low-potency drugs such as chlorpromazine generally are avoided since they can reduce the seizure threshold. High-potency drugs such as haloperidol (Haldol) also can reduce the seizure threshold, but less commonly. Haloperidol and related agents are available for oral, intramuscular, and IV administration. Clinicians should note that since antipsychotics can lower the seizure threshold, their use during alcohol withdrawal should be undertaken with great care and close supervision of the patient is required.

### *Relapse prevention agents*

Relapse prevention agents such as naltrexone and acamprosate are under consideration as additional therapies during late withdrawal treatment, although they are not effective for alcohol detoxification. Since one-third to one-half of outpatients detoxifying with benzodiazepines will either drink or leave treatment prematurely, naltrexone and acamprosate may be valuable in assisting in reducing the probability of the individual drinking during late detoxification. High-dose naltrexone therapy has been associated with some liver toxicity, but this has not been reported in individuals taking therapeutic doses to enhance relapse

prevention. Acamprosate may produce diarrhea and this may be already present in some individuals in alcohol withdrawal. Thus far no well-controlled studies have been conducted to provide guidelines as to when these medications should be introduced during detoxification or whether it would be better to wait until the early phase of rehabilitation. For an extended review, see Kranzler and Jaffe (2003).

### *Other medications*

Abecarnil (Anton et al. 1997), and more recently baclofen (Addolorato et al. 2002), have both shown promise in the treatment of alcohol withdrawal. However, insufficient information has been accumulated on these drugs, and therefore they are not recommended for use in clinical patient settings. Their use in alcohol withdrawal should be considered experimental and premature for the present.

## **Management of Delirium and Seizures**

Delirium and seizures are the two most pathologic responses seen in alcohol withdrawal. The major goal of medical management is to avoid seizures and a special state of delirium called delirium tremens (DTs) with aggressive use of the primary detoxification drug (e.g., higher doses of a benzodiazepine). Prevention is essential where DTs are concerned. DTs do not develop suddenly but instead progress from earlier withdrawal symptoms. Properly administered symptom-triggered medication approaches will prevent DTs and limit overmedication that can occur when high-dose benzodiazepines are administered without regard to clinical response. It can be challenging clinically to differentiate impending DTs versus benzodiazepine toxicity on day 3 of detoxification. When in doubt, in most cases it is safer to overmedicate than to undertreat and allow DTs to develop. Flumazenil (Romazicon) can be used to reverse benzodiazepine overdose.

Death and disability may result from DTs or seizures without medical care. Several factors are related to severity of alcohol withdrawal: high amounts of alcohol being consumed in the

weeks prior to treatment, the severity of the last withdrawal episodes, and the number of previously treated or untreated withdrawal episodes. Other factors such as increasing age; the patient's general health, including nutritional status; the presence of co-occurring medical, surgical, and psychiatric disorders; and the use of medications (prescription, over-the-counter, or herbal) also can amplify severity of withdrawal symptoms. Early proper medical management of alcohol withdrawal reduces the probability of these complications, assuming early recognition.

For patients with a history of DTs or seizures, early benzodiazepine treatment is indicated at the first clinical contact setting (e.g., doctor's office, clinic, urgent care, emergency department). Patients with severe withdrawal symptoms, multiple past detoxifications (more than three), and co-occurring unstable medical and psychiatric conditions should be managed similarly.

Once an initial clinical screening and assessment have been made, and the diagnosis is reasonably certain, medication should be given. Giving the patient a benzodiazepine should not be delayed by waiting for the return of laboratory studies, transportation problems, or the availability of a hospital bed. Early thiamine and multivitamin administration also should be done at this time. Once full DTs have developed, they tend to run their course despite medication management, and there is little evidence in the medical literature to suggest that any medication treatment can immediately abort DTs.

Patients presenting in severe DTs should have emergency medical transport to a qualified emergency department and generally will require hospitalization. If the DTs are severe, patients may need to be placed in an intensive care unit (ICU), and in such settings continuous monitoring of cardiac rhythm, pulse, blood pressure, oxygen saturation, temperature, and respiration rates begins with the emergency medical system and continues in the emergency department and ICU.

Early care will depend on medical and surgical complications and may involve protocols from advanced cardiac life support (ACLS) and/or advanced trauma life support. Correction of fluids and electrolytes (salts in the blood), hyperthermia (high fever), and hypertension are vital. Loading doses (rapid administration of initial high doses) of IV diazepam or lorazepam are recommended, as are IV thiamine (prior to IV glucose) and multiple vitamins. The physician should consider intramuscular or intravenous haloperidol (Haldol and others) to treat agitation and hallucinations. Nursing care is vital, with particular attention to medication administration, patient comfort, soft restraints, and frequent contact with orienting responses and clarification of environmental misperceptions.

Alcohol withdrawal seizures represent another management challenge (Ahmed et al. 2000), since no large-scale clinical studies have been conducted to establish firmly best treatment practices. The majority of alcohol withdrawal seizures occur within the first 48 hours after cessation or reduction of alcohol, with peak incidence around 24 hours (Victor and Adams 1953). Most alcohol withdrawal seizures are singular, but if more than one occurs they tend to be within several hours of each other. While alcohol withdrawal seizures can occur several days out, a higher index of suspicion for other causes is prudent. Someone experiencing an alcohol withdrawal seizure is at greater risk for progressing to DTs, whereas it is extremely unlikely that a patient already in DTs will also then experience a seizure.

The occurrence of an alcohol withdrawal seizure happens quickly, usually without warning to the individual experiencing the seizure or anyone around him. The patient loses consciousness, and if seated usually slumps over, but if standing will immediately fall to the floor. The patient's body is rigid, and breathing ceases. This part of the seizure is called the tonic phase, which usually lasts for a few seconds and rarely more than a minute.

The next part of the seizure (more dramatic and generally remembered by witnesses) con-

sists of jerking of head, neck, arms, and legs. Breathing resumes during this clonic phase of the seizure but may be irregular. During the clonic phase, the lips, tongue, or inside of the cheeks may be bitten. Involuntary urination or a bowel movement may occur. Immediately after the jerking ceases, the patient generally has a period of what appears to be sleep with more regular breathing. Vomiting may occur at this time. The period of sleep may be a few seconds with awakening or a few minutes. Rarely, the patient may appear not to waken at all and have a second period of rigidity followed by muscle jerking. This is known as status epilepticus. Upon awakening, the individual usually is mildly confused as to what has happened and may be disoriented as to where she or he is. This period of post-seizure confusion generally lasts only for a few minutes but may persist for several hours in some patients. Headache, sleepiness, nausea, and sore muscles may persist in some individuals for a few hours. See the text box on the next page for what to do in the event of a seizure.

Patients who start to retch or vomit should be gently placed on their side so that the vomitus (stomach contents vomited) may exit the mouth and not be taken into the lungs. Vomitus taken into the lungs is a severe medical condition leading to immediate difficulty breathing and, within hours, severe pneumonia.

Predicting who will have a seizure during alcohol withdrawal cannot be accomplished with any great certainty. There are some factors that clearly increase the risk of a seizure, but even in individuals with all of these factors, most patients will not have a seizure. Out of 100 people experiencing alcohol withdrawal only two or three of them will have a seizure. The best single predictor of a future alcohol withdrawal seizure is a previous alcohol withdrawal seizure. Individuals who have had three or more documented withdrawal episodes in the past are much more likely to have a seizure regardless of other factors including age, gender, or overall medical health. However, certain other factors may increase the risk of seizures for all patients:

## What To Do in the Event of a Seizure

- At the first sign of what appears to be a seizure, lay witnesses should summon trained medical personnel.
- Depending on the setting, this may mean calling 911 or calling the nurse or physician who is on duty for the clinic or hospital unit.
- While awaiting medical help, a layperson witnessing an alcohol withdrawal seizure should gently attempt to prevent injury to the person as he or she slumps or falls to the floor by protecting the individual's head and body from hard or sharp objects. Often, though, the initial loss of consciousness and fall is not seen by anyone.
- In the jerking phase of the seizure, if the jerking is extreme, it is important to protect the head from extreme head-banging by placing a soft object under the head and neck. Sometimes placing one's hand or shoe under the head is adequate.
- No attempt should be made to insert anything in the mouth (such as spoons, pencils, pens, tongue blades). Such attempts at object insertion may cause damage to the teeth and tongue, or objects may get partially swallowed and obstruct the airway.
- Patients who start to retch or vomit should be gently placed on their side so that the vomitus (stomach contents vomited) may exit the mouth and not be taken into the lungs. Vomitus taken into the lungs is a severe medical condition leading to immediate difficulty breathing and, within hours, severe pneumonia.
- Even if the individual appears to become fully awake, alert, and oriented without any harm following a seizure, it is strongly recommended that he be referred for medical evaluation.
- Individuals who awaken confused and disoriented should be given brief reassuring and soothing messages to reorient them as to what happened and where they are.

- Having drunk for more than two decades
- Having poor general medical health and poor nutritional status
- Having had previous head injuries
- Having had disturbances of serum calcium, sodium, potassium, or magnesium

Patients having a witnessed seizure can be treated with IV diazepam or lorazepam and ACLS protocol procedures. This reduces but does not completely prevent the likelihood of a second seizure (D'Onofrio et al. 1999). In the rare patient with recurrent multiple seizures or status epilepticus (continuous seizures of several minutes) an anesthesiology consultation may be required for general anesthesia. Evaluation of electrolyte disturbances, central nervous system (CNS) trauma, and consideration of sedative-hypnotic withdrawal should be reviewed.

Patients who have had a single witnessed or suspected alcohol withdrawal seizure should be immediately given a benzodiazepine,

preferably with IV administration. The study by D'Onofrio and colleagues (1999) indicated that a single dose of 1mg of IV lorazepam reduced recurrent seizure risk, reduced rates of return to emergency departments, and lowered hospitalization rates. Despite this report, the consensus panel agrees that hospitalization for further detoxification treatment is strongly advised to monitor and ameliorate other withdrawal symptoms, reduce suffering, and stabilize the patient for rehabilitation treatment.

The addition of anti-epileptic drugs (AEDs) has not been established as effective (Chance 1991; Hillbom and Hjelm-Jager 1984; Rathlev et al. 1994). This is primarily based on evaluations of phenytoin (Dilantin and others). Newer AEDs have not been studied extensively for preventing alcohol withdrawal seizures. The consensus panel suggests that AED therapy should be considered in alcohol withdrawal patients with multiple past seizures (of any cause), a history of recent head injury, past

meningitis, encephalitis, or family history of seizures. Further evaluation of a first seizure often warrants neurologic evaluation (computerized tomography and electroencephalogram), even if the seizure may be suspected to have been due to alcohol withdrawal.

## Patient Care and Comfort

Interpersonal support and hygienic care along with adequate nutrition should be provided. Staff assisting patients in detoxification should provide whatever assistance is necessary to help get patients cleaned up after entering the facility and bathed thoroughly as soon as they have been medically stabilized. Attention to the treatment of scabies, body lice, and other skin conditions should be given. Screening for tuberculosis should be done. Dental and oral care should be made available. The patient should be screened for physical trauma, including bruises and lacerations. Tetanus immunization may be necessary. Patients with an altered mental status or altered level of consciousness should be seen in emergency departments, evaluated, and possibly hospitalized. Staff should continue to observe patients for head injuries after admission because some head injuries, such as subdural hematomas, may not immediately be evident and cost considerations may preclude obtaining a brain scan in some settings.

## Other Immediate Concerns

Alcohol may interact with several classes of medicine to produce serious CNS depression. Some examples include benzodiazepines, barbiturates, meprobamate, and other sedative hypnotic groups. Metoclopramide and sedating antipsychotic medicines such as phenothiazines also can produce CNS suppression. A disulfiram-like (Antabuse) reaction characterized by flushing, sweating, tachycardia, nausea, and chest pain has been reported for metronidazole and several antibiotics including, but not limited to, cefamandole, cefoperazone, and cefotetan. Acetaminophen in low doses may act acutely with alcohol to produce hepatotoxicity (liver damage). Clinicians also should deter-

mine whether the patient is using aspirin or nonsteroidal anti-inflammatory medications (for example, Motrin or Advil, both containing ibuprofen) in conjunction with alcohol use. Antidiabetic agents in concert with alcohol may produce hypoglycemia (low blood sugar) and lactic acidosis (blood that has become too acidic). The therapeutic efficacy and margin of safety for the use of anti-anxiety medications, antidepressants, and antipsychotic medication is thought by some to be lessened by alcohol use, but this is based largely on anecdotal information. Alcohol interacts with numerous other classes of medications that lead to less serious results. Some important examples are sedatives, tranquilizers, antiseizure medications, and anticoagulants (blood thinners) such as Coumadin. Patients who may be taking such medications need to be carefully observed and have their medications carefully monitored.

## Opioids

Opioids are highly addictive, and their chronic use leads to withdrawal symptoms that, although not medically dangerous, can be highly unpleasant and produce intense discomfort. All opioids (e.g., heroin, morphine, hydromorphone, oxycodone, codeine, and methadone) produce similar effects by interacting with endogenous (produced by the body itself) opioid ( $\mu$ ,  $\delta$ , and  $\kappa$ ) receptors (that is, specific sites on cells where these substances bind to the cell). Opioid agonists stimulate these receptors and opioid antagonists block them, preventing their action.

## Opioid Withdrawal Symptoms

All opioid agents produce similar withdrawal signs and symptoms with some variance in severity, time of onset, and duration of symptomatology, depending on the agent used, the duration of use, the daily dose, and the interval between doses. For instance, heroin withdrawal typically begins 8 to 12 hours after the last heroin dose and subsides within a period of 3 to 5 days. Methadone withdrawal typically begins 36 to 48 hours after the last dose, peaks

after about 3 days, and gradually subsides over a period of 3 weeks or longer. Physiological, genetic, and psychological factors can significantly affect intoxication and withdrawal severity. Figure 4-4 summarizes many of the common signs and symptoms of opioid intoxication and withdrawal.

The clinician uses intoxication and withdrawal measures as guides to avoid under- or over-medicating patients during medically supervised detoxification; the number and intensity of signs determine the severity of opioid withdrawal. It is important to appreciate that untreated opioid withdrawal gradually builds in severity of signs and symptoms and then diminishes in a self-limited manner. *Repeated assessments* should be made during detoxification to determine whether symptoms are improving or worsening. Repeated assessments also should address the effectiveness of pharmacological interventions. Detoxification strategies should aim to establish control over

the opioid withdrawal syndrome, after which dose reductions can be made gradually.

Medical complications associated with opioid withdrawal can develop and should be quickly identified and treated. Unlike alcohol and sedative withdrawal, uncomplicated opioid withdrawal is not life-threatening. Rarely, severe gastrointestinal symptoms produced by opioid withdrawal, such as vomiting or diarrhea, can lead to dehydration or electrolyte imbalance. Most individuals can be treated with oral fluids, especially fluids containing electrolytes, and some might require intravenous therapies. In addition, underlying cardiac illness could be made worse in the presence of the autonomic arousal (increased blood pressure, increased pulse, sweating) that is characteristic of opioid withdrawal. Fever may be present during opioid withdrawal and typically will respond to detoxification. Other causes of fever should be evaluated, particularly with intravenous users,

**Figure 4-4**  
**Signs and Symptoms of Opioid Intoxication and Withdrawal**

Opioid Intoxication	Opioid Withdrawal
<p><b>Signs</b>                      Bradycardia (slow pulse)                      Hypotension (low blood pressure)                      Hypothermia (low body temperature)                      Sedation                      Meiosis (pinpoint pupils)                      Hypokinesia (slowed movement)                      Slurred speech                      Head nodding</p> <p><b>Symptoms</b>                      Euphoria                      Analgesia (pain-killing effects)                      Calmness</p>	<p><b>Signs</b>                      Tachycardia (fast pulse)                      Hypertension (high blood pressure)                      Hyperthermia (high body temperature)                      Insomnia                      Mydriasis (enlarged pupils)                      Hyperreflexia (abnormally heightened reflexes)                      Diaphoresis (sweating)                      Piloerection (gooseflesh)                      Increased respiratory rate                      Lacrimation (tearing), yawning                      Rhinorrhea (runny nose)                      Muscle spasms</p> <p><b>Symptoms</b>                      Abdominal cramps, nausea, vomiting, diarrhea                      Bone and muscle pain                      Anxiety</p>
<p><i>Source:</i> Consensus Panelist Charles Dackis, M.D.</p>	

Methadone is the most frequently used agent approved for detoxification by the FDA, and a new medication, buprenorphine, has been approved for use.

because HIV infection, viral hepatitis, abscesses, infected injection sites, and pneumonia occur commonly in this population and always require medical attention. Anxiety disorders, especially those involving panic anxiety, also might show increased intensity during opioid withdrawal. Finally, any condition involving pain is likely to worsen during opioid withdrawal because of a reduced pain threshold and the lack of analgesia (pain relief) afforded by opioid use.

This phenomenon is particularly common with dental pain and chronic back pain.

## Management of Withdrawal Without Medications

It is not recommended that clinicians attempt to manage significant opioid withdrawal symptoms (causing discomfort and lasting several hours) without the effective detoxification agents discussed below. Even mild levels of opioid use commonly produce uncomfortable levels of withdrawal symptomatology.

Management of this syndrome without medications can produce needless suffering in a population that tends to have limited tolerance for physical pain.

## Management of Withdrawal With Medications

The management of opioid withdrawal with medications is most commonly achieved through the use of methadone (in addition to adjunctive medications for nausea, vomiting, diarrhea, and stomach cramps). Federal regulations restrict the use of methadone for opioid withdrawal to specially licensed programs, except in cases where the patient is hospitalized for treatment of another acute medical condition. Methadone is the most frequently used agent approved for detoxification by the Food and Drug Administration (FDA), and a new medication, buprenorphine (discussed below), has been approved for use. Methadone can be used for detoxification from heroin and all opioid agonists.

Another commonly used agent is clonidine (Gold et al. 1984), an  $\alpha$ -adrenergic agonist that relieves most opioid withdrawal symptoms without producing opioid intoxication or drug reward. However, since clonidine detoxification is less effective against many opioid withdrawal symptoms, adjunctive medicines often are necessary to treat insomnia, muscle pain, bone pain, and headache. Adjunctive agents should not be used in the place of an adequate detoxification dosage. Additional opioid agonists could be used theoretically for detoxification but would have to be administered “off label,” because the FDA has approved only methadone for this purpose. Off-label use (prescribing an agent approved for another condition) could be difficult to justify, given the efficacy of methadone in reversing opioid withdrawal.

Detoxification is indicated for treatment-seeking persons who display signs and symptoms sufficient to warrant treatment with medications and for whom maintenance is declined or for some reason is not indicated or practical. In addition, individuals dependent on opioids sometimes are hospitalized for other health problems and may require hospital-based detoxification even though they are not

seeking substance abuse treatment. Such patients also can be maintained on methadone during the course of hospitalization for any condition other than opioid addiction. The hospital does not have to be a registered opioid treatment program, as long as the patient was admitted for a detoxification treatment for some substance other than opioids. On the other hand, some persons may not have used sufficient amounts of opioids to develop withdrawal symptoms, and for others sufficient time may have elapsed since their last dose to extinguish withdrawal and eliminate the need for detoxification.

## **Methadone**

This section discusses methadone as an agent for detoxification. For detailed information on methadone maintenance, readers are referred to TIP 43 *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs* (CSAT 2005d). While methadone is one of the more common medications for opioid detoxification, its use is highly regulated and it can only be prescribed for withdrawal by a doctor at a Substance Abuse and Mental Health Services Administration (SAMHSA)-certified methadone clinic or if the patient is being hospitalized for another medical condition. (Detoxification programs may become certified to prescribe methadone by undergoing the process described in TIP 43.) Federal regulations allow for the use of methadone in both a short-term detoxification treatment of less than 30 days and a long-term treatment of 30 to 180 days. The regulations also specify that if a patient has failed two detoxification attempts in a 12-month period he or she must be evaluated for a different course of treatment (e.g., ongoing opioid substitution therapy).

Methadone is a long-acting agonist at the  $\mu$ -opioid receptor site that, in effect, displaces heroin (or other abused opioids) and restabilizes the site, thereby reversing opioid withdrawal symptoms. If maintained for long enough, this stabilizing effect can even reverse the immunologic

and endocrinologic defects caused by long-term heroin addiction. This is one of many important reasons to consider conversion to maintenance during most methadone detoxification admissions.

Once the dose requirement for methadone has been established, methadone can be given once daily and generally tapered over 3 to 5 days in 5 to 10mg daily reductions. The initial dose requirement is determined by estimating the amount of opioid use and gauging the patient's response to administered methadone. Clinicians should take care not to underdose patients with methadone; adequate dosage is vitally important. Patients sometimes exaggerate their daily consumption to receive greater dosages of methadone. For this reason, history is no substitute for a physical examination that screens for signs of opioid withdrawal. Treating clinicians should not only be familiar with the intoxication and withdrawal signs that are set forth in Figure 4-4 (p. 67), but also should be skilled in discerning these features of opioid withdrawal. Avoidance of overmedicating is crucial during methadone detoxification because excessive doses of this agent can produce overdose, whereas opioid withdrawal does not constitute a medical danger in otherwise healthy adults. For more information on methadone and other medications used to treat opioid addiction, see TIP 43, *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs* (CSAT 2005d).

Patients with significant opioid dependence may require a starting dose of 30 to 40mg per day; this dose range should be adequate for even the most severe withdrawal. If the degree of dependence is unclear, withdrawal signs and symptoms can be reassessed 1 to 2 hours after giving a dose of 10mg of methadone. The practice of giving a dose of methadone and later assessing its effect (also termed a challenge dose) is an important intervention of detoxification. Sedation or intoxication signs after a methadone challenge dose indicate a lower starting dose. Similarly, intoxication at any point of the detoxification

signals the need to hold or more rapidly wean (reduce to a zero dose) the methadone. Care should be taken to avoid giving methadone to newly admitted patients with signs of opioid intoxication, since overdose could result. Note that methadone stabilization is the treatment of choice for patients who are pregnant and opioid dependent.

### **Clonidine (Catapres)**

Clonidine was originally marketed and approved for the treatment of high blood pressure but also has been used for opioid detoxification since 1978. While clonidine is not FDA approved for treatment of opioid withdrawal, it is widely used “off label” for this purpose (Alling 1992) because the research literature substantiates its effectiveness for this condition. Advantages of clonidine over methadone in the treatment of opioid withdrawal are as follows:

- Clonidine does not produce opioid intoxication and is not reinforcing.
- The FDA does not classify clonidine as having abuse potential. Yet some abuse has been reported. (See p. 107 under the section on pregnant women and opioids.)
- Since clonidine does not interact with the  $\mu$ -opioid receptor, detoxification occurs without opioids.
- No special licensing is required for the dispensing of this medication.

One disadvantage to methadone detoxification with naltrexone (an opioid antagonist), compared with clonidine, is that naltrexone, when it is prescribed for abstinence, can precipitate opioid withdrawal if given too soon after the last methadone dose. This problem does not exist with clonidine, making this agent particularly beneficial in a drug-free treatment program or a therapeutic community.

Nevertheless, patients addicted to opioids generally prefer methadone over clonidine detoxification. Although clonidine alleviates some symptoms of opioid withdrawal, it usually is relatively ineffective for insomnia,

muscle aches, and drug craving. Completion rates for opioid detoxification using clonidine have been low (ranging from 20 to 40 percent); those patients who complete the procedure are more likely to be dependent on opioids other than heroin, have private health insurance, and report lower levels of subjective withdrawal symptoms than those who do not complete (Strobbe et al. 2003).

An appropriate protocol for clonidine is 0.1mg administered orally as a test dose. A dose of 0.2mg might be used initially for patients with severe signs of opioid withdrawal or for those patients weighing more than 200 pounds. The sublingual (under the tongue) route of administration also may be used. Clinicians should check the patient’s blood pressure prior to clonidine administration and clonidine should be withheld if systolic blood pressure is lower than 90 or diastolic blood pressure is below 60. These parameters can be relaxed to 80/50 in some cases if the patient continues to complain of withdrawal and is not experiencing symptoms of orthostatic hypotension (a sudden drop in blood pressure caused by standing). Clonidine (0.1 to 0.2mg orally) can then be given every 4 to 6 hours on an as-needed basis. Clonidine detoxification is best conducted in an inpatient setting, as vital signs and side effects can be monitored more closely in this environment. In cases of severe withdrawal, a standing dose (given at regular intervals rather than purely “as needed”) of clonidine might be advantageous (Alling 1992). The daily clonidine requirement is established by tabulating the total amount administered in the first 24 hours, and dividing this into a three or four times per day dosing schedule. Total clonidine should not exceed 1.2mg the first 24 hours and 2.0mg after that, with doses being held in accordance with parameters noted above. The standing dose is then weaned over several days. Clonidine must be tapered to avoid rebound hypertension.

The clonidine transdermal (administered through the skin) patch, FDA approved in

1986 for the treatment of hypertension (high blood pressure), also is used in opioid detoxification. However, the safety of the patch for treatment of opioid withdrawal has not been sufficiently studied in controlled clinical trials. The transdermal route of administration has the disadvantage of continued clonidine action even after the patch has been removed. Blood pressure effects of clonidine can therefore be prolonged, leading to undesirable and persistent reductions of blood pressure. For this reason, it has been recommended that the patch be used only if the patient's blood pressure is monitored regularly (Alling 1992).

The clonidine patch is available in three sizes that deliver a total daily oral equivalent clonidine dose of 0.2mg (3.5 cm<sup>2</sup>), 0.4mg (7.0 cm<sup>2</sup>), or 0.6mg (10.5 cm<sup>2</sup>). The patch supplies clonidine for up to 7 days and one patch application usually is sufficient. The convenience of one application allows the clinician to avoid the disruption that multiple dosing might have during rehabilitative programming. In particular, patients can focus on rehabilitative treatment without being distracted by the need to ask repeatedly for oral clonidine doses. Vital signs should be monitored at least four times daily to assess persistent signs and symptoms of withdrawal or undesirable effects of clonidine on blood pressure.

## **Buprenorphine**

Buprenorphine, a partial  $\alpha$ -opioid agonist that is FDA approved in an injectable form (Buprenex) for the treatment of pain, has recently been approved as a detoxification agent and for opioid maintenance treatment as an alternative to methadone maintenance. A number of clinical trials have reported it to be effective for heroin detoxification (Becker et al. 2001; Bickel et al. 1988; Diamant et al. 1998), and the medication should play an important role in gradually removing patients from methadone maintenance (Amass et al. 2004; Banys et al. 1994; Johnson et al. 2000).

Buprenorphine is available in oral form as Subutex, which contains only buprenorphine, and is meant for patients who are starting treatment for drug dependence. Another form, Suboxone, contains buprenorphine and naloxone and is intended for persons dependent on opioids who have already started and are continuing medication therapy.

Buprenorphine has great affinity for the  $\mu$ -opioid receptor, in spite of being only a partial agonist, and can displace other opioids such as heroin. This feature gives buprenorphine the ability to precipitate opioid withdrawal when administered to patients who have recently used heroin (Kosten and McCance-Katz 1995).

An advantage to buprenorphine is its safety. Because of the partial agonist action, buprenorphine has a "ceiling effect" with regard to overdose potential (Walsh et al. 1994).

That is, unlike methadone, which produces increasing respiratory suppression with increasing dose, respiratory effects of buprenorphine tend to level off due to its partial agonist action. Another advantage of buprenorphine is that it can be dispensed at a physician's office, unlike methadone, which can be dispensed only at designated treatment centers. This makes access to this medication for opioid dependence much more convenient for both patient and clinician. See TIP 40, *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction* (CSAT 2004a).

One advantage of buprenorphine is that it can be dispensed at a physician's office, unlike methadone, which can be dispensed only at designated treatment centers.

Unlike methadone, buprenorphine may be prescribed by physicians who are not connected with a certified opioid treatment program. However, there is still a specific

training and certification process physicians must undergo in order to prescribe the medication. Information on the legal aspects of prescribing buprenorphine and rules for carrying out detoxification in the physician's office can be found at [www.buprenorphine.samhsa.gov/](http://www.buprenorphine.samhsa.gov/). Information given at the site includes the following on the Drug Addiction Treatment Act (DATA) of 2000: "[DATA 2000] expands the clinical context of medication-assisted opioid

addiction treatment by allowing qualified physicians to dispense or prescribe specifically approved Schedule III, IV, and V narcotic medications for the treatment of opioid addiction in treatment settings other than the traditional Opioid Treatment Program (i.e., methadone clinic). In addition, DATA 2000 reduces the regulatory burden on physicians who choose to practice opioid addiction therapy by permitting qualified physicians to apply for and receive waivers of the special registration requirements defined in the Controlled Substances Act" (SAMHSA 2002).

## Terminating Methadone Maintenance Treatment

Individuals seeking the discontinuation of methadone maintenance require a much more lengthy detoxification process than that

described above for heroin. The methadone dose should be tapered gradually by 5 to 10mg/week until a daily dose of 30 to 40mg has been attained. At that time, detoxification with either clonidine or smaller doses of methadone can be instituted. The use of clonidine has the advantage of brevity as a complete clonidine detoxification usually can be conducted within 2 to 3 weeks (Gold et al. 1984).

Once the daily dose requirement has been established by using the principles outlined above, the patient can be placed on a standing dose of clonidine. The dose required usually is in the range of 0.2mg, three to four times daily, although titration (adjustment of dosage in light of drug response) is necessary based on the information gathered during the clinical examination. Additional doses as needed (sometimes abbreviated "PRN") of 0.2mg clonidine also can be given and blood pressure parameters must be followed prior to the administration of standing and PRN doses to avoid orthostatic hypotension. The initial standing dose can be reduced to 0.1mg, given three to four times daily, after one week of detoxification, with PRN doses of 0.1mg available. After a period of 1 week on this reduced dosage, clonidine is given for an additional week only if needed. Because clonidine does not reverse all opioid withdrawal symptoms, especially insomnia, adjunctive medications for symptom relief of insomnia, nausea, diarrhea, etc. usually are required. Clonidine detoxification is best conducted on an inpatient basis to ensure appropriate vital sign monitoring. Inpatient treatment also reduces the impulse to relapse, especially if the detoxification is difficult.

Methadone detoxification can be continued once a daily dose of 30 to 40mg is achieved, as described above. The dose can be reduced to 20mg per day by a reduction of 5 to 10mg/week. Once the patient is on 20mg/day, methadone can be reduced by 1 to 2mg daily, depending on clinical measures of withdrawal. As with clonidine detoxification, the final 2 to 3 weeks of methadone detoxification is associated with recidivism (relapsing).

Inpatient treatment can provide additional support, medical supervision, and rehabilitative treatment that serve as disincentives to relapse.

Inpatient treatment, if available, can provide additional support, medical supervision, and rehabilitative treatment that serve as disincentives to relapse.

## **Rapid and Ultrarapid Detoxification**

Although there are few data showing that the rapid or ultrarapid methods of opioid detoxification show a positive correlation with the likelihood of a patient's being abstinent a few months later, efforts persist to make the detoxification process shorter and easier. This stems in part from the desire of the person addicted to opioids for a rapid, painless procedure, and in part from an attempt to coax more such persons into treatment (fewer than one in five people with substance use disorders in the United States are in treatment at any time) (Office of National Drug Control Policy 2002). Another contributing factor is the American culture's search for rapidity in most endeavors. Finally, the desire for rapid opioid detoxification is a remnant of the belief system of a century ago, when detoxification often was erroneously equated with cure.

Rapid methods of detoxification have at their core the use of narcotic antagonists; for example, naloxone, naltrexone, or nalmefene, to precipitate narcotic withdrawal by displacing exogenous opioids (those not produced by the body itself) from the receptor sites. The ensuing severe symptoms then are managed by a variety of medications and techniques. This procedure was tried in the mid-1970s (Blachly et al. 1975; Resnick et al. 1977), using naloxone combined with benzodiazepines or propranolol to ameliorate symptoms, but relief was insufficient for the technique to be considered useful.

With the discovery of clonidine as a nonopioid that could successfully treat much of the withdrawal syndrome (Gold et al. 1978), the method became more successful, but was still problematic. Using combinations of clonidine, naltrexone, benzodiazepines, and other adjunct medications, the method was refined

and shortened during the 1980s (Charney et al. 1982, 1986; Kleber et al. 1987; Riordan and Kleber 1980; Vining et al. 1988) so that a blocking dose of naltrexone—at least 25mg—usually was used by the second or third day of treatment. The rate-limiting factor of this rapid clonidine-naltrexone method is its capacity to adequately relieve the precipitated withdrawal symptoms in the conscious patient. Golden and Sakhрани (2004) found that 25 percent of the 20 patients they studied who were undergoing rapid detoxification using clonidine and naltrexone developed delirium and had to discontinue the procedure after the first day, and another patient dropped out before completion.

The 1990s witnessed a variety of attempts to overcome this barrier by using general anesthesia or heavy sedation. Although the ultrarapid procedure under anesthesia has received wide publicity, controlled studies that would make it possible to evaluate the risk/benefit ratio are absent. The procedure is still unproven and controversial. For a brief review of studies done in this area, see Stine and colleagues (2003).

## **Patient Care and Comfort**

Opioid detoxification, when properly conducted, usually can be concluded without significant patient discomfort. Aside from the compassionate goal of preventing unnecessary suffering, appropriate opioid detoxification strengthens the therapeutic alliance between the patient and clinician and prevents patients from leaving treatment prematurely.

Discomfort also can indicate that too low a dose of the detoxification agent is being administered. Mere symptomatic treatment is not a substitute for reversing opioid withdrawal and care should be taken to avoid masking symptoms that would better respond to detoxification.

Nevertheless, patients receiving adequate detoxification doses still may complain of symptoms that can be treated with adjunctive

medications. Insomnia can be treated with diphenhydramine (Benadryl) 50 to 100mg, trazodone (Desyrel) 75 to 200mg, or hydroxyzine (Vistaril) 25 to 50mg at bedtime. Benzodiazepines should be avoided unless required for concomitant alcohol or sedative detoxification. Headache, muscle aches, and bone pain can be managed with acetaminophen (e.g., Tylenol), aspirin, or ibuprofen (e.g., Motrin) as needed. Abdominal cramps are rare when the detoxification dose is sufficient but can be ameliorated with dicyclomine (e.g., Bentyl) 10 to 20mg every 6 hours. Mylanta or Maalox can be administered for epigastric complaints and bismuth subcarbonate (e.g., Pepto-Bismol) 30 cc can be given every 2 to 3 hours for diarrhea. Constipation, a frequent complaint during methadone maintenance, usually can be managed with milk of magnesia at 30 cc daily.

Opioid dependence, particularly intravenous heroin dependence, is associated with a number of medical conditions. For this reason, a complete physical examination, review of systems, and laboratory evaluation (when indicated) should be conducted. The patient should be screened for tuberculosis as well as for commonly encountered medical complications. These include HIV/AIDS, viral hepatitis (especially B and C), other sexually transmitted diseases, and opportunistic infections. Injection sites should be examined for infection or abscess and patients should be queried about night sweats, chills, nutritional intake, diarrhea and gastrointestinal distress, fever, and cough. History or evidence of trauma also should be elicited as part of a comprehensive assessment upon which a full treatment plan will be based. In general, patients should be ambulatory and able to participate in rehabilitative activities during detoxification. However, during the first 24 hours they may require bed rest or reduced activity.

## **Benzodiazepines and Other Sedative-Hypnotics**

### **Intoxication and Withdrawal Symptoms Associated With Benzodiazepines and Other Sedative-Hypnotics**

Patients intoxicated with sedative-hypnotics appear similar to individuals intoxicated with alcohol. Slurred speech, ataxia, and poor physical coordination are prominent. If benzodiazepines are used alone, breath and blood alcohol levels should be zero. It should be remembered that benzodiazepines, when ingested alone, intentionally, or accidentally in overdose, rarely lead to death by themselves. Unfortunately, most individuals who ingest benzodiazepines also may be using alcohol, other sedative-hypnotics, or other drugs of abuse, which in combination with benzodiazepines could be fatal if not managed appropriately.

Management of benzodiazepines and other sedative-hypnotics in overdose is in part supported following principles of ACLS with particular attention to ventilation. Additionally, removal of the benzodiazepine from the gastrointestinal tract using lavage and a cathartic is generally carried out, particularly if the overdose is recent. Flumazenil (Romazicon) is a competitive antagonist that acts at the benzodiazepine receptor. It can reverse the sedative and overdose effects of benzodiazepines but not of alcohol or other sedative-hypnotics. The medication is administered via IV by slow push (2 to 3 minutes) and dosage varies, depending on whether one is treating sedation reversal or overdose coma-reversal. Flumazenil is only effective in benzodiazepine overdose and is not an effective antidote against other drugs. Clinicians should be aware that in chronic benzodiazepine users who are physically dependent, flumazenil may induce seizures, high blood pressure,

and delirium. So patients who are comatose from benzodiazepines and are benzodiazepine dependent may move quickly from coma to acute benzodiazepine withdrawal symptoms when flumazenil is administered.

Assessing the potential or actual severity of a benzodiazepine and other sedative-hypnotic abstinence syndrome is based primarily on clinical information obtained from the patient, significant others, and physical assessment. Confirmation of length of benzodiazepine treatment with significant others, local pharmacies, and treating physicians is useful. Specific name of medication, dose, and duration of therapy are vital. The presence or absence of alcohol use is also important to know, as with the use of other sedative-hypnotics, such as medications for sleep. The existence of co-occurring psychiatric disorders such as panic disorder also are important factors and should be investigated. Cigarette smoking tends to induce the metabolism of some benzodiazepines and this can be a factor in scheduling a taper. Physical assessment, with particular attention to mental status, and neurologic exams are important. Determination of vital signs also provides guidance. A urine drug screen may confirm the presence of benzodiazepines but otherwise will not be particularly helpful. Although sedative-hypnotic withdrawal scales have been used in research studies, they are not widely available for clinical practice.

Medical complications of withdrawal from benzodiazepines include problems similar to those seen in alcohol withdrawal. Seizures are particularly worrisome and may occur without being preceded by other evidence of withdrawal. As in alcohol withdrawal, seizures and delirium represent the most extreme pathology seen. Anecdotal reports appearing in the literature also have described distortions in taste, smell, and other perceptions. Since many individuals who take benzodiazepines have underlying anxiety disorders, it often is difficult during periods of withdrawal to determine whether symptomatology is related to withdrawal or the emergence of panic attack symptoms. Elderly patients who are being withdrawn from benzo-

diazepine are at risk for falls and myocardial infarctions. Delirium without marked autonomic hyperactivity (no elevations of pulse, blood pressure, or temperature) also may be seen in the elderly. The management of benzodiazepine withdrawal is not recommended without medical supervision. All benzodiazepines should be tapered rather than stopped abruptly, regardless of dose or duration of use—unless it is a matter of use for only a few days (Ashton 2002).

### **Management of Withdrawal With Medications**

There are a limited number of controlled trials that can provide guidance regarding the management of benzodiazepine and other sedative-hypnotic withdrawal. For reviews, see Rickels and colleagues (1999) and Eickelberg and Mayo-Smith (1998). One strategy that is appropriate is to begin with a slow taper of the benzodiazepine that the patient already is taking. This taper may be conducted over several weeks or perhaps even months. This may be effective in cases of long-acting benzodiazepines but often is not effective in detoxification from short half-life benzodiazepines. Sometimes switching to another benzodiazepine in a patient who has had serious loss of control and abuse problems with his primary agent is therapeutic. Another strategy is to switch the patient to another benzodiazepine with a long half-life. Frequently chlorodiazepoxide and

Patients intoxicated with sedative-hypnotics appear similar to individuals intoxicated with alcohol. Slurred speech, ataxia, and poor physical coordination are prominent.

clonazepam are recommended. Figures 4-5 and 4-6 (p. 78) give the equivalent doses of these medicines along with numerous other sedative-hypnotics and benzodiazepines.

Another alternative is phenobarbital substitution. For patients who have used high doses of benzodiazepines for an extended period of time, hospitalization is always prudent. Outpatient detoxification should be reserved for patients whose doses of benzodiazepines were mainly in therapeutic ranges, who do not have polysubstance dependence, and who are reliable and have reliable significant others to aid in monitoring and supervising their progress. In the outpatient setting, patients and families need to be informed that even with sound withdrawal treatment, seizures and delirium are possible. The individual should be instructed not to drive or operate dangerous machinery during treatment and perhaps for several weeks thereafter. Recurring assessment will be necessary, particularly around times of dosage reductions. Pregnant patients will need to be detoxified slowly and in consultation with an obstetrician.

A variety of cognitive and behavioral techniques have been proposed to assist in the presence of a medication taper. These techniques alter negative cognitions regarding medication cessation, provide patient education, and provide alternative cognitive and behavioral techniques for anxiety reduction and sleep enhancement during detoxification (Spiegel 1999).

Anticonvulsants such as carbamazepine and valproate, as well as sedating antidepressants such as trazodone and imipramine, have been advocated for use in withdrawal (Dickinson et al. 2003). Rickels and colleagues (1999) assert that these drugs have some beneficial effect in the management of relatively low-dose benzodiazepine discontinuation in their ability to reduce patients' subjective complaints, but

that, in more severe withdrawal syndromes, they do not decrease symptoms. Imipramine can lower the seizure threshold and therefore is not recommended. The use of anticonvulsants is probably best reserved as an adjunctive medicine to the long-acting benzodiazepine or phenobarbital. The use of buspirone for benzodiazepine detoxification is ineffective and should not be considered. For patients with major autonomic symptoms during withdrawal that cannot be controlled by the primary treating agent, consideration of the use of a low dose of clonidine or propranolol may be helpful.

Preparing patients and starting detoxification during a period of low external stressors, with patient commitment to tapering, and a plan to manage underlying anxiety disorders, also are important in detoxification. A flexible detoxification schedule is advised. During periods of increased withdrawal symptoms, dosage should be stabilized or even increased for a period of days. Frequent in-person or phone contact with the patient is vital. Patients being detoxified in the outpatient setting may need to be seen several times per week, especially at times of dosage reductions.

## Stimulants

Cocaine and amphetamines (such as methamphetamine) are the most frequently abused central nervous system stimulants. These agents are intensely rewarding and are self-administered by laboratory animals to the point of death. Individuals dependent on stimulants experience profound loss of control over stimulant intake, presumably in response to the stimulation and disruption of endogenous (originating internally) reward centers (Dackis and O'Brien 2001). They often use stimulants in a binge pattern that is followed by periods of withdrawal. It is not clear whether craving occurs predominantly during stimulant with-

**Figure 4-5**  
**Benzodiazepines and Their Phenobarbital Withdrawal Equivalents**

Generic name	Trade name	Therapeutic dose range (mg/day)	Dose equal to 30mg of phenobarbital for withdrawal (mg)**	Phenobarbital conversion constant
<b>Benzodiazepines</b>				
alprazolam	Xanax	0.75–6	1	30
chlordiazepoxide	Librium	15–100	25	1.2
clonazepam	Klonopin	0.5–4	2	15
clorazepate	Tranxene	15–60	7.5	4
diazepam	Valium	4–40	10	3
estazolam	ProSom	1–2	1	30
flumazenil	Mazicon	***	***	***
flurazepam	Dalmane	15–30*	15	2
halazepam	Paxipam	60–160	40	0.75
lorazepam	Ativan	1–16	2	15
midazolam	Versed	***	***	***
oxazepam	Serax	10–120	10	3
prazepam	Centrax	20–60	10	3
quazepam	Doral	15*	15	2
temazepam	Restoril	15–30*	15	2
triazolam	Halcyon	0.125–0.50*	0.25	120

\* Usual hypnotic dose.

\*\* Phenobarbital withdrawal conversion equivalence is not the same as therapeutic dose equivalency. Withdrawal equivalence is the amount of the drug that 30mg of phenobarbital will substitute for and prevent serious high-dose withdrawal signs and symptoms.

\*\*\* Not applicable.

*Source:* American Psychiatric Association (APA) 1990; Wesson and Smith 1985.

**Figure 4-6**  
**Other Sedative-Hypnotics and Their Phenobarbital  
Withdrawal Equivalents**

Generic name	Trade name(s)	Common therapeutic indication	Dose equal to 30mg of therapeutic dose range (mg/day)	Phenobarbital for withdrawal (mg)**	Conversion constants
<b>Barbiturates</b>					
amobarbital	Amytal	sedative	50–150	100	0.33
butabarbital	Butisol	sedative	45–120	100	0.33
butalbital	Fiorinal, Sedapap	sedative/ analgesic*	100–300	100	0.33
pentobarbital	Nembutal	hypnotic	50–100	100	0.33
secobarbital	Seconal	hypnotic	50–100	100	0.33
<b>Others</b>					
bupirone	Buspar	sedative	15–60	***	***
chloral hydrate	Noctec, Somnos	hypnotic	250–1,000	500	0.06
ethchlorvynol	Placidyl	hypnotic	500–1,000	500	0.06
glutethimide	Doriden	hypnotic	250–500	250	0.12
meprobamate	Miltown, Equanil, Equagesic	sedative	1,200–1,600	1,200	0.025
methylprylon	Noludar	hypnotic	200–400	200	0.15
<p>* Butalbital usually is available in combination with opioid or non-opioid analgesics.  ** Phenobarbital withdrawal conversion equivalence is not the same as therapeutic dose equivalency. Withdrawal equivalence is the amount of the drug that 30mg of phenobarbital will substitute for and prevent serious high-dose withdrawal signs and symptoms.  *** Not cross-tolerant with barbiturates.</p>					
<i>Source:</i> APA 1990; Wesson and Smith 1985.					

drawal or after these symptoms have largely disappeared. While the processes that govern addiction to cocaine and amphetamines are believed to be similar, recent animal research suggests that there are also subtle differences in the ways in which these two types of drugs create sensitization (and perhaps addiction) in regular users (Li et al. 2005).

## Stimulant Withdrawal Symptoms

Stimulants are associated with withdrawal symptoms that differ markedly from those seen with opioid, alcohol, and sedative dependence (see Figure 4-7). While most clinicians believe that alcohol and heroin withdrawal should be treated aggressively with detoxification, there has been little emphasis on treating symptoms of stimulant withdrawal. Consequently, no medications have been developed for this purpose. This situation is understandable because stimulant withdrawal usually does not involve medical danger or intense patient discomfort. However, if stimulant withdrawal predicts poor outcome, it may be a reasonable target for clinical interventions.

An often overlooked but potentially lethal “medical danger” during stimulant withdrawal is the risk of a profound dysphoria (depression, negative thoughts and feelings) that may include suicidal ideas or attempts. This may be, in part, a physiological response to cocaine

or amphetamine withdrawal and, in part, a reaction to individuals’ acute realization of the devastating psychosocial consequences after a binge ends. While both cocaine and amphetamine users may experience depression during withdrawal, the period of depression experienced by amphetamine users is more prolonged and may be more intense. Amphetamine users, in particular, should be monitored closely during detoxification for signs of suicidality and treated for depression if appropriate.

Although the literature on cocaine withdrawal is controversial, reasonable consensus supports the constellation of symptoms depicted in Figure 4-7 (Coffey et al. 2000; Cottler et al. 1993). These symptoms often disappear after several days of stimulant abstinence but can persist for 3 to 4 weeks (Coffey et al. 2000). In addition, since individuals addicted to stimulants often fail to achieve abstinence, withdrawal symptoms can be a persistent component of active addiction. In addition, individuals addicted to stimulants may experience impairment in hedonic function (ability to experience pleasure) that has been ascribed to stimulant-induced disruptions of endogenous reward centers (Dackis and O’Brien 2002). Research on animals has found that exposure to high doses of methamphetamine results in changes to both the dopaminergic and serotonergic systems of the brain (Nordahl et al. 2005) and dopamine abnormalities among animals and humans who had been ingesting cocaine (Schuckit 2000).

**Figure 4-7  
Stimulant Withdrawal Symptoms**

- |   |   |
|---|---|
| <ul style="list-style-type: none"> <li>• Depression</li> <li>• Hypersomnia (or insomnia)</li> <li>• Fatigue</li> <li>• Anxiety</li> <li>• Irritability</li> </ul> | <ul style="list-style-type: none"> <li>• Poor concentration</li> <li>• Psychomotor retardation</li> <li>• Increased appetite</li> <li>• Paranoia</li> <li>• Drug craving</li> </ul> |
|---|---|

Source: Consensus Panelist Robert Malcolm, M.D.

Researchers have also observed abnormalities in regions of the brain that govern attention and memory in animals that were regularly administered methamphetamine (Nordahl et al. 2005).

Although cocaine withdrawal has traditionally been viewed as relatively mild (Satel et al. 1991; Weddington et al. 1990), evidence suggests that individuals dependent on cocaine with severe stimulant withdrawal are more likely to have a poor clinical outcome (Kampman et al. 2001a). The level of withdrawal symptoms, therefore, may be clinically significant and should be monitored and recorded for future treatment (Kampman et al. 2001b). Kampman reported significantly higher dropout rates in individuals dependent on cocaine who scored high on the Cocaine Selective Severity Assessment (CSSA), a reliable and valid structured interview designed to capture cocaine withdrawal symptoms (Kampman et al. 1998). Patients with high scores on the CSSA were five times more likely to leave treatment and four times more likely to resume cocaine use than those with low scores (Mulvaney et al. 1999). The CSSA is an easily administered 18-item questionnaire. Each item is a 7-point rating scale, so that a person can score a number of points on any given question. Scores in excess of 22 indicate the presence of significant cocaine withdrawal. See appendix C for more information on the CSSA. Given the poor prognosis associated with cocaine withdrawal, it is reasonable that more clinical attention be directed toward this phenomenon.

## Medical Complications of Stimulant Withdrawal

As previously noted, stimulant withdrawal is not usually associated with medical complications. However, patients with recent cocaine use can experience persistent cardiac complications, including prolonged QTc interval and vulnerability for arrhythmia and myocardial infarction (Chakko and Myerburg 1995). QT is an interval of time that can be measured on an

electrocardiogram (between the q wave and the t wave), while QTc is the relative (or “corrected”) QT interval. Some conditions and many drugs (LAAM, other opioids, and even antibiotics) can cause the interval to lengthen and this can result in cardiac rhythm disturbances. Anterior chest pain or cardiac symptoms should therefore be fully evaluated in these individuals. Seizures also may be a complication of stimulant abuse and can occur during detoxification. Persistent headaches could represent a subdural, subarachnoid, or intracerebral bleed (bleeding in or around the brain) and should be appropriately evaluated. It also should be emphasized that people who abuse stimulants usually become addicted to other substances, such as alcohol, sedatives, or opioids, and therefore can experience any of the complications ascribed to detoxification from these substances. Covert (secretive) use of other substances should be suspected and assessed with urine toxicology.

## Management of Withdrawal Without Medications

The most effective means of treating stimulant withdrawal involves establishing a period of abstinence from these agents. Access to brief hospitalization, a level of care previously available for those who abuse stimulants, has been largely eliminated by managed care initiatives. In its place, intensive outpatient treatment can assist the patient to cease use long enough for withdrawal symptoms to abate entirely. Rehabilitative approaches to achieve stimulant abstinence have been reviewed elsewhere (Dackis and O’Brien 2001). The avoidance of cue-induced craving is particularly important in these individuals, especially in light of research that shows limbic activation (activity in a certain part of the brain) in response to cue-induced craving (Childress et al. 1999). It also is important that individuals dependent on stimulants abstain from other addictive substances.

## Management of Withdrawal With Medications

There are no medications with proven efficacy to treat stimulant withdrawal. However, researchers have investigated some medications for cocaine detoxification. Amantadine may help reduce cocaine use in patients with more severe withdrawal symptoms (Kampman et al. 2000). Modafinil, an antinarcotism agent with stimulant-like action, is currently under investigation by one research group as a cocaine detoxification agent (Dackis and O'Brien 2002). One small study in Thailand found the antidepressant mirtazapine (Remeron) was effective at reducing a number of the symptoms associated with amphetamine withdrawal (Kongsakon et al. 2005). None of these medications, however, are approved for use in treating stimulant withdrawal and further research is needed. Gorelick and colleagues (2004) review the full range of clinical literature on pharmacological intervention for cocaine addiction.

## Patient Care and Comfort

Since stimulant withdrawal is not associated with severe physical symptoms, adjunctive medications are seldom required. These patients often are sleep deprived and might be unable to benefit from therapeutic activities during the first 24 to 36 hours of abstinence. They often are hungry and in need of large meal portions initially as their food intake may have been inadequate during active addiction. Stimulant users also may be irritable and care should be taken to avoid needless confrontation during the initial withdrawal phase. Headaches often are reported and can be treated symptomatically. Persistent headaches should be evaluated, as cocaine can produce cerebrovascular disease. Similarly, chest pain of possible cardiac origin should be evaluated medically with electrocardiography, cardiac enzymes, and appropriate medical attention. On occasion, patients undergoing withdrawal from cocaine or amphetamines report insomnia and may benefit from diphenhydramine (Benadryl) 50 to 100mg, trazodone (Desyrel) 75 to 200mg,

or hydroxyzine (Vistaril) 25 to 50mg at bedtime. Benzodiazepines should be avoided unless required for concomitant alcohol or sedative detoxification. As stimulant withdrawal symptoms wane, patients are best treated with an active rehabilitative approach that combines entry into substance abuse treatment with support, education, and changes in lifestyle.

## Other Immediate Concerns

Central nervous system stimulants exert most of their toxic effects through vasoconstriction (constriction of the blood vessels).

Consequently, a number of medical conditions can arise from

ischemia (lack of proper blood supply) or infarction (death of tissue as the result of lack of blood supply) as a result of stimulant use.

Myocardial (heart muscle) infarction and stroke are widely recognized complications of stimulant use. However, other problems such as spontaneous abortion, bowel necrosis (tissue death), and renal (kidney) infarction also have been reported from cocaine-induced vasoconstriction. Cardiac arrhythmias also are common. Other medical problems that are associated with stimulant dependence include dental disease, neuropsychiatric abnormalities, and movement disturbances/disorders.

Antidepressants, such as selective serotonin reuptake inhibitors, can be prescribed for the depression that often accompanies methamphetamine or other amphetamine withdrawal.

Intensive outpatient treatment can assist the patient to cease use long enough for withdrawal symptoms to abate entirely.

# Inhalants/Solvents

## Withdrawal Symptoms Associated With Inhalants/Solvents

The term “inhalants” is used to describe a large and varied group of psychoactive substances that all share the common characteristic of being inhaled for their effects. They are commonly found in household, industrial, and medical products. These drugs are used primarily by adolescents, although some, especially the nitrates, are used by adults as well (NIDA 2000). Figure 4-8 presents some of the more commonly abused inhalants.

Dependence on inhalants and subsequent withdrawal symptoms are both relatively uncommon phenomena (Balster 2003). There is no *specific* or characteristic withdrawal syndrome that would include all drugs in the inhalant class. Intoxication with the solvents, aerosols, and gases often produces a syndrome most like that of alcohol intoxication but lasting only 15 to 45 minutes (Miller and Gold 1990). Rarely, symptoms similar to sedative withdrawal have been described, including “fine tremors, irritability, anxiety, insomnia, tingling sensations, seizures and muscle cramps” (Miller and Gold 1990, p. 87). Toluene withdrawal has been reported to cause delirium tremens (Miller and Gold 1990). Longtime users also may exhibit weakness, weight loss, inattentive behavior, and depression (NIDA 2005). It has been reported that withdrawal symptoms can occur with as little as 3 months of regular usage (Ron 1986). When present, the withdrawal typically lasts 2 to 5 days (Evans and Raistrick 1987).

In addition to their short-term intoxicating affects, nitrates are used to enhance sexual pleasure by vasodilation (dilation of blood vessels) that produces a rush and sensation of warmth. There is no withdrawal syndrome that has been associated with nitrate abuse.

There are no specific assessment instruments available to measure inhalant withdrawal symptoms. A patient who presents with a history of inhalant use and symptoms of sedative-like withdrawal should alert the clinician to the possibility of inhalant withdrawal. These patients require a complete history and physical exam. Additionally, a blood alcohol level and urine drug screen are helpful in the cases of suspected polydrug abuse.

## Medical Complications of Withdrawal From Inhalants/Solvents

There are a large number of medical complications associated with inhalant abuse and intoxication. Many of these complications are not the result of withdrawal but may still be seen when the patient presents to the clinician. Most inhalants produce some neurotoxicity with cognitive, motor, and sensory involvement. Additionally, damage to internal organs including the heart, lungs, kidneys, liver, pancreas, and bone marrow has been reported.

## Management of Withdrawal Without Medications

It is crucial to provide the patient with an environment of safety that removes him from access to inhalants. This can pose a challenge due to the almost universal availability of these drugs in society. Many of the medical consequences of inhalant usage will remit once the patient achieves abstinence (Balster 2003). The patient should be monitored for withdrawal symptoms and changes in mental status.

Most patients presenting for treatment of inhalant dependence will be adolescents. Ideally, they should be entered into an age-appropriate treatment program that meets their medical and psychosocial needs. Supportive care, including helping them to get enough sleep and a well-balanced diet, usually will be sufficient to get patients safely through withdrawal (Frances and Miller 1998).

**Figure 4-8**  
**Commonly Abused Inhalants/Solvents**

Type	Example	Chemicals in Inhalant/Solvent
Adhesives	Airplane glue	Toluene, ethyl acetate
	Other glues	Hexane, toluene, methyl chloride, acetone, methyl ethyl ketone, methyl butyl ketone
	Special cements	Trichloroethylene, tetrachloroethylene
Aerosols	Spray paint	Butane, propane (U.S.), fluorocarbons, toluene, hydrocarbons, "Texas shoe shine" (a spray containing toluene)
	Hair spray	Butane, propane (U.S.), chlorofluorocarbons (CFCs)
	Deodorant; air freshener	Butane, propane (U.S.), CFCs
	Analgesic spray	CFCs
	Asthma spray	CFCs
	Fabric spray	Butane, trichloroethane
	PC cleaner	Dimethyl ether, hydrofluorocarbons
Anesthetics	Gaseous	Nitrous oxide
	Liquid	Halothane, enflurane
	Local	Ethyl chloride
Cleaning agents	Dry cleaning	Tetrachloroethylene, trichloroethane
	Spot remover	Xylene, petroleum distillates, chlorohydrocarbons
	Degreaser	Tetrachloroethylene, trichloroethane, trichloroethylene

## Management of Withdrawal With Medications

Patients presenting with only inhalant withdrawal are unusual. Clinicians should promptly ascertain if the patient has been abusing any other substances and proceed with appropriate detoxification as clinically indicated. When a patient presents with (1) a history of extensive inhalant usage, (2) a sedative-like withdrawal syndrome, and (3) no significant history or laboratory data that supports other substances, then the clinician can assume that the patient is in inhalant withdrawal.

As noted before, withdrawal from inhalants is similar to withdrawal from sedative-hypnotics. No systematic detoxification protocol

has been established, although some clinicians have found phenobarbital useful (CSAT 1995*d*). The usefulness of benzodiazepines is unknown but would seem a reasonable alternative given our current understanding of inhalant withdrawal (Brouette and Anton 2001). No other medications have been routinely used for inhalant withdrawal.

## Patient Care and Comfort

For patients who have only been abusing inhalants, treatment of insomnia during withdrawal is not usually necessary. Sedative substitution during the period of detoxification may allow the patient to sleep. However, a period of postdetoxification insomnia should be expected and usually can be treated by the

**Figure 4-8 (continued)**  
**Commonly Abused Inhalants/Solvents**

Solvents and gases	Nail polish remover	Acetone, ethyl acetate
	Paint remover	Toluene, methylene chloride, methanol acetone, ethyl acetate
	Paint thinner	Petroleum distillates, esters, acetone
	Correction fluid and thinner	Trichloroethylene, trichloroethane
	Fuel gas	Butane, isopropane
	Lighter	Butane, isopropane
	Fire extinguisher	Bromochlorodifluoromethane
Food products	Whipped cream	Nitrous oxide
	Whippets	Nitrous oxide
“Room odorizers”	Locker Room, Rush, Poppers	Isoamyl, isobutyl, isopropyl or butyl nitrate (now legal), cyclohexyl

*Source:* Balster 2003.

recommendation of good sleep hygiene practices such as avoiding caffeine, daytime napping, and overstimulation in the evening.

If the patient is able to refrain from inhalant (and other substance) use and has no serious psychiatric or medical consequences, then outpatient treatment should be the first option. Inpatient or residential treatment should be used for those patients who cannot achieve abstinence or have serious co-occurring medical or psychiatric disorders. Hospitalized patients will need a thorough history and physical exam. Therapy to address denial, addiction, and pertinent psychosocial issues should be initiated as soon as possible during the hospitalization. Supportive care and abstinence will resolve most medical problems associated with chronic inhalant usage (Balster 2003).

## Nicotine

In 2004, approximately 44.5 million adults were cigarette smokers (23.4 percent were men and 18.5 percent were women) (CDC 2005a). Nicotine addiction in the form of cigarette smoking accounts for more deaths each year than AIDS, alcohol, cocaine, heroin, homicide, suicide, motor vehicle crashes, and fires combined (U.S. Department of Health and Human Services [U.S. DHHS] 2000b). Between 1995 and 1999, there were 490,000 smoking-related premature deaths annually, and smoking cost the country at least \$157 billion yearly in health-related economic losses. This amounts to approximately \$7.18 per pack of cigarettes (Fellows et al. 2002), a truly staggering figure.

Smokers are at increased risk for several medical problems, including myocardial infarction, coronary artery disease, hypertension, stroke, peripheral vascular disease,

chronic obstructive lung disease, chronic bronchitis, and several types of cancer (lung, stomach, head and neck, and bladder). Other problems associated with nicotine addiction include gastro-esophageal reflux disease and gastric ulcerations, cataracts, and premature wrinkling of the skin. There also appears to be an antiestrogen effect (suppression of an important hormone) that may lead to early development of osteoporosis in women (Okuyemi et al. 2000).

In 1988, the U.S. Surgeon General's Report concluded that nicotine is the principal addictive agent in tobacco. Nicotine binds to nicotinic acetylcholine receptors in the brain and has the direct ability to stimulate the release of dopamine in the nucleus accumbens area. The nucleus accumbens has long been considered the "reward center" in the brain. This increase in dopamine is similar to what occurs when patients use stimulants and is felt to be an essential element in the reward process of addiction (Glover and Glover 2001).

As many as 90 percent of patients entering treatment for substance abuse are current nicotine users (Perine and Schare 1999). There has long been controversy in the field of addiction medicine as to how best to handle the problem of nicotine dependence in patients seeking treatment for other types of substance abuse. Traditionally, it has been argued that patients would find that trying to stop smoking while also contending with other (more pressing) addiction problems would be too difficult and distracting in early abstinence. However, others argue that nicotine dependence is a lethal disease and that physicians have the responsibility to intervene in this addiction with the same aggressiveness they show toward other addictive substances. This pro-intervention position has received increasing attention from clinicians, inasmuch as it is now understood that alcohol consumption is associated with increased nicotine usage (Henningfield et al. 1984). Gulliver and colleagues (1995) have demonstrated that the urge to smoke is correlated with the urge to

drink, and others have shown that continued nicotine dependence may be a relapse trigger for resumption of drinking (Stuyt 1997). The concern that smoking cessation may precipitate relapse to other substances of abuse has not been supported in the literature (Hughes 1995).

Treatment programs that have attempted to treat nicotine dependence in conjunction with other drugs of addiction have met with limited success (Bobo and Davis 1993; Burling et al. 1991; Hurt et al. 1994) and have generated increased interest in smoking cessation as a part of a patient's overall substance abuse treatment (Sees and Clark 1993). One study reported that forcing unmotivated patients (or patients who did not consider smoking a problem) to quit was countertherapeutic (Trudeau et al. 1995).

Moreover, it has traditionally been accepted that nicotine detoxification concurrent with detoxification from other substances makes the undertaking more difficult. Several factors are involved including the following: (1) patient ambivalence and/or lack of interest in smoking cessation; (2) physician ambivalence about the importance of smoking cessation early in treatment; (3) staff's use of nicotine; (4) staff's ambivalence about the importance of nicotine cessation early in treatment; (5) easy availability of cigarettes from peers, family, visitors, staff, and at 12-Step meetings; (6) lack of sufficient training and expertise on the part of physicians and staff in managing nicotine withdrawal; and (7) staff resistance to patient smoking cessation because withdrawal symptoms include irritability, anxiety, and depression, all of which can make patients more difficult to manage.

## **Withdrawal Symptoms Associated With Nicotine**

*The Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR) (APA 2000) notes that typically, a person in nicotine withdrawal will have four*

or more of the signs presented in Figure 4-9, though some clinicians believe that three or more is sufficient to make the diagnosis of nicotine withdrawal. Furthermore, it should be noted that symptoms vary in duration and intensity, with decreased heart rate and light-headedness resolving in 48 hours, while increased appetite may remain present for weeks to months (Glover and Glover 2001). Smokers who have severe craving during withdrawal are less likely to be successful in their attempt at quitting (Hughes and Hatsukami 1992). Depression during withdrawal also has been linked to relapse to smoking (Covey et al. 1993).

### Assessing Severity

Since 1978, the standard instrument used to measure physical dependence on nicotine has been the eight-item Fagerstrom Tolerance Questionnaire (FTQ) (Fagerstrom 1978). A later revision known as the Fagerstrom Test for Nicotine Dependence (FTND) (see Figure

4-10) has been reduced to six questions (Giovino et al. 1995; Heatherton et al. 1991). Scores greater than seven are consistent with nicotine dependence.

While both the FTQ and FTND are very useful for estimating a patient's physical dependence on nicotine, there is still a need to assess more accurately the degree to which smoking behavior plays a role in maintaining addiction. The Glover-Nilsson Smoking Behavioral Questionnaire (GN-SBQ) is an 11-question, self-administered test that evaluates the impact of behaviors and rituals associated with smoking (see Figure 4-11, p. 88). It was designed to assist clinicians in identifying and quantifying behavioral aspects of smoking that play a role in maintaining nicotine dependence, which can then help the clinician develop a cessation strategy that takes into account both physical dependence and behavioral dependence (Glover et al. 2002).

**Figure 4-9**  
**DSM-IV-TR on Nicotine Withdrawal**

- A. Daily use of nicotine for at least several weeks.
- B. Abrupt cessation of nicotine use, or reduction in the amount of nicotine used, followed within 24 hours by 4 or more of the following signs:
  1. Dysphoric or depressed mood
  2. Insomnia
  3. Irritability, frustration, or anger
  4. Anxiety
  5. Difficulty concentrating
  6. Restlessness
  7. Decreased heart rate
  8. Increased appetite or weight gain
- C. The symptoms of Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Source: APA 2000, pp. 244–245.

**Figure 4-10**

**Items and Scoring for the Fagerstrom Test for Nicotine Dependence**

Questions	Answers	Points
1. How soon after you wake up do you smoke your first cigarette?	Within 5 minutes	3
	6–30 minutes	2
	31–60 minutes	1
	After 60 minutes	0
2. Do you find it difficult to refrain from smoking in places where it is forbidden (e.g., in church, at the library, in the cinema, etc.)?	Yes	1
	No	0
3. Which cigarette would you hate most to give up?	The first thing in the morning	1
	All others	0
4. How many cigarettes/day do you smoke?	10 or less	0
	11–20	1
	21–30	2
	31 or more	3
5. Do you smoke more frequently during the first hours of waking than during the rest of the day?	Yes	1
	No	2
6. Do you smoke if you are so ill that you are in bed most of the day?	Yes	1
	No	0

Source: APA 1996.

To better understand a patient’s level of nicotine dependence, providers can assess biochemical markers including nicotine, cotinine, and carbon monoxide. Nicotine and its metabolite cotinine can be measured in urine, blood, or saliva. Cotinine continues to be present in bodily fluids for up to 7 days after cessation. Clinicians should use caution when interpreting the meaning of nicotine and cotinine assays, as they are not specific to tobacco-derived nicotine and may indicate the patient’s compliance with nicotine replacement therapy rather than smoking.

Carbon monoxide is easily measured in expired breath and can show whether the patient has been smoking within a few hours prior to the test. It can be used to monitor smoking cessation for patients receiving nico-

tine replacement therapy and patients often find it a helpful motivator in their attempt to maintain abstinence (Benowitz 1983).

### Medical Complications of Withdrawal From Nicotine

There are no major medical complications precipitated by nicotine withdrawal itself. However, patients frequently experience uncomfortable withdrawal symptoms starting within a few hours of cessation. In addition to the symptoms previously noted, patients may complain of increased coughing, a desire for sweets, and difficulty concentrating (Hughes and Hatsukami 1992). Clinicians should be aware that withdrawal symptoms can masquer-

**Figure 4-11****The Glover-Nilsson Smoking Behavioral Questionnaire (GN-SBQ)**

Please indicate your choice by circling the number that best reflects your choice.

0 = Not at all; 1 = Somewhat; 2 = Moderately so; 3 = Very much so; 4 = Extremely so

How much do you value the following (Specific to Questions 1–2)?

- |   |   |   |   |   |   |
|---|---|---|---|---|---|
| 1. My cigarette habit is very important to me.                            | 0 | 1 | 2 | 3 | 4 |
| 2. I handle and manipulate my cigarette as part of the ritual of smoking. | 0 | 1 | 2 | 3 | 4 |

Please indicate your choice by circling the number that best reflects your choice.  
(Specific to Questions 3–11).

0 = never; 1 = seldom; 2 = sometimes; 3 = often; 4 = Always

- |  |   |   |   |   |   |
|--|---|---|---|---|---|
| 3. Do you place something in your mouth to distract you from smoking?  | 0 | 1 | 2 | 3 | 4 |
| 4. Do you reward yourself with a cigarette after accomplishing a task?   | 0 | 1 | 2 | 3 | 4 |
| 5. If you find yourself without cigarettes, will you have difficulties in concentrating before attempting a task?  | 0 | 1 | 2 | 3 | 4 |
| 6. If you are not allowed to smoke in certain places, do you then play with your cigarette pack or a cigarette?  | 0 | 1 | 2 | 3 | 4 |
| 7. Do certain environmental cues trigger your smoking (e.g., favorite chair, sofa, room, car, or drinking alcohol)?  | 0 | 1 | 2 | 3 | 4 |
| 8. Do you find yourself lighting up a cigarette routinely (without craving)?   | 0 | 1 | 2 | 3 | 4 |
| 9. Do you find yourself placing an unlit cigarette or other objects (pen, toothpick, chewing gum, etc.) in your mouth and sucking to get relief from stress, tension or frustration, etc.? | 0 | 1 | 2 | 3 | 4 |
| 10. Does part of your enjoyment of smoking come from the steps (ritual) you take when lighting up?   | 0 | 1 | 2 | 3 | 4 |
| 11. When you are alone in a restaurant, bus terminal, party, etc., do you feel safe, secure, or more confident if you are holding a cigarette?   | 0 | 1 | 2 | 3 | 4 |

TOTAL \_\_\_\_\_

Scoring for Behavioral Dependence

<12 Mild

12–22 Moderate

23–33 Strong

>33 Very Strong

Source: Glover et al. 2002

ade as other psychiatric conditions, especially anxiety and depression (see Figure 4-12).

Smoking cessation also may affect the metabolism of other drugs primarily through the Cytochrome P 450 (CYP450) system. This system is one of many hepatic liver enzyme systems that is responsible for the metabolic breakdown of various drugs into inactive compound products. Different drugs and compounds have varying affinities for the CYP450 system. The higher the affinity, the faster the breakdown of the drug or compound in the body. Some compounds can slow the metabolism or breakdown of other drugs with a lower affinity, leading to a buildup of that drug or compound in the body.

During detoxification from nicotine, some medications will have their metabolism altered, including theophylline, caffeine, tacrine, imipramine, haloperidol, pentazocine, propranolol, flecainide, and estradiol; in general, these effects are short-lived and seldom drastic. Nicotine also reduces beta blockers' ability to lower blood pressure and heart rate and decreases the amount of sedation from benzodiazepines as well as decreases the amount of pain relief provided by some opioids, most likely because of its stimulant effects (Zevin and Benowitz 1999). A complete discussion of nicotine's effects on medications is beyond the scope of this TIP and physicians are encouraged to consult the *Physicians' Desk Reference* (2004) or equivalent

pharmaceutical guide. Figure 4-13 (p. 90) shows the effects of abstinence from smoking on blood levels of a number of medications.

## Management of Withdrawal Without Medications

About one third of current smokers attempt to quit smoking each year and more than 90 percent of these try to do so without any formal nicotine cessation treatment. Most smokers will make several attempts on their own to quit and ultimately, only about 50 percent are successful over a lifetime (U.S. DHHS 2000b). While some smokers are able to quit on their own, others may require intervention in the form of behavioral treatment and/or pharmacotherapy.

There are insufficient data available to determine who will benefit most from a particular type of treatment. Some patients may prefer to stop smoking without the use of medication. An elevated score on the GN-SBQ would indicate a strong behavioral component to smoking that might guide the clinician in recommending behavioral treatment as a primary intervention. Patients who also have elevated FTQ scores may benefit by a combination of behavioral and pharmaceutical intervention.

**Figure 4-12**  
***Some Examples of Nicotine Withdrawal Symptoms That Can Be Confused With Other Psychiatric Conditions***

Anxiety  
Depression  
Increased REM (rapid eye movement) sleep  
Insomnia  
Irritability  
Restlessness  
Weight gain

*Source:* APA 1996.

**Figure 4-13**  
**Effects of Abstinence From Smoking on Blood Levels of Psychiatric Medications**

Abstinence Increases Blood Levels	Abstinence Does Not Increase Blood Levels	Effect of Abstinence on Blood Levels Is Unclear
Clomipramine Clozapine Desipramine Desmethyldiazepam Doxepin Fluphenazine Haloperidol Imipramine Oxazepam Nortriptyline Propranolol	Amitriptyline Chlordiazepoxide Ethanol Lorazepam Midazolam Triazolam	Alprazolam Chlorpromazine Diazepam

Source: APA 1996.

The U.S. Public Health Service’s *Treating Tobacco Use and Dependence: Clinical Practice Guideline* is a comprehensive review of the smoking cessation literature (Fiore et al. 2000a). It discusses a range of nonpharmacological interventions for the management of withdrawal from nicotine; these can be separated into two basic categories: self-help interventions and behavioral interventions (Anderson and Wetter 1997).

### **Self-help interventions**

Many tobacco users prefer to attempt to quit without any assistance from professionals. A number of self-help products are available that can assist them in their cessation attempts. These include a wide array of pamphlets, manuals, video- and audiotapes (e.g., from the American Lung Association and the National Cancer Institute), 12-Step self-help support groups, and telephone helplines. The U.S. Public Health Service’s *Guideline*, which analyzed all types of self-help interventions together, found that the self-help approach to cessation yielded results only slightly better than no intervention at all. To date, self-help

interventions alone have not been very successful at helping people achieve abstinence from tobacco. The *Guideline* suggests, however, that self-help can be a useful adjunct to other forms of treatment (Fiore et al. 2000a).

One type of self-help intervention that shows some promise is the use of computer-generated personalized written feedback for patients. The computer makes recommendations based on an individual’s response to standardized questions about her smoking (Etter and Perneger 2001; Shiffman et al. 2000).

### **Behavioral interventions**

The U.S. Public Health Service study noted that when physicians took as little as 3 minutes to advise their patients to stop smoking, long-term quit rates were modestly improved from 7.9 percent to 10.2 percent (Fiore et al. 2000a). Westmaas and colleagues note that “simple, clear advice from a physician can be considered an easy, cost-effective intervention that not only moves smokers closer to the decision to quit, but also may motivate some smokers to make an actual attempt”

(Westmaas et al. 2000, p. 58). The greater the amount of time in face-to-face interventions, the higher the success rate for patients, but interventions as short as 3 minutes have been found to be effective (Fiore et al. 2000a). A counseling session of longer than 10 minutes produced a cessation rate of 20.1 percent compared to a rate of 10.9 percent for no treatment. The guideline also indicated that if cessation information is given by multiple types of providers (e.g., physician, psychologist, dentist, nurse, and pharmacist) it can have a dramatic effect on cessation rates, increasing the rate to 23 percent compared to 10.8 percent for patients who had no provider contact.

A review of behavioral intervention studies concluded that both supportive care by a clinician and the ability of patients to develop problemsolving and coping skills improved success rates for smoking cessation (Anderson and Wetter 1997). Other components such as cigarette fading (gradually decreasing the number of cigarettes smoked over a period of time), establishing a quit date, enhanced environmental support, improved diet and increased exercise, relaxation training, and contingency contracting were not associated with improved outcome. Aversive conditioning, such as rapid smoking techniques, is

effective but not routinely recommended (Fiore et al. 2000a).

## Management of Withdrawal With Medications

A U.S. Public Health Service panel recommends that all primary care physicians provide a five-step intervention, known as the “5 A’s,” to all tobacco users. The panel recommends that all smokers who want to quit should be offered active medication that has been approved for assisting in smoking cessation unless there is a medical contraindication (Fiore et al. 2000a). Figure 4-14 provides a summary of the “5 A’s” for brief intervention.

## Nicotine Replacement Therapy (NRT)

Nicotine polacrilex gum was approved by the FDA in 1984. In the 1990s other NRTs received FDA approval, including the nicotine transdermal patch, the nicotine nasal spray, and the nicotine inhaler. Nicotine gum and nicotine transdermal patch are now available over the counter. After the acute withdrawal period, patients are then weaned off the medication until they become nicotine free. All NRTs are

**Figure 4-14**  
**The “5 A’s” for Brief Intervention**

Ask about tobacco use. Identify and document tobacco use status for every patient at every visit.
Advise to quit. In a clear, strong, and personalized manner urge every tobacco user to quit.
Assess willingness to make a quit attempt. Is the tobacco user willing to make a quit attempt at this time?
Assist in quit attempt. For the patient willing to make a quit attempt, use counseling and pharmacotherapy to help him or her quit.
Arrange followup. Schedule followup contact, preferably within the first week after the quit date.
<i>Source:</i> Fiore et al. 2000a, p. 26.

effective, with 1-year quit rates between 11 and 34 percent (Okuyemi et al. 2000).

There has been some concern about the addictive potential of NRTs, and it has been reported that 5 to 20 percent of patients using nicotine polacrilex gum continue to use it for more than 1 year (Hughes 1989). There was also initial concern that the nicotine nasal spray, with its rapid onset of action and high plasma concentrations, might become a drug of abuse. This has not been reported in the

literature, and it could be speculated that this is because of the nasal spray's relatively uncomfortable side effects that cause many patients to dislike the product (Schuh et al. 1997). In general, withdrawal symptoms from NRTs are mild compared to those that occur in smoking cessation, and continued use of these products may be the result of patients' fear of returning to active smoking (APA 1996). For those patients who continue to use NRTs, providers

should balance the patient's continued dependence on nicotine with the considerable health benefit of decreasing active tobacco usage. It is clear that constituents of tobacco other than nicotine are responsible for causing cancer. No ill effects have been attributed to long-term use of nicotine replacement therapy (Benowitz and Gourlay 1997).

Patients should be encouraged to use combined NRT treatments if they are unable to quit using a single type of first line pharmacotherapy.

## **Bupropion SR**

Bupropion SR (Sustained Release) was initially manufactured under the name Wellbutrin as a treatment for major depressive disorder. In 1997, the FDA approved bupropion SR for smoking cessation, and it has been marketed under the name Zyban. Bupropion is a novel antidepressant that is involved primarily with dopamine but also affects adrenergic mechanisms in the central nervous system. Its exact mechanism of action is unknown, but it is not a nicotine substitute or replacement like the NRTs. The recommended dose is 150mg daily for 3 days and then 150mg twice daily for 7 to 12 weeks. Typically patients set their quit date 1 to 2 weeks from the time they start the medication in order to get the drug to therapeutic levels. This is an ideal time for the patient to focus on making behavioral changes and enlisting social support to augment his quit attempt. Bupropion SR has proven useful in smoking cessation with a 12-month abstinence rate of 35.5 percent compared to a placebo at 15.6 percent and the nicotine patch at 16.4 percent (Westmaas et al. 2000). The most commonly reported side effects include dry mouth and insomnia. Bupropion SR should not be used in patients with a history of seizures, heavy alcohol use, head trauma, or with anorexia or bulimia.

## **Other nonnicotine pharmacotherapy**

Covey and colleagues examined nonnicotine pharmaceutical products that have been evaluated in controlled trials of smoking cessation (Covey et al. 2000). These drugs include the following:

- The alpha-2 agonist antihypertensive, clonidine
- The tricyclic antidepressant, nortriptyline
- The monoamine oxidase inhibitor (MAOI) antidepressant, moclobemide
- The serotonin 5-HT<sub>1A</sub> agonist anxiolytic, buspirone

- The antihypertensive CNS nicotinic receptor blocker, mecamylamine
- Oral dextrose tablets

Although none of these agents has been approved by the FDA for smoking cessation, clonidine, nortriptyline, and moclobemide have all been found to be effective treatments (Covey et al. 2000). Clonidine may be a helpful adjunct to nicotine replacement during acute nicotine withdrawal. Doses of 0.05mg to 0.1mg three times a day can be tried as tolerated (sedation and low blood pressure are concerns), and the medication needs to be tapered when discontinued to avoid rebound hypertension.

The Public Health Service's *Treating Tobacco Use and Dependence: Clinical Practice Guideline* (Fiore et al. 2000a) has classified nortriptyline and clonidine as second-line treatments. Clonidine is an antihypertensive and may be appropriate for patients addicted to certain types of drugs but not appropriate for others. The antidepressant selective serotonin reuptake inhibitor (SSRI) fluoxetine has been tested in a number of multisite trials (Cook et al. 2004; Hitsman et al. 1999; Niaura et al. 2002) and found to have a small benefit at best, although for patients who experience mild depressive states it may be a worthwhile adjunctive treatment. The usefulness of other SSRIs for smoking cessation is unknown, but studies have generally been unfavorable. More information on smoking cessation for people with co-occurring substance use and other mental disorders can be found in appendix D of TIP 42, *Substance Abuse Treatment for Persons With Co-Occurring Disorders* (CSAT 2005c).

## **Combination drug therapy**

### **Combining NRT products**

NRT products typically provide less than half the nicotine plasma levels that cigarette users achieve through smoking (Benowitz et al. 1997; Dale et al. 1995; Gupta et al. 1995; Lawson et al. 1998). To attempt to increase nicotine lev-

els, several clinical trials have evaluated the effectiveness of combining available products. The simultaneous use of nicotine gum and the nicotine patch has been evaluated in several studies. Short-term gains in cessation were seen with the combination compared to either medication alone, but no long-term benefits in abstinence were demonstrated (Anderson and Wetter 1997). Blondal and colleagues (1999) compared the combination of nicotine nasal spray and the nicotine patch to the patch alone and found that at 3 months 37 percent of the patients were smoke free (compared to 25 percent for the patch alone). An open-label study of the combined use of nicotine inhaler and the nicotine patch found a 12-week cessation rate of 30 percent and good tolerability for the combination (Westman et al. 2000).

So-called “combination NRT” involves combining different types of nicotine replacement products, such as the patch and gum, on the premise that doing so will boost nicotine blood levels. Further rationale for this practice is that a “passive” nicotine delivery system (i.e., patch) produces relatively steady levels of nicotine in the body that prevent the user from going below a threshold minimum while “active” NRTs (i.e., gum, inhaler, spray, sublingual tablet, etc.) permit the user to respond to situational cravings with ad libitum dosing on an acute basis. Several clinical trials have evaluated the effectiveness of combining available NRT products (for a review see Silagy et al. 2000). After reviewing available data, the *Guideline* panel (Fiore et al. 2000a) felt that there was moderately strong evidence to conclude that “Combining the nicotine patch with a self-administered form of nicotine replacement therapy (either the nicotine gum or nicotine nasal spray) is more efficacious than a single form of nicotine replacement, and patients should be encouraged to use such combined treatments if they are unable to quit using a single type of first-line pharmacotherapy” (Fiore et al. 2000a, p. 77).

## ***NRT using high-dose nicotine patch therapy***

The highest dose of nicotine available by patch is 22mg. Several studies have evaluated whether higher doses of nicotine (up to 44mg) improve abstinence rates. The effect of this strategy has been small and the routine use of higher dose patches is not recommended (Hughes et al. 1999; Killen et al. 1999).

## ***Combining nicotine patch and bupropion SR***

In a double-blind, placebo-controlled study, the combination of bupropion SR and the nicotine transdermal patch showed higher abstinence rates at 12 months (35.5 percent) compared to bupropion SR alone (30.3 percent), nicotine patch alone (16.4 percent), or placebo patch and pill group (15.6 percent) (Jorenby et al. 1999). This combination was well tolerated. Clinicians who use this combination should first start the patient on bupropion SR 150mg for 3 days and then increase the dosage to 150mg twice daily for 1 to 2 weeks prior to the day of smoking cessation. On the “quit day,” nicotine patch therapy should be initiated and the combination treatment continued for 3 to 6 months (Okuyemi et al. 2000).

## ***Patient Care and Comfort***

Most smokers attempt cessation on an outpatient basis and without any assistance from professionals. However, if a patient decides that she or he wants help with smoking cessation, it is important for the clinician to present a supportive and nonjudgmental attitude and develop a therapeutic alliance with the patient. It must be emphasized that nicotine dependence is a chronic relapsing disorder and that patients often make several attempts at quitting before succeeding.

Most smokers who want treatment will seek help from their primary care physician. The physician has the responsibility of providing pharmaceutical treatment, education about common problems associated with cessation,

and emotional support to patients attempting to quit. Discussing nicotine withdrawal symptoms can often help allay patient concerns.

Fear of weight gain is a barrier for many who want to quit smoking (French et al. 1995). This is an especially important issue for women and may deter their attempts to stop smoking (Gritz et al. 1989). Though the health gains of stopping smoking clearly outweigh the health risks of weight gain, this argument does little to assuage patients’ fears. Dieting during smoking cessation is not recommended in general and has been shown to increase the likelihood of smoking relapse (Hall et al. 1992). Physicians should, however, recommend both exercise and proper nutrition for patients attempting to stop smoking. Patients should be informed that alcohol use also is considered a risk factor for relapse to smoking by most clinicians (Shiffman 1982), and patients who can abstain from drinking during the withdrawal period should do so.

Patients generally will find a smoke-free environment helpful during quit attempts. If the patient lives in a household where others smoke, household members and friends can help by not smoking in front of the patient and limiting the number of smoking cues in their residence.

Patients with more severe nicotine dependence may benefit from enrollment in a specialized smoking cessation program. They might also benefit from more intensive medical management using several drugs (NRT + anti-craving), medication for longer periods of time, closer followup, and longer enrollment in treatment. There are a number of cessation programs available from organizations such as the American Lung Association ([www.lungusa.org](http://www.lungusa.org)) and the American Cancer Society ([www.cancer.org](http://www.cancer.org)). Some community and local organizations also sponsor smoking cessation programs. For the most severely dependent smokers, there are a limited number of residential facilities that treat nicotine dependence on an inpatient basis (Hurt et al. 1992). Providers of detoxification services

should be familiar with the programs available in their communities in order to make referrals.

## Marijuana and Other Drugs Containing THC

Marijuana and hashish are the two substances containing THC (delta-9-tetrahydrocannabinol) commonly used today. The field of addiction medicine has given considerable attention to the question of whether there is a specific withdrawal syndrome associated with cessation from prolonged THC use. In the past, many have stated that there is no acute abstinence syndrome that develops in people who abruptly discontinue THC (CSAT 1995*d*). More recently this has been called into question and most experts now believe that a THC-specific withdrawal syndrome does occur in some patients who are heavy users (Budney et al. 2001), though cannabis withdrawal is not yet included in the APA's *Diagnostic and Statistical Manual of Mental Disorders*.

The THC abstinence syndrome usually starts within 24 hours of cessation. The amount of THC that one needs to ingest in order to experience withdrawal is unknown. It can be assumed, however, that heavier consumption is more likely to be associated with withdrawal symptoms. The most frequently seen symptoms of THC withdrawal are anxiety, restlessness and irritability, sleep disturbance, and change in appetite (usually anorexia). Other symptoms of withdrawal are less frequently seen and appear to include tremor, diaphoresis (sweating), tachycardia (elevated heart rate), and GI disturbances, including nausea, vomiting, and diarrhea. Cognitive difficulties including depression also have been reported and may persist but usually improve with time. There are no medical complications of withdrawal from THC, and medication is generally not required to manage withdrawal.

Clinicians may see a variety of the symptoms mentioned above, but these generally require

no immediate medication during the detoxification period and usually are self-limiting. However, the clinician should be aware of the potential for more persistent problems. Screening the patient for suicidal ideation or other mental health problems is warranted. Some reviews have advocated the use of buspirone as an alternative to benzodiazepines for the management of persistent generalized anxiety (Gatch and Lal 1998). Other common problems encountered during withdrawal can be managed with nonaddictive, supportive medications. For patients with more persistent difficulty sleeping, clinical experience suggests that Trazodone may be useful. Trazodone can lead to low blood pressure upon standing, dizziness, and may increase falls, particularly in individuals over age 60. Benzodiazepines and other addictive medications should be avoided.

The patient should be encouraged to maintain abstinence from THC as well as other addictive substances. Some patients will require a substance-free, supportive environment to achieve and maintain abstinence. Clinicians should educate all patients about the effects of withdrawal, validate their complaints, and reassure them that their symptoms will likely improve with time. Symptomatic relief may be provided in order to increase the patient's comfort.

Most experts now believe that a THC-specific withdrawal syndrome does occur in some patients who are heavy users, though cannabis withdrawal is not yet included in the APA's *Diagnostic and Statistical Manual of Mental Disorders*.

There are no clinical assessment instruments available that measure THC withdrawal. Both animal and human studies indicate that a withdrawal syndrome starts within 24 hours of cessation and may last for up to a week.

## Anabolic Steroids

Anabolic steroids, as differentiated from corticosteroids and female gonadotropic hormones, are androgens (male hormones) and subject to abuse as a means of increasing

muscle mass. These agents also can produce aggressive, manic-like behavior that may include delusions (Lukas 1998). Males involved in professional sports, weight lifting, body building, or other pursuits that value muscular mass are more likely to use these substances than are women, although use in women has been reported.

Adolescents use anabolic steroids to improve their appearance and may have increased access to these compounds (Yesalis et al. 1993). The large numbers of anabolic steroid preparations that have medical and veterinary uses are primarily

obtained illegally through diversion. High doses of anabolic steroids can be medically dangerous but side effects, usually involving endocrine, liver, central nervous system, and cardiac function, tend to be reversible upon cessation of anabolic steroid

use. However, neither cessation nor disclosure of anabolic steroid use can be assumed when treating these individuals.

## Withdrawal Symptoms Associated With Steroids

Anabolic steroids can be associated with withdrawal symptoms emerging after their abrupt discontinuation. Withdrawal symptoms include (in descending order of prevalence) craving for more steroids, fatigue, depression, restlessness, anorexia (loss of appetite), insomnia, reduced libido (sex drive), headaches, and nausea (Lukas 1998). It is not known how commonly this syndrome occurs, but steroid withdrawal appears more likely in heavy users. The clinician's index of suspicion should be raised when evaluating individuals who are predisposed to steroid misuse and who exhibit these symptoms. Also indicative of possible steroid abuse are certain physiological signs of androgen exposure, including hair loss, acne, dysuria (difficult or painful urination), small testicles, edema of the extremities, and rapid weight gain. Females can develop decreased breast size, acne, virilism (clitoral enlargement, excessive and abnormal bodily hair growth, male pattern baldness) and amenorrhea (suppression of menstruation). Males who abuse steroids have been reported to possess a distorted body image and may inaccurately view themselves as small and weak (Pope et al. 1993).

## Medical Complications of Steroid Withdrawal

Due to anabolic steroids' long duration of action, side effects that might emerge cannot be quickly reversed by the discontinuation of these substances. Therefore, related side effects might require medical management beyond the simple recommendation that steroids immediately be discontinued. Persistent side effects include urinary tract infections, bladder irritability, skin blistering (at the injection site), erythema (abnormal skin redness) when given as a skin patch, and

Interventions directed toward cessation should involve patient education regarding the dangers and medical complications of anabolic steroids, their behavioral effects, and a thorough evaluation of the patient's rationale for misuse.

priapism (prolonged erections lasting hours). The latter condition involves a painful penile erection and constitutes an emergency that requires specialized medical attention. Edema (swelling) of the hands or feet, commonly seen with anabolic steroids, can be treated with diuretics (medications that increase urine flow). Elevated liver function tests and jaundice usually resolve with cessation of anabolic steroid administration, although hepatic carcinoma (cancer of the liver) has been reported. Other side effects such as headache, nausea, vomiting, acne, insomnia, and lethargy are time-limited and resolve after steroid cessation. Behavioral disturbances, such as psychosis or severe aggressiveness, should be treated symptomatically with appropriate psychopharmacological interventions. In extreme cases of psychotic or manic presentations, emergency psychiatric hospitalization might be necessary to address dangerousness to self or others.

## **Management of Steroid Withdrawal**

There is no recommended detoxification protocol for anabolic steroids. The key medical goal is that of persuading the patient to cease steroid misuse. This intervention should be followed by evaluating and treating any side effects (discussed above) that might be present. Interventions directed toward cessation should involve patient education regarding the dangers and medical complications of anabolic steroids, their behavioral effects, and a thorough evaluation of the patient's rationale for misuse. A family meeting often is helpful if agreed upon by the patient. Unfortunately, education alone often is insufficient. Patients with distorted body images might be especially difficult to dissuade from steroid misuse, and referral to psychotherapy by a qualified clinician trained in the treatment of body image disorder should be considered. Similarly, patients who derive significant muscle gain from anabolic steroids might be resistant to cessation and may conceal continued steroid use.

## **Patient Care and Comfort**

Patient comfort during steroid withdrawal can be achieved by addressing side effects, if present, that are discussed above. Counseling also is a useful intervention and specialized psychiatric interventions may be necessary. If the individual also is using other substances of abuse, referral to drug or alcohol rehabilitative treatment should be made.

## **Club Drugs**

Club drugs represent diverse classes of drugs that include sedative-hypnotic type agents as well as stimulant/hallucinogens. Club drugs are illicit drugs used in the setting of nightclubs, dance clubs, parties, and "raves." Raves are overnight dance parties, usually with several hundred people in attendance.

Abuse of these drugs by adolescents and young adults has risen greatly in recent years. All healthcare professionals need familiarity with their short- and long-term effects.

Although withdrawal syndromes have been reported with some of these drugs, this is not the most common clinical problem.

Intoxication and severe intoxication with overdose are more frequent problems. With some of these compounds, there appears to be the potential for neurotoxicity (destructive effects on the nervous system) and persistent psychiatric and neurologic syndromes. At the present time, much of the available information regarding club drugs comes from surveys and anecdotal case reports. Human laboratory studies and rigorously controlled clinical trials are not common.

One difficulty in assessing the effects of intoxication, overdose, withdrawal, and long-term health consequences of club drugs is that in general, there are no baseline evaluations of individuals before they used club drugs. Also, these individuals abuse more than one substance. Some of these patients may have had moderate to severe psychopathology (including psychosis) prior to their introduction to club drugs. In the past, some club drugs were

referred to as “designer drugs” because of their production in a laboratory rather than being processed from plant products.

## Hallucinogens

Hallucinogens are a broad group of substances that can produce sensory abnormalities and hallucinations. Most hallucinogens have some adrenergic effects as well. Hallucinogens also are referred to as psychedelics and psychomimetics. The more traditional hallucinogens such as lysergic acid diethylamide (LSD) are considered primarily serotonergic-acting agents. Some of the other compounds include phenylethylamines which have hallucinogenic properties but act like amphetamines as well. These drugs include mescaline and MDMA (3,4-methylenedioxy-N-methylamphetamine). Other drugs include MDA (3,4-methylenedioxyamphetamine) and DOM (dimethyloxymethylamphetamine). (See section on ecstasy below.) Other hallucinogens are acetylcholine antagonists. These include belladonna, drugs such as benzotrophine used to treat parkinsonian symptoms, and many common over-the-counter antihistamines.

Hallucinogen intoxication often begins with autonomic effects, sometimes nausea and vomiting, and mild increases of heart rate, body temperature, and slight elevations of systolic blood pressure. Dizziness and dilated pupils may occur. The prominent effects during intoxication are sensory distortions with illusions and hallucinations. Visual distortions are more common than auditory or tactile ones. So-called “bad trips” may involve anxiety including panic attacks, paranoid reactions, anger, violence, and impulsivity. Either due to delusions or misperceptions, individuals may feel they can fly or have special powers, and thus injure themselves in falls or other accidents. Suicide attempts also can occur during “bad trips” and possible suicidal ideation should be carefully evaluated, even though it may be quite transient.

Withdrawal syndromes have not been reported with hallucinogens; however, considerable attention has been paid to residual effects such as delayed perceptual illusions with anxiety, “flashbacks,” residual psychotic symptoms, and long-term cognitive impairment. Controversies around these issues are not important in the clinical setting. The important thing is to determine whether residual symptoms are present and provide an appropriate environment and appropriate care for the individual who has them. Generally, staff of emergency rooms, clinics that treat people who abuse substances, and social detoxification centers have individuals who are very familiar with “talking down” individuals with bad hallucinogenic trips.

Acute intoxication and bad trips usually can be managed with placement of the individual in a quiet, nonstimulating environment with immediate and direct supervision so that the patient does not cause harm to herself or to others. Occasionally, a low dose of a short- or intermediate-acting benzodiazepine may be useful to control anxiety and promote sedation. Individuals with chronic depressive-like reactions may require antidepressant therapy. Individuals with residual psychotic symptoms are likely to require antipsychotic medications. On rare occasions, the use of a low dose, high-potency antipsychotic medication may be required orally or parenterally (any method other than the digestive tract, e.g., intravenously, subcutaneously, or intramuscularly). Assessment of residual psychiatric and cognitive symptoms should be made prior to treatment referral.

## Gamma-hydroxybutyrate (GHB)

GHB use has increasingly been reported in night clubs and at raves by adolescents and young adult populations. GHB is a compound that is produced in the central nervous system, and it acts as an inhibiting neurotransmitter similar to GABA (Shannon and Quang 2000). In pharmacologic (medication-propor-

tioned) doses, GHB serves as a sedative-hypnotic medication. GHB intoxication may look like alcohol or sedative-hypnotic intoxication.

Although GHB is illegal, psychotropic compounds similar to GHB such as gamma-hydroxy lactone (GHL) and 1,4-butanediol (1,4-BD) are widely available chemical compounds and may be obtained through catalogs and the Internet. These compounds produce effects similar to those of GHB. At the present, overdose syndromes are more likely to be seen than withdrawal syndromes.

Overdose syndromes may require airway and respiratory management. GHB has been studied in Europe (Addolorato et al. 1999a) in a randomized, single-blind study comparing it to diazepam as a treatment for alcohol withdrawal. GHB was as effective as diazepam in suppressing alcohol withdrawal symptoms and was said to be quicker in reducing anxiety and agitation with less sedation than diazepam. Because of its history of abuse in the United States, it is unlikely to be viewed as a therapeutic agent any time in the near future.

Miotto and Roth (2001) describe a GHB withdrawal syndrome, noting that it shares features of both alcohol and benzodiazepine withdrawal. They have found this syndrome most pronounced in patients who have taken GHB around-the-clock, at 2- to 4-hour intervals. The GHB withdrawal syndrome has the prolonged duration of symptoms found in benzodiazepine withdrawal and features delirium tremens that appear early (often within an hour) with peak manifestations occurring within 24 hours; the delirium may last up to 14 days. Confusion, psychosis, and delirium are the most prominent features of GHB withdrawal, and the autonomic effects (i.e., tremor, diaphoresis [sweating], hypertension, and temperature changes) are less severe than found in alcohol withdrawal. They note that brief periods of significant tachycardia (rapid heart rate) begin early in GHB withdrawal. Garvey and Fitzmaurice (2004) also report seizure activity in a case of GHB withdrawal in a male who had been

using the substance regularly over a 2-year period, and Rosenberg and colleagues (2003) note that in severe cases GHB withdrawal may be life-threatening.

Milder cases of GHB withdrawal syndrome may be managed with benzodiazepines such as lorazepam and supportive care. However, in more severe cases high doses of intravenous benzodiazepines (e.g., lorazepam) or barbiturates (e.g., phenobarbital, pentobarbital) may be required (Miotto and Roth 2001; Rosenberg et al. 2003). Patients experiencing GHB withdrawal are likely to have a high tolerance for the sedative effects of benzodiazepines and require large and frequent doses to manage the withdrawal (Miotto and Roth 2001); in cases where high doses of lorazepam prove ineffective, pentobarbital may be effective (Sivilotti et al. 2001). Clonidine may be used to treat episodes of tachycardia (rapid heart rate) (Miotto and Roth 2001).

## Ecstasy

MDMA (3, 4-methylenedioxy-methamphetamine) commonly known as ecstasy, was synthesized around the turn of the century and patented by Merck Pharmaceuticals in 1914 (Christophersen 2000; Parrot et al. 2000). These drugs are phenel-ethylene stimulants

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with various substitution groups off the benzene ring that give the medications hallucinogenic properties. There are a number of related compounds that are designated by their initials (MDMA, MDA, MDEA, DOM, 2-CB, and DOT). Clinicians are likely to have to manage the complications of intoxication and overdose but not withdrawal.

Patients using MDMA or related compounds frequently are hyperactive and hyperverbal, reporting heightened tactile and visual sensations. They frequently will use camphor on the skin in facial masks, gloves, and other clothing to heighten their tactile sensations. Sometimes light sticks are used to heighten visual experiences at raves. Hyperthermia, dehydration, water intoxication with low sodium, rhabdomyolysis (severe muscular injury and breakdown of muscle fibers), renal failure, cardiac arrhythmia, and coma have been reported.

MDMA has been proven to be toxic to serotonergic neurons in several animal studies. Heavy ecstasy users can have paranoid thinking, psychotic symptoms, obsessional thinking, and anxiety (Parrott et al. 2000). Impaired cognitive performance in heavy ecstasy users also has been identified (Gouzoulis-Mayfrank et al. 2000). Ecstasy users performed more poorly than control groups in complex attention, memory, and learning tasks. The duration or permanence of such effects has not yet been well studied.

## **Ketamine and PCP (Phencyclidine)**

Ketamine and PCP (phencyclidine) were both developed in the 1950s as anesthetic agents for humans. Phencyclidine was briefly marketed for human anesthetic use but taken off the market because of an unusual high incidence of psychotic symptoms. PCP remains in legitimate use for veterinarian anesthesia for large animals as does ketamine for small animals. Although both drugs were originally developed for intravenous use, they are now manufac-

tured illicitly as oral drugs of abuse. PCP frequently is sold as LSD.

Some studies have found that ketamine and PCP act specifically at the MDMA/glutamate receptor as noncompetitive MDMA receptor antagonists. Research in animals indicates that both drugs are reinforcing, in that animals will press a bar to obtain doses of either drug. Furthermore, in these same animal models, abstinence syndromes have been observed. Withdrawal symptoms in humans have included depression, drug craving, increased appetite, and hypersomnolence (excessive sleep).

In the clinical setting, syndromes of acute intoxication with hallucinations, delusions, agitation, and violence are the most pressing problems. A human laboratory study (Lahti et al. 2001) conducted a comparison of ketamine and placebo in normal volunteers never exposed to ketamine and to people with schizophrenia with a previous history of ketamine use. In both groups, ketamine produced a dose-related, but brief, increase in psychotic symptoms. The magnitude of ketamine-induced positive psychotic symptoms was similar for both groups, although the schizophrenia group had higher baseline scores.

Although originally MDMA receptor antagonists were felt to have neuroprotective effects (preventing damage to brain cells) and have been explored as post-stroke medications, there is some evidence now that ketamine and PCP may in fact have some neurotoxic effects. Studies (e.g., Curran and Monaghan 2001) have found greater memory impairment among chronic ketamine users than infrequent ketamine users. Acute human laboratory studies by this group indicate persistent memory impairment with ketamine exposure. This same study did not find persistent psychotic features beyond acute use.

In the clinical setting, ketamine and PCP use require management for the agitation and psychotic features produced during acute use. Occasionally, patients will have such large

overdoses, intentionally or accidentally, that they will require airway management and ventilatory support for some hours. The behavioral management of the agitation and violence that may be seen is best managed in a controlled environment with limited stimuli and very close supervision. Occasionally, oral or parenteral uses of sedating medications such as benzodiazepines will be required. In extreme cases, restraints may be required for protection of the patient and staff.

Following acute management, assessment of persistent mood and cognitive effects must be made prior to any treatment attempts. The persistence of psychotic symptoms may represent an underlying psychiatric disorder that may require medication treatment. There are no studies to guide the treatment of ketamine or PCP detoxification. The need to manage withdrawal symptoms from these drugs is unlikely, but if it should arise, benzodiazepines should be administered.

## Other

Rohypnol is a benzodiazepine that is sold under trade names in Europe and Mexico as a sedative-hypnotic. Rohypnol is occasionally used as a club drug and at dance clubs. In the last decade it began to be smuggled into the United States and was commonly used among homeless youth involved in the sex industry. Rohypnol has a reputation as a “date rape” drug because it can produce powerful amnesic and hypnotic effects, as well as coma. For further details on benzodiazepines, see the benzodiazepine section regarding intoxication and potential withdrawal reactions.

## Management of Polydrug Abuse: An Integrated Approach

One of the most significant changes in detoxification services in recent years has been the increase in the number of patients requiring detoxification from more than one substance.

In an evaluation of admissions to publicly funded detoxification programs in Massachusetts between 1984 and 1996, McCarty and colleagues (2000) found a steady increase in the number of patients using both alcohol and other substances in the month prior to admission. In 1988, 26 percent of admissions reported using two or more substances in the previous month; by 1996 that number had nearly doubled to 50 percent (McCarty et al. 2000). There is no reason to believe that this trend has not appeared elsewhere in this country. As Miller and colleagues (1990*a*) note, “For the contemporary drug addict, multiple drug use and addiction that includes alcohol is the rule” (p. 597).

In the Massachusetts evaluation, which did not include marijuana or nonopioid prescription medication use, the most commonly seen combination of substances was alcohol and cocaine. Thirty percent of patients admitted for detoxification in 1996 reported using this combination; 12 percent used alcohol, cocaine, and heroin together; 10 percent combined alcohol and cocaine; and 7 percent combined heroin and cocaine (McCarty et al. 2000). Other studies, evaluating patient populations at inpatient treatment centers, found that between 70 and 90 percent of patients who reported cocaine abuse also abused alcohol. Rates of alcohol dependence among methadone patients and patients dependent on heroin were between 50 and 75 percent,

One of the most significant changes in detoxification services in recent years has been the increase in the number of patients requiring detoxification from more than one substance.

## **An Example of Potential Problems: Detoxification for Polydrug Abuse**

Mr. L is a 43-year-old male with a 25-year heroin dependence. He is well known to the detoxification center, having been through the program there (which consisted primarily of support and hydration) on many occasions over the years. Though he looked more gaunt and, not surprisingly, a bit more ill each time he arrived, his course usually was about the same: 2 or 3 days of serious stomach cramps, nausea, and diarrhea, then a few days of feeling poorly, and then a return to the community. This time, however, was different. He looked “sicker” than usual. Mr. L usually was a compliant patient; now he was hostile and belligerent. He seemed to be talking to himself and did not seem as alert as he should have been. The staff asked him several times if he had used anything else and each time he denied it. His drug of choice was always heroin—he drank alcohol once in a while, and occasionally smoked marijuana when he could not get anything else. On the third day of detoxification, Mr. L seemed acutely more ill. On his way to the bathroom he was observed staggering, and as he reached for the door he fell, striking his head, and suffered a grand mal seizure. At the local hospital, a toxicological screen showed the presence of PCP, high levels of barbiturates, opioids, and trace amounts of benzodiazepines

and 80 to 90 percent who were being treated for cannabis abuse also reported alcohol abuse (Miller et al. 1990a).

Clinicians need to be constantly aware that a patient may be abusing multiple substances. Even if a patient admits the abuse of one substance he may not admit to using others. Patients may not see that other substances are a problem, they may be worried about the legal consequences of use, or they sometimes may not even be aware of what substances they have been using. For these reasons, clinicians should not rely on patients’ self-reports to determine which substances are being used. Interviews with family, friends, or others who know the patient may be helpful, but these also are insufficient. The consensus panel strongly recommends that all patients receive an immediate urine drug screening upon admission to a detoxification program to determine the types of substances being abused. It is not necessarily true that the person is drug free simply because a drug is not detected on a drug screen. It is possible that the toxicology is not able to detect the class or type of drug. Staff should be aware of what the program/detoxification center/hospital tests for, what is not tested for, what cannot be tested for or found, and the limitations of “dip” tests.

## **Prioritizing Substances of Abuse**

While substances of abuse may have complex interactions, it is not always possible to determine how those interactions will affect withdrawal. Therefore, it is generally best practice to prioritize the substances an individual has been dependent on and treat them sequentially according to the severity of the withdrawal produced by the substance. The substances with the most serious withdrawal syndromes, those where the withdrawal syndrome can be fatal, are alcohol and the sedative-hypnotics. When detoxifying a patient who has been dependent upon multiple substances, the sedative-hypnotics must be addressed first.

Oral methadone, LAAM, or buprenorphine should be used to stabilize withdrawal from opioids while tapering the dose of the sedative-hypnotic or anxiolytic (anti-anxiety medication) by 10 percent each day. After the patient has been tapered off of the sedative-hypnotic or anxiolytic, withdrawal from the substitute opioid can begin (Wilkins et al. 1998). Some patients can successfully be detoxified from both sedative-hypnotics and opioids simultaneously, but this requires a great deal of medical and nursing attention. Most patients will benefit from opioid mainte-

nance for an extended period of time following the completion of sedative withdrawal.

If the patient has been abusing multiple sedative-hypnotic substances or a sedative-hypnotic and alcohol, withdrawal should be handled in the same way as withdrawal from one such substance. The patient should be administered a regularly decreasing dosage of sedative-hypnotic, usually a benzodiazepine that the clinician is comfortable with and accustomed to using. The dosage should be decreased according to the patient's physiologic response. Providers also may administer an anticonvulsant such as carbamazepine (Tegretol XR), even in the absence of epilepsy or withdrawal seizures, to help ensure patient safety (Wilkins et al. 1998). Phenobarbital also may be used for detoxifying patients who have been abusing both alcohol and benzodiazepines. When the dose of alcohol and sedative-hypnotics that a patient is taking is not known, tolerance testing as previously described can be helpful in determining the dose of phenobarbital.

When treating patients detoxifying from substances other than sedative-hypnotics, management of opioid detoxification should be the next priority. Generally, other substances of abuse, including stimulants, marijuana, hallucinogenics (LSD and similar drugs), and inhalants, will not require specific treatment in patients who are being detoxified from sedative-hypnotics and/or opioids.

Patients may abuse a wide range of substances in various combinations, and the clinician must be vigilant in assessing and treating withdrawal from multiple substances. The case study above illustrates some of the serious problems the clinician faces in evaluating and treating patients withdrawing from multiple substances.

In the private sector, where money for toxicological screening is readily available, the first question many would ask concerning the case of Mr. L. is, "Why wasn't the drug screen done sooner?" However, those working in public facilities will recognize that such screenings often are unavailable or available only after an extended turnaround time. Toxicological

screening, even a hand-held screening, can be an expensive item for what often is a very limited budget. Besides, in this case, the patient was believed to be a known quantity—someone who only used heroin.

This scenario is not uncommon. It is likely that the patient himself was unaware of what was in his body. One of the more frightening facts concerning the purchase of illicit drugs is the lack of knowledge of what is in them. To make buyers believe that they are buying a higher-quality product than they are, drugs often are cut with adulterants (inferior ingredients) that can produce effects similar to the drug they think they are buying. In this case, Mr. L. may have been buying barbiturates and benzodiazepines in his heroin for some time without knowing it, a fact that could have had deadly consequences. Both are sedating and could have given him some of the comfortable sedation and euphoria he was seeking from his drug of choice. Unfortunately, however, where opioid withdrawal is not life-threatening, withdrawal from barbiturates can be. Furthermore, he could have gotten PCP in the marijuana he occasionally used, again without knowing it.

## Alternative Approaches

Alternative methods that have been studied scientifically do not claim to be stand-alone withdrawal methods, nor stand-alone treatment modalities. Alternative approaches are designed to be used in a comprehensive, integrated substance abuse treatment system that promotes health and well-being, provides palliative symptom relief, and improves treatment retention. Therefore, because isolation of any of these approaches as an independent variable in rigorous controlled studies is difficult, if not impossible, there are no conclusive data on the effectiveness of alternative methods (Trachtenberg 2000).

Auricular (ear) acupuncture has been used throughout the world, beginning in Hong Kong, as an adjunctive treatment during opioid

detoxification for about 30 years. Its use in the United States originated in California (Seymour and Smith 1987) and New York (Mitchell 1995) but has not been subjected to rigorous controlled research. One report (Washburn et al. 1993) noted that patients dependent on heroin with mild habits appeared to benefit more than those with severe withdrawal symptoms, which acupuncture did not alleviate. The 1997 National Institute of Health Consensus Statement on acupuncture stated that acupuncture treatment for addiction could be part of a comprehensive management program. The National Acupuncture Detoxification Association has developed acupuncture protocols involving ear acupuncture in group settings that originated at Lincoln Hospital in the Bronx and are used by over 400 drug treatment programs and 40 percent of drug courts. SAMHSA's National Survey of Substance Abuse Treatment Services (NSSATS) found that 5.4 percent of the 13,720 facilities polled in 2001 offered acupuncture as a service (Office of Applied Studies 2002b).

Acupuncture is one of the more widely used alternative therapies within the context of addictions treatment. It has been used as an adjunct to conventional treatment because it seems to reduce the craving for a variety of substances of abuse and appears to contribute to improved treatment retention rates. In particular, acupuncture has been viewed as an effective adjunct to treatment for alcohol and cocaine disorders, and it also has played an important role in opioid treatment (i.e., methadone maintenance). It is used as an adjunct during maintenance, such as when tapering methadone doses. The ritualistic aspect of the practice of acupuncture as part of a comprehensive treatment program provides a stable, comfortable, and consistent environment in which the client can actively participate. As a result, acupuncture enhances the client's sense of engagement in the treatment process. This may, in part, account for reported improvements in treatment retention (Boucher et al. 2003). A 1999 CSAT-funded study showed that patients

choosing outpatient programs with acupuncture were less likely to relapse in the 6 months following discharge than were patients who had chosen residential programs (Shwartz et al. 1999).

Ear acupuncture detoxification, which was originally developed as an alternative treatment for opioid agonist pharmacotherapy, is now augmenting pharmacotherapy treatment for patients with coexisting cocaine problems (Avants et al. 2000). The advocates of acupuncture have joined with the advocates of opioid agonist pharmacotherapy to create a holistic synthesis. Each has contributed to the success of the other, both clinically and in public perception.

Care must be taken to ensure sterile acupuncture needles in the heroin-dependent population, given the high incidence of HIV infection, viral hepatitis, and other infections. Acupuncture is not recommended as a stand-alone treatment for opioid withdrawal.

Other alternative management approaches that are not supported by controlled studies include neuroelectric therapy (the administration of electric current through the skin) and herbal therapy. In fact, the former has been shown to be no better than placebo in a controlled study (Gariti et al. 1992). The use of herbs for healing purposes dates back to the dawn of civilization, while the use of herbs in the treatment of substance abuse has been documented since 1981 in methadone programs, free clinics, therapeutic communities, outpatient programs, and hospitals (Nebelkopf 1981). Herbal remedies are used in substance abuse detoxification and treatment in a number of cultures around the world. However, in no scientific studies have herbs been isolated as a discrete variable to test their efficacy. Much research is currently being conducted on the effectiveness of herbal medicine on a wide variety of physical conditions.

## Considerations for Specific Populations

All individuals undergoing detoxification are especially vulnerable. Patients who experience negative attitudes from staff may experience further loss of self-esteem, may leave detoxification prematurely, or may experience other psychologically damaging feelings. Negative experiences can undermine the recovery process. It is important to recognize that individuals do not fit into just one population category. A person will be a member of several populations (e.g., a Latina woman who is pregnant, bisexual, and has psychiatric diagnoses of post-traumatic stress disorder and major depression) and may benefit from a number of the considerations discussed below. It also should be noted that the information in the specific populations sections should not be used to categorize individuals or leave the reader with the impression that the information below will fit all individuals who are members of a group.

### Pregnant Women

While in detoxification, pregnant women should receive comprehensive medical care, especially since this may be the first time they have sought any type of care or treatment. Ideally, programs detoxifying pregnant women from alcohol and illicit drugs should include the following services:

- Detoxification on demand
- Woman-centered medical services
- Transportation services to and from detoxification (as well as to substance abuse treatment afterward)
- Childcare services
- Counseling and case management services
- Access to drug-free, safe, affordable housing
- Help with legal, nutritional, and other social service needs

While it is recognized that provision of all of these services is an ideal to be striven for, at a minimum detoxification programs must have

strong linkages to agencies that provide the above-mentioned services and should set up systems to ensure that pregnant women can access the additional services they need.

Pregnant women who present for detoxification will benefit from a comprehensive medical examination that includes a careful obstetrical component. Since it is estimated that approximately 44 to 70 percent of women who abuse substances have a history of physical, emotional, and sexual abuse (Moylean et al. 2001; Stevens et al. 1997), care should be given to the comfort of the patients during the examination. One of the major internal barriers that prevents pregnant women from seeking treatment is the shame and stigma attached to substance use, especially during pregnancy. Any negative experience encountered during detoxification can lead these women to leave treatment and not return.

Detoxification during pregnancy poses a special risk in that care should be taken to ensure the health and safety of both the mother and fetus. From a clinical standpoint, before giving any medications to pregnant women it is of vital importance that they understand the risks and benefits of taking these medications and sign informed consent forms verifying that they have received and understand the information provided to them. Since pregnant women often present to treatment in mid- to late-second trimester and poly-drug use is the norm rather than the exception (Jones et al. 1999), it is important first to

Pregnant women who present for detoxification will benefit from a comprehensive medical examination that includes a careful obstetrical component.

screen these women for dependence on the two classes of substances that can produce a life-threatening withdrawal: alcohol and sedative-hypnotics. Pregnant women should be made aware of all wraparound services that will assist them in dealing with newborn issues, including food, shelter, medical clinics for inoculations, as well as programs that will help with developmental or physical issues that the neonate (newborn baby) may experience as a result of substance exposure.

A National  
Institutes of  
Health consensus  
panel  
recommended  
methadone  
maintenance as  
the standard of  
care for pregnant  
women with  
opioid  
dependence.

### **Alcohol**

When pregnant women are detoxified from alcohol, benzodiazepine tapers appear to be the current practice of choice. The current state of knowledge suggests that benzodiazepine therapy in general does not have as much of a teratogenic (producing a deformed baby) risk as do other anticonvulsants as long as they are given over a short time period. It appears that short-acting benzodiazepines, like the ones described to treat alcohol withdrawal above, can

be used in low doses for acute uses such as detoxification, even in the first trimester (Robert et al. 2001). Long-acting benzodiazepines should be avoided—their use during the third trimester or near delivery can result in a withdrawal syndrome in the baby (Garbis and McElhatton 2001).

Although no teratogenic effects have been observed, little is known about the effects of

naltrexone, naloxone, or nalmefene administration during pregnancy. Although propranolol (Inderal), labetalol (Trandate), and metoprolol (Lopressor) are the beta blockers of choice for treating hypertension (high blood pressure) during pregnancy (McElhatton 2001), the impact of using them for alcohol detoxification during pregnancy is unclear. The use of SSRIs, a class of antidepressant medication, is safer for the mother and fetus than are tricyclic antidepressants (Garbis and McElhatton 2001). Fluoxetine (Prozac) is the most studied SSRI in pregnancy and no increased incidence in malformations was noted, nor were there neurodevelopmental effects observed in preschool-age children (Garbis and McElhatton 2001). However, possible neonatal withdrawal signs have been observed. Given that the greatest amount of data are available for fluoxetine, this is the recommended SSRI for use during pregnancy (Garbis and McElhatton 2001).

The use of anticonvulsants, such as valproic acid, is associated with several disfiguring malformations. If this type of medication must be used during pregnancy, the woman must be told that there is substantial risk of malformations (Robert et al. 2001). Barbiturate use during pregnancy has been studied to some extent, and phenobarbital is used therapeutically during pregnancy, but the risk of any anticonvulsive medication should be discussed with the patient (Robert et al. 2001). There also are reports of a withdrawal syndrome in the neonate following prenatal exposure to phenobarbital (Kuhn et al. 1988).

### **Opioids**

While it is not recommended that pregnant women who are maintained on methadone undergo detoxification, if these women require detoxification, the safest time to detoxify them is during the second trimester. For further information, consult the forthcoming TIP *Substance Abuse Treatment: Addressing the Specific Needs of Women* (CSAT in development *e*) and TIP 43

*Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs* (CSAT 2005*d*). In contrast, it is possible to detoxify women dependent on heroin who are abusing illicit opioids by using a methadone taper.

Before starting a detoxification, women should weigh the risks and benefits of detoxification, since many women eventually relapse to drug use and thus place themselves and their fetuses at risk for adverse consequences (Jones et al. 2001*b*). During pregnancy, the protein binding of many drugs, including methadone and diazepam (a benzodiazepine), is decreased (e.g., Adams and Wachter 1968; Dean et al. 1980; Ganrot 1972) with the greatest decrease noted during the third trimester (Perucca and Crema 1982). This decreased binding may be due to the decreased levels of albumin reported during pregnancy (Yoshikawa et al. 1984). From a clinical standpoint, it may be that pregnant women could be at risk for developing greater toxicity and side effects, yet at the same time an increase in metabolism of the drug may result (such as found with methadone). This may result in reduced therapeutic effect from the drug, since many women require an increase in their dose of methadone during the last trimester (Pond et al. 1985).

Other medications used to treat the withdrawal signs and symptoms include clonidine. Clonidine is used as a second-line drug to treat hypertension (high blood pressure) during pregnancy and appears to lack teratogenic effects (McElhatton 2001). It has reportedly been abused by pregnant women. Some pregnant women take clonidine with their methadone because it is hard to detect in urine and it increases the high they get from methadone. However, little is known about its effects on the baby following therapeutic doses given in a detoxification context or doses taken in higher than therapeutic amounts (Anderson et al. 1997*a*). Buprenorphine has been examined in pregnancy and appears to lack teratogenic effects

but may be associated with a withdrawal syndrome in the neonate (Jones and Johnson 2001).

A National Institutes of Health consensus panel recommended methadone maintenance as the standard of care for pregnant women with opioid dependence. Methadone currently is the only medication recommended for medication-assisted treatment for pregnant women. Clinical trials are being conducted to determine the efficacy and safety of buprenorphine with pregnant women but it has not yet been approved for use with this population. Two early studies on treatment of pregnant women with opioid dependence with buprenorphine showed promising results (Fischer et al. 2000; Johnson et al. 2001). Comer and Annitto (2004) conclude, from their review of the research literature, that buprenorphine should be used more aggressively to detoxify pregnant women who want to be opioid-free at delivery.

Because of the potential for premature labor and delivery and risks of morbidity and mortality to the fetus related to withdrawal from opioids, it is recommended that a pregnant woman who is dependent on opioids be maintained during pregnancy (Kaltenbach et al. 1998). Other reasons to stabilize a pregnant woman on methadone rather than attempt withdrawal are the risks of relapse, consequences associated with HIV and use of multiple needles, and the potential lack of prenatal care.

The Federal government mandates that prenatal care be available for pregnant women on methadone. It is the responsibility of treatment providers to arrange this care. More than ever, there is need for collaboration involving obstetric, pediatric, and substance abuse treatment caregivers. Comprehensive care for the pregnant woman who is opioid dependent must include a combination of methadone maintenance, prenatal care, and substance abuse treatment.

Pregnant women should be maintained on an adequate (i.e., therapeutic) methadone dose. An effective dose prevents the onset of withdrawal for 24 hours, reduces or eliminates drug craving, and blocks the euphoric effects of other narcotics. An effective dose usually is in the range of 50–150mg (Drozdzick et al. 2002). Dosage must be individually determined, and some pregnant women may be able to be successfully maintained on less than 50mg while others may require much higher doses than 150mg. The dose often needs to be increased as a woman progresses through gestation, due to increases in blood volume and metabolic changes specific to pregnancy (Drozdzick et al. 2002; Finnegan and Wapner 1988).

Generally, dosing of methadone is for a 24-hour period. However, because of metabolic changes during pregnancy it might not be possible to adequately manage a pregnant woman during a 24-hour period on a single dose. Split dosing, particularly during the third trimester of pregnancy, may stabilize the woman's blood methadone levels and effectively treat withdrawal symptoms and craving.

Breastfeeding is not contraindicated for women who are on methadone. Very little methadone comes through breast milk; the American Academy of Pediatrics (AAP) Committee on Drugs lists methadone as a “maternal medication usually compatible with breastfeeding” (AAP 2001, pp. 780–781).

## ***Benzodiazepines***

The principles of detoxification from benzodiazepines are the same for pregnant and nonpregnant patients. It is important to taper the dose of benzodiazepine slowly in order not to induce fetal withdrawal or other adverse consequences in the fetus or mother. Detoxification is most likely safest during the second trimester in order to avoid spontaneous abortion or premature labor. For more information, see the forthcoming TIP *Substance Abuse Treatment: Addressing the*

*Specific Needs of Women* (CSAT in development *e*). There is a documented withdrawal syndrome in neonates who have been prenatally exposed to benzodiazepines (Sutton and Hinderliter 1990), and this syndrome may be delayed in onset more than that associated with other drugs.

## ***Stimulants***

The principles of detoxification from stimulants such as cocaine are the same for pregnant and nonpregnant women. Since there is no current pharmacotherapy to use in tapering individuals from stimulant use, the use of any medications to treat medical complications that might arise from the withdrawal should only be done after discussion with the patient of the risks and benefits of each medication.

## ***Solvents***

The principles of detoxification from solvents are the same for pregnant and nonpregnant women. It should be noted that based on a review of case reports, there is a complex array of characteristics that appear to be similar to fetal alcohol effects. Fetal Alcohol Syndrome (FAS) is characterized by growth deficiency (born small for gestational age; failure to grow at a normal rate), particular facial features (e.g., eyes are too close together, ears are set low on the head), and CNS dysfunctions (mental retardation, microcephaly [small brain size] and brain malformations (Costa et al. 2002). Thus fetal development in pregnant women who have a history of solvent abuse should be evaluated and carefully monitored (Jones and Balster 1998).

## ***Nicotine***

There is extensive documentation that smoking during pregnancy causes numerous adverse fetal consequences (see Schaefer 2001). Cigarette smoking during pregnancy is the largest modifiable risk for pregnancy-related morbidity and mortality in the United States (Dempsey and Benowitz 2001). While women

are undergoing detoxification, they should be offered education about the risk of cigarette smoking during pregnancy and, ideally, prevented from smoking. This is especially important since cigarette smoking is strongly associated with decreased birth weight, which is a predictor of developmental problems in newborns (Ernst et al. 2002). If women are unable to stop smoking using behavioral interventions, nicotine replacement products may be used; however, the woman should fully understand the possible risks and benefits of these pharmacotherapies (Jones and Johnson 2001).

It also is important to point out to patients that there are data to suggest that women may derive less benefit from NRT than do men and that they may derive greater benefit from some non-NRT medications (e.g., bupropion), thus producing quit rates in women comparable with those in men (Perkins 2001). However, the data regarding the use of bupropion during pregnancy are limited.

Examinations of the acute effects of NRT in pregnant women reveal that nicotine has minimal impact on the maternal and fetal cardiovascular systems. NRT may well be viewed as the lesser of two evils, inasmuch as smoking cigarettes delivers, in addition to nicotine, thousands of chemicals. Among these are many that also are viewed as developmental toxins (e.g., carbon monoxide and lead). It is doubtful that the reproductive toxicity of cigarette smoking is primarily related to nicotine. Thus, if NRT is to be used during pregnancy, the dose of nicotine in NRT should be similar to the dose of nicotine that the pregnant woman received from her ad lib (when desired) smoking. Although intermittent-use formulations of NRT (e.g., chewing gum) have been recommended over continuous-use formulations (e.g., transdermal patch) due to reductions in the total dose of nicotine delivered to the fetus (Dempsey and Benowitz 2001), it is unknown what the impact of intermittent acute doses followed by withdrawal of nicotine has on the fetus.

## **Marijuana, anabolic steroids, and club drugs**

The principles of detoxification from these drugs is the same for pregnant and nonpregnant women. The use of anabolic steroids during pregnancy is rare; however, these can be catastrophic to a pregnancy, and if use is found, a detailed ultrasound examination is recommended to determine the morphological (physical or structural) development of the fetus (Scialli 2001).

Although the class of club drugs is relatively new there have been a few reports (McElhatton et al. 1999) suggesting that there is an increased risk of congenital malformation in neonates prenatally exposed to ecstasy. Other club drugs such as flunitrazepam (Rohypnol) may have effects similar to those of some benzodiazepines; however, this is speculative. For comprehensive information on the treatment of this specific population, see the forthcoming TIP

*Substance Abuse Treatment:*

*Addressing the Specific Needs of Women* (CSAT in development *e*).

## **Older Adults**

It has been recommended that, when treating older adults, there should be a policy of using age-specific group treatment that is both supportive and nonconfrontational (Royer et al. 2000; West and Graham 1999). Older adults may be dealing with depression, loneliness,

While women are undergoing detoxification, they should be offered education about the risk of cigarette smoking during pregnancy and, ideally, prevented from smoking.

and loss of career or a loved one. Thus, as a standard policy, older adults should be screened for depression and grief or loss-related issues. Similar to the situation with other specific populations, the detoxification setting should ideally have in place a policy that mandates, at a minimum, well-established linkage with general medical services and specialized services for the aging, because of their increased vulnerability to physical ailments. Establishing policies that create an environment that is positive and does not tolerate “ageism”—a general tendency to react negatively toward elderly adults—is important for the optimal treatment of older individuals.

Alcohol and other drug-related disorders in elderly individuals often are more severe than those of younger individuals and they are at increased risk for co-occurring medical disorders. It is the medical complications rather than age itself for which detoxification in a medical setting is needed. The elderly may have slower metabolism of medications making dosage adjustments necessary in some cases. The elderly also may be at greater risk for drug interactions, since they may be receiving medications to treat other problems. A complete and careful assessment with ongoing monitoring should be done to examine the existence of diseases such as, but not limited to, heart disease, respiratory disease, diabetes, and dementia. Potential for falls also should be evaluated in the context of prescribed medications. The previously presented protocols for detoxification from alcohol, opioids, benzodiazepines, stimulants, solvents, nicotine, marijuana, anabolic steroids, and club drugs (anabolic steroids and club drug abuse are rare in this population) appear to be applicable to the elderly population as long as sensitivity to the withdrawal medication is considered. TIP 26, *Substance Abuse Among Older Adults* (CSAT 1998f), provides comprehensive information on the treatment of this population.

## People With Disabilities or Co-Occurring Conditions

In any patient population, the clinician should expect to encounter persons with disabilities including co-occurring medical or mental disorders. These patients often will require special assistance to overcome both physical and psychological barriers in undergoing detoxification and treatment, including their own psychological barriers that must be overcome, as well as those attitudinal and communication barriers that often prevent complete and clear understanding between patient and clinician or clinician and institution. Effective communication is essential for effective services. Accommodations must take into consideration the expressed preference of the individual with a disability. Substance abuse treatment programs need to be in compliance with two Federal laws regarding this matter: the 1992 Amendments to the Rehabilitation Act of 1973 and the Americans with Disabilities Act [ADA] of 1990.

According to the ADA, programs must remove or compensate for physical or architectural barriers to existing facilities when accommodation is readily achievable, meaning “easily accomplishable and able to be carried out without much difficulty or expense” (P.L. 101-336 § 301). Providers should examine their programs and modify them to eliminate four fundamental groups of barriers to treatment for people with disabilities and/or co-occurring disorders: (1) attitudinal barriers; (2) discriminatory policies, practices, and procedures; (3) communications barriers; and (4) architectural barriers. Federal, State, and other sources of assistance might be available to fund ADA-related improvements. See TIP 29, *Substance Use Disorder Treatment for People With Physical and Cognitive Disabilities* (CSAT 1998g) for further information.

The following passage clarifies terms and addresses the basic issues presented by patients with disabilities and/or co-occurring disorders. Diseases, disorders, and injuries,

whether congenital or acquired, can have diverse effects on organs and body systems. Conditions (and *diseases*) such as multiple sclerosis, traumatic brain injury, spinal cord injury, diabetes, and cerebral palsy can lead to *impairments*, such as impaired cognitive ability, paralysis, blindness, or muscular dysfunction. These impairments in turn cause *disabilities*, which limit an individual's ability to function in various areas of life, such as learning, reading, and mobility. While diseases, impairments, and disabilities are distinct categories, they often are used interchangeably. These essential terms are defined in Figure 4-15.

The field of disability services has developed its own terminology to discuss physical, sensory, and cognitive disabilities (see definitions below), and many treatment providers of people with substance use disorders will not be familiar with these terms as the profession defines them. WHO has devised a method for the classification of impairments and disabili-

ties (WHO 1980). This complex system has been simplified here into four main categories:

1. *Physical* impairments are caused by congenital or acquired diseases and disorders or by injury or trauma. For example, spinal cord injury is a disorder that can cause paralysis, an impairment.
2. *Sensory* impairments include blindness and deafness, which may be caused by congenital disorders, diseases such as encephalopathy or meningitis, or trauma to the sensory organs or the brain.
3. *Cognitive* impairments are disruptions of thinking skills, such as inattention, memory problems, perceptual problems, disruptions in communication, spatial disorientation, problems with sequencing (the ability to follow a set of steps in order to accomplish a task), misperception of time, and perseveration (constant repetition of meaningless or inappropriate words or phrases).

### **Figure 4-15** **Some Definitions Regarding Disabilities**

**Disease:** An interruption, cessation, or disorder of body functions, systems, or organs.

**Impairment:** Any loss or abnormality of psychological, physiological, or anatomical structure or functions.

**Disability:** Any restriction or lack (resulting from an impairment) of the ability to perform an activity in the manner or within the range considered normal for a human being. A disability is always perceived in the context of certain societal expectations, and it is only within that context that the disadvantages resulting from a disability can be properly evaluated.

**Functional capacities:** The degree of ability possessed by an individual to meet or perform the behaviors, tasks, and roles expected in a social environment.

**Functional limitations:** The inability to perform certain behaviors, fulfill certain tasks, or meet certain social roles as a consequence of a disability. Those limitations can be anatomical (e.g., amputation), physiological (e.g., diabetes), cognitive (e.g., traumatic brain injury), sensory (e.g., blindness, deafness), or affective (e.g., depression) in origin and nature. They represent substandard performance on the part of the individual in meeting life activities and reflect the interaction between the person and the environment. (A list of the areas of functional capacity and disabilities most often assessed is in Figure 4-16, p112.)

*Sources:* Livneh and Male 1993; Stedman 1990; World Health Organization (WHO) 1980.

**Figure 4-16**  
**Impairment and Disability Chart**

Impairment Category	Common Disabilities
Physical	Spina bifida Spinal cord injury Amputation Diabetes Chronic fatigue syndrome Carpal tunnel Arthritis
Sensory	Blindness Hearing impairment Deafness Deaf-blindness Visual impairment
Cognitive	Learning disabilities Traumatic brain injury Mental retardation Attention deficit disorder
Affective	Depression Bipolar disorder Schizophrenia Eating disorder Anxiety disorder Posttraumatic stress disorder

*Source:* CSAT 1998e.

4. *Affective* impairments are disruptions in the way emotions are processed and expressed. For the purposes of this discussion, affective impairments are considered to include problems caused by both affective and mood disorders, such as major depression and mania. These impairments include the symptoms of mental disorders, such as disorganized speech and behavior, markedly depressed mood, and anhedonia (joylessness).

One of the most important practices that should be in place as a standard in any detoxification setting is routine screening for dis-

abilities and co-occurring medical and/or psychiatric conditions. The failure to recognize these problems in patients can result in poor outcomes (Cook et al. 1992). Additionally, intoxicated individuals with co-occurring depressive disorders are at high risk for suicide attempts. Of course, an individual patient may present with two or more disabilities and/or co-occurring disorders. Clinicians treating people with co-occurring substance use and mental disorders should consult TIP 42, *Substance Abuse Treatment for Persons With Co-Occurring Disorders* (CSAT 2005b).

All programs should make a good faith effort to provide equal access in as comprehensive a manner as possible for all patients. Individual unique needs should be taken into account when providing services. For example, patients with physical, sensory, or cognitive disabilities may need help with self-care (e.g., eating, grooming), moving (e.g., using stairs, walking), communication (e.g., reading, speaking), learning, social skills, and executive functions (e.g., planning and organization, decisionmaking). Unresponsiveness to instructions, lack of participation in discussions and activities, forgetfulness, or confusion by an individual with cognitive disabilities should not be viewed as a lack of motivation, resistance, or denial. Programs may need to develop the expertise or engage an expert on cognitive disabilities to determine the limitations resulting from the substance abuse and those resulting from the disability. Both require patience in the response. Information presented to the person with a cognitive disability should include different and complementary media; for example, visual and tactile materials can reinforce the usual verbal interaction.

Programs also may need to alter their policies regarding the use of drugs prescribed for pain control, since most medications of this class are drugs with a high abuse potential. A number of patients with substance use disorders also live with chronic pain. Living in a drug-free state may not be desirable if it is associated with unrelieved pain, which can be quite disabling. The clinician should explore with patients what pain management options have been tried in the past, and which management medications are being used currently. Patients should be encouraged to discuss their feelings about pain and how it affects their daily life, and especially to what extent it curtails or prevents their participation in the activities of daily living.

There are a number of alternative treatments for chronic pain. Acupuncture is already in use in some treatment programs for detoxification to help relieve symptoms of withdraw-

al. Physical therapy and exercise, chiropractic care, biofeedback, hypnotism, and therapeutic heat or cold are some other approaches to caring for persons with physical problems. Most of these alternative treatments have limited or no research support of their efficacy; yet some clinicians believe they work. Thus, consultation with experts on their use is necessary before starting a person with chronic pain on these remedies.

An alternative model supports the idea that patients should be treated simultaneously in substance abuse treatment, mental/physical health, and detoxification settings, yet treatments may occur in separate facilities and be conducted by separate staff. The consequent task for all is to be supportive and knowledgeable about each other's interventions. The severity of the addiction and medical/psychiatric problems at the time of detoxification entry should determine which acute services the patient receives first. Naturally, a person's medical and psychiatric disabilities must be accounted for in the preparation of any treatment plan. In some cases, substance abuse treatment cannot begin until issues relating to medical and psychiatric disabilities are settled.

There are a number of resources for clinicians to employ, including experts in the field of disability services. Figure 4-17 (p. 114) discusses ways of locating expert help for treating patients with disabilities and/or co-occurring disorders.

Finally, integrated treatment combines substance abuse treatment, treatment for co-occurring disorders, and detoxification services into one program. For more complete information on the treatment of many of these disorders, see chapter 5.

## **African Americans**

For African Americans, entrance into detoxification has been associated with enrolling in further treatment, reductions in HIV/AIDS risk behaviors, and linkages with social and health-

## Figure 4-17 Locating Expert Assistance

“Experts” in disability services can be located in several ways, depending upon the nature of the patient’s disability and the local resources available. Patients who understand their disability may in fact be the best “experts” on their condition and specific needs; however, it is not uncommon that persons requiring treatment for substance use disorders will not understand basic aspects of their situation or condition. In such cases, immediate family members or close friends may be important sources of information and guidance. The treatment team also should consider contacting other sources:

- A disability-specific service organization (e.g., United Cerebral Palsy, organizations for the blind or deaf such as the National Association of the Deaf and American Deafness and Rehabilitation Association, the Association for Retarded Citizens)
- Social workers
- Case managers
- Rehabilitation specialists
- Psychologists
- Nurses or physicians associated with a social service agency providing disability services for the individual patient in question (e.g., vocational rehabilitation, family services for people who are deaf and hard of hearing, the Department of Veterans Affairs’ physical rehabilitation unit, community case management services)
- Other organizations recognized by the disability community (e.g., Centers for Independent Living, governors’ committees for persons with disabilities, Paralyzed Veterans of America, local or State consumer coalitions for persons with disabilities)

Source: CSAT 1998e.

care services (Lundgren et al. 1999). African Americans are at greater risk than other populations for the co-occurrence of diabetes and hypertension (high blood pressure) that can predispose them to a risk of stroke. This should be taken into account when placing and monitoring them on withdrawal medications.

In treating African-American patients, treatment efficacy and therapist efficacy may be associated with the therapist’s understanding of how race plays a role in recovery (Luborsky et al. 1988; Pena et al. 2000). In addition, when working with counselors from other cultures, African Americans may display mistrust and a reluctance to show any weakness. To overcome this mistrust and to build rapport, especially when the clinician is discussing the detoxification process, it is particularly important for the clinician to keep in

mind the standard of respecting the client as an equal partner in treatment. For further information on this subject (as well as information on working with members of other cultural/ethnic groups), see the forthcoming TIP *Improving Cultural Competence in Substance Abuse Treatment* (CSAT in development a).

The previously discussed protocols for detoxification from all substance of abuse appear adequate for the detoxification of African Americans. However, there are a few further aspects to consider:

- If treating African Americans with beta blockers, propranolol is less effective in treating African Americans than Caucasians (Pi and Gray 1999).
- African Americans are more likely (15 to 25 percent) to have less of the enzyme activity

needed to eliminate diazepam than others, so it may have a longer half-life in African Americans than it does in other ethnic groups (Pi and Gray 1999).

- Since co-occurring disorders such as depression frequently are seen in people with substance use disorders, it is important to know that African Americans may require lower doses and may be at greater risk of developing toxic side effects when prescribed antidepressants, since they are likely to metabolize tricyclic antidepressants and SSRIs less efficiently than Caucasians (Pi and Gray 1999).
- Although the clearance of nicotine is similar for African Americans and Caucasians, the clearance of cotinine, a metabolite of nicotine, is slower in African Americans, which may cause different smoking patterns than found in Caucasians (Ahijevych 1998).

## Asians and Pacific Islanders

This group is the most diverse in nations of origin and has widely differing languages, beliefs, practices, dress, and values. Often the only common thread among these people is their geographic origin (Chang 2000). Although this group appears to have lower rates of alcohol and illicit drug use, these problems should not be overlooked; members of this group may not seek treatment until the problems are quite severe. Successful treatment involves the family and important values include balance, harmony, wisdom, and modesty. Thus, it may be important to talk to the family about the process of detoxification and dispel their fears and concerns as well as the patient's.

Asians and Pacific Islanders tend to be concerned about the clinician's credibility and trustworthiness. Generally speaking, maleness, mature age, the projection of self-confidence, possession of sound cultural competence skills, good educational background, and level of experience are of importance. In addition, a concrete logical approach to the problem at hand is valued (Brems 1998). The previously discussed protocols for detoxification from all substances of abuse appear ade-

quate for the detoxification of Asians and Pacific Islanders. During the detoxification process, there are a number of issues to consider:

- If possible and appropriate, incorporate traditional healing methods (e.g., meditation and religious exercises). These can help reduce stress and anxiety and promote recovery (Chang 2000). While there is a large immigrant population among many Asian-American groups, it is erroneous to assume that all are foreign born. Variation in practice of traditional healing methods is considerable and consistent with generational differences. When considering detoxification, recognize the importance of bicultural practices, values, and beliefs that might influence responsiveness to treatment.
- When discussing detoxification medications, discuss with patients their feelings about taking "Western" medications for detoxification. In some Southeast Asian cultures, Western medications are believed to be too strong for the Asian person. It is important to assess a person's feelings about these since the patient may not wish to disagree with the clinician yet may be noncompliant in taking the medications. Compliance with detoxification medication may be better achieved if doses are reduced or regimens shortened, yet this should only be attempted if it is in the best interest of the patient.
- Racial differences in alcohol sensitivity among Asians and Caucasians have long been recognized, with more than 80 percent of some Asians compared to 10 percent of Caucasians being sensitive to alcohol (i.e., having a flushing reaction) (Wolff 1972, 1973). This is the result of genetic differences in alcohol metabolizing enzymes. Approximately 50 percent of Asians lack the enzyme ALDH2, found in the liver, that helps the body get rid of alcohol (Hsu et al. 1985; Yoshida et al. 1985). One reason for lower drinking rates among Asians may be the flushing reaction in the face and body following alcohol ingestion and an increase in skin temperature. Other uncomfortable signs and symptoms associated with the negative reac-

tion to alcohol ingestion can include nausea, dizziness, headache, fast heartbeat, and anxiety (Caetano et al. 1998).

- Five studies have shown that the metabolism of codeine is slower in Chinese people than in Caucasians. Chinese patients seem to require lower doses of codeine, since the slower metabolism leads to a higher concentration of codeine in the blood (Smith and Lin 1996).
- If treated with beta blockers, Asians require much lower doses than Caucasians, since they are very sensitive to this medication's blood pressure and heart rate effects (Pi and Gray 1999).
- Asians as a group have a higher number of individuals than other ethnic groups who are poor metabolizers of diazepam. This may result in the need for lower doses, since they report greater sedative effects with a typical dose (Lesser et al. 1997). It also may be that a lower body fat, which is typical of Asian-American individuals, can lead to differences in the pharmacokinetics of lipophilic drugs (Lesser et al. 1997).
- In treatment for co-occurring depression and a substance use disorder, Asians appear to metabolize clomipramine more slowly than Caucasians (Pi and Gray 1999). In contrast, Asians may metabolize phenelzine faster, resulting in the need for a higher dose relative to that which would be appropriate for Caucasians (Pi and Gray 1999).
- Chinese Americans tend to metabolize nicotine 35 percent more slowly than Hispanics/Latinos and Caucasians. Thus, they may need to smoke less frequently and take in less nicotine to achieve the same nicotine levels as do Hispanics/Latinos and Caucasians. This may have implications for the dosing of NRTs (Benowitz et al. 2002).
- Smoking rates among male Asian Americans, especially immigrant males, are exceedingly high and masked by the lower rates among Asian-American females.

## American Indians

There are currently more than 500 federally recognized American-Indian tribes, and there is among them great variability in appearance, dress, values, religious beliefs, practices, and traditions. More than 200 different languages are spoken by American-Indian tribes. Alcohol use varies widely among tribes (Mancall 1995). Of all ethnic and racial groups, American Indians have the greatest rates of alcohol and illicit drug use (Office of Applied Studies 2002a).

An early study of treatment utilization by American Indians found that there was a significant association between involvement in society and treatment outcomes. Those involved in either the traditional Indian society or both the traditional Indian society and Caucasian society had more than a 70 percent success rate, whereas those involved in neither society had a 23 percent success rate (Ferguson 1976). At a 10-year followup, those who had reported greater Indian culture affiliation and more severe liver dysfunction at baseline had better alcohol treatment outcomes (Westermeyer and Neider 1984).

When engaging an American Indian in the process of detoxification, moving through the process too quickly or abruptly can be perceived as showing a lack of caring and is considered contrary to trust building (Brems 1998). The pace of conversation is important; a slower pace is more agreeable than a rapid conversation. Moreover, a confrontational approach also is not advised with this population (Abbott 1998). American Indians may want a close and involved relationship with their therapists and often want the clinician to be a friend or relative (Brems 1998). The trust often is built by idle small talk to a level of shared understanding. Use of fables and illustrative stories to express ideas can be extremely helpful. According to the forthcoming TIP *Improving Cultural Competence in Substance Abuse Treatment* (CSAT in development a), avoidance of eye contact also is traditional. The Talking Circle is a native tra-

dition that can be helpful in the treatment process (Canino et al. 1987; Coyhis 2000). The previously discussed protocols for detoxification from all substances of abuse appear adequate for the detoxification of American Indians. The following are some issues to consider during detoxification.

- Fetal Alcohol Syndrome is 33 times higher in this population than the national average (CSAT in development *a*). This may be important for pregnant women coming to detoxification and also may be important if the adult has FAS.
- Indian women who drink have a six-fold increase in cirrhosis of the liver relative to Caucasian women (Heath 1989).
- Although some American Indians have reported a flushing response to alcohol, it appears that the flushing reaction in American Indians is milder and less adverse than that experienced by Asians (Gill et al. 1999).
- If Alcoholics Anonymous or other 12-Step programs are to be introduced, framing the steps in terms of a circle rather than a ladder may be better received, since the circle is important concept in Indian culture (CSAT in development *a*).
- If possible and appropriate, other traditional methods that can help recovery are sweat lodges, vision quests, smudging ceremonies, sacred dances, and four circles (Abbott 1998).
- Overall, detoxification for this population is the same as for other populations, but American Indians are likely to seek treatment later and have more medical complications and poorer nutrition (Abbott 1998).

## Hispanics/Latinos

Hispanics/Latinos are now the largest ethnic minority group in America. Assessment of the patient's level of acculturation can be helpful in understanding substance abuse patterns. Language is one of the most difficult barriers to treatment entry and success for Hispanics/Latinos. However, simply knowing

Spanish or Portuguese does not guarantee cultural sensitivity or competence. For instance, it is important that the treatment staff understand the role of the family. The functional family can be extended and should take into account people who have day-to-day contact with and a role in the family (Markarian and Franklin 1998).

Hispanics/Latinos are likely to view drug dependency as moral failing or personal weakness. Traditional healing such as folk remedies and folk healers may provide benefit. The previously discussed protocols for detoxification from alcohol, opioids, benzodiazepines, stimulants, solvents, nicotine, marijuana, anabolic steroids, and club drugs appear adequate for the detoxification of Hispanics/Latinos.

## Gays and Lesbians

Approximately 5 to 33 percent of all lesbian and gay individuals are estimated to have a substance abuse problem (Cochran and Mays 2000; Hughes and Wilsnack 1997). A

contributing factor may be the stress and anxiety associated with the social stigma attached to homosexuality. Further, alcohol and drugs may serve as an escape and ease social interactions at social settings such as bars. More information on this subject will be available in the forthcoming TIP *Improving Cultural Competence in Substance Abuse Treatment* (CSAT in development *a*). The previously discussed protocols for detoxifica-

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tion appear adequate for gay and lesbian patients. Since numerous misconceptions and stereotypes exist concerning gay and lesbian individuals, it is important for the clinician to assess his beliefs and take care not to impose them on the patient.

There are a number of principles of care for treating gay and lesbian individuals, which are outlined in *A Provider's Introduction to Substance Abuse Treatment for Lesbian, Gay, Bisexual, and Transgender Individuals* (CSAT 2001). These principles include: (1) counselors' being able to monitor their own feelings about working with this population of patients in order to provide professional, ethical, and competent care; (2) helping patients heal from the negative experiences of homophobia and heterosexism; (3) helping patients understand their reactions to discrimination and prejudice; and (4) helping patients accept personal power over their own lives by helping them improve their self-images and build support networks.

## Adolescents

The previously discussed protocols for detoxification from all substances of abuse appear adequate for the detoxification of adolescents; however, there are several additional aspects to consider:

- Physical dependence generally is not as severe, and response to detoxification is more rapid than in adults.
- Retention is a major problem in adolescent treatment (Thurman et al. 1995).
- Peer relationships play a large role in treatment. Among adolescents who do not use drugs, few of their friends reported use. In one study, among those who reported specific drug use, over 90 percent of their friends reported using the same drug (Dinges and Oetting 1993).
- It is estimated that 75 percent of those reporting steroid use are high school students, and most of them are male. Detoxification from steroids does not typically require specific pharmacological intervention unless

there is liver toxicity or suicidal intent (Giannini et al. 1991). The use of club drugs is higher in this population than in others.

TIP 31, *Screening and Assessing Adolescents for Substance Use Disorders* (CSAT 1999d), and TIP 32, *Treatment of Adolescents With Substance Use Disorders* (CSAT 1999f), provide comprehensive information on the treatment of adolescents.

## Incarcerated/Detained Persons

Substance use disorders are common among inmate populations. At the time of arrest and detention, it has been estimated that 70 to 80 percent of all inmates in local jails and State and Federal prisons had regular drug use or had committed a drug offense, and 34 to 52 percent of these inmates were intoxicated at the time of their arresting offense (Federal Bureau of Prisons 2000; Mumola 1999). Although women comprise a small proportion of the incarcerated population (12.3 percent in jails and 7.4 percent in State and Federal prisons) than men (Harrison et al. 2004), females have a greater prevalence of illicit drug use (i.e., 40 percent compared to 32 percent were under the influence of drugs at the time the crime was committed) than do males (Greenfeld and Snell 1999).

Persons who are incarcerated or detained in holding cells or other locked areas should be screened for physical dependence on alcohol, opioids, and benzodiazepines and provided with needed detoxification and treatment. Screening should occur over time, since the onset and intensity of withdrawal is dependent on the type of drug taken, when the person last took the drug, and how long the drug lasts in the person's body. The duration of detention will affect what detoxification services can be provided, and many facilities will not be able to provide detoxification or continuing care services. There are some special considerations for the detoxification of this population:

- Abrupt withdrawal from alcohol can be life-threatening.

- Abrupt withdrawal from opioids or benzodiazepines is not life-threatening but can cause severe withdrawal signs and symptoms and great distress.
- It should be determined whether dependence on either opioids or benzodiazepines is the result of illicit use and not the result of taking medications that have been prescribed to treat pain or anxiety disorders.
- If medically supervised withdrawal is indicated, the substitution of a long-acting drug from the same class of substances the patient is using (e.g., giving methadone to treat heroin dependence) and the gradual tapering of that substance (no faster than 10 to 20 percent per day) should be conducted under closely monitored settings.
- There are cases when individuals maintained on opioid agonist medications are detained or incarcerated. If the incarceration is 30 days or less, the individual should be maintained on her usual dosage. If the incarceration is longer, the individual may be appropriate for gradual dose tapering.
- Persons who transition from a state of opioid dependence to a drug- or medication-free state are at greater risk of overdose upon relapse to opioid use.
- Many correctional facilities have restrictions on the use of methadone or LAAM and special provisions for maintaining or tapering the individual may need to be made.
- If medications are provided to medically detoxify inmates, the Federal Bureau of Prisons' *Clinical Practice Guidelines for Detoxification of Chemically Dependent Inmates* (2000) suggest retaining strict control over access to these medications to prevent diversion or misuse (e.g., eating clonidine patches to obtain a state of euphoria).

TIP 44, *Substance Abuse Treatment for Adults in the Criminal Justice System* (CSAT 2005b), and TIP 30, *Continuity of Offender Treatment for Substance Use Disorders From Institution to Community* (CSAT 1998b), provide more detailed information about the treatment of this population. TIP 21, *Combining Alcohol and Other Drug Abuse Treatment With Diversion for Juveniles in the Justice System* (CSAT 1995b), also provides information about incarcerated youth.