Detoxification and Substance Abuse Treatment

A Treatment Improvement Protocol

TIP 45

Substance Abuse and Mental Health Services Administration
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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Substance Abuse and Mental Health Services Administration

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5 Co-Occurring Medical and Psychiatric Conditions

In This Chapter...

Patients undergoing detoxification frequently present with medical and psychological conditions that can greatly affect their overall well-being and the process of detoxification. These may simply be pre-existing medical conditions not related to substance use or the direct outcome of the substance abuse. In either case, the detoxification process can negatively affect the co-occurring disorder or vice versa. Furthermore, people who abuse substances often present with medical conditions in advanced stages or in a medical crisis. Co-occurring mental disorders also are likely to be exacerbated by substance abuse. For more on treating patients with co-occurring psychiatric disorders, the reader should refer to TIP 42, *Substance Abuse Treatment for Persons With Co-Occurring Disorders* (Center for Substance Abuse Treatment [CSAT] 2005*c*).

This chapter is intended primarily for medical personnel treating patients in detoxification settings, though nonmedical staff may find it informative as well. This chapter is not meant to take the place of authoritative sources from internal medicine. Rather, it presents a cursory overview of special conditions, modifications in protocols, and the use of detoxification medications in patients with co-occurring conditions or disorders. Overall treatment of specific conditions is not addressed unless modification of such treatment is needed.

General Principles of Care for Patients With Co-Occurring Medical Conditions

Patients who use substances can present with any of the conditions or combinations of conditions that can be found in the general population. In most cases, the management of the medical condition in the patient with a substance use disorder diagnosis does not differ from that of any other patient. However, the medication used for detoxification and the actual detoxification protocol may need to be modified to minimize potentially harmful effects relevant to the co-occurring condition.

Detoxification staff providing support should be familiar with the signs and symptoms of common co-occurring medical disorders. Likewise, personnel at medical facilities (i.e., emergency rooms, physicians' offices) should be aware of the signs of withdrawal and how it affects the treatment of the presenting medical conditions.

The setting in which detoxification is carried out should be appropriate for the medical conditions present and should be adequate to provide the degree of monitoring needed to ensure safety (e.g., oximetry [a measurement of the amount of oxygen present in the blood], greater frequency of taking vital signs, etc.). Acute, life-threatening conditions need to be addressed concurrently with the withdrawal process and intensive care unit monitoring may be indicated.

Clinicians should keep in mind that consultation with specialists in infectious diseases, cardiology, pulmonary medicine, hematology, neurology, and surgery may be warranted. Whenever possible, consent should be sought to involve the patient's primary healthcare provider in the coordination of care. Attending medical staff should be aware that co-occurring medical conditions present an opportunity to engage patients. By focusing on the adverse effects of the substance abuse on the overall health of patients, staff members are in a position to help patients see the importance of engaging in treatment for their substance use disorders. Patients should have appointments for followup care made prior to detoxification discharge for all chronic medical conditions, conditions needing further evaluation, and substance abuse treatment.

This section highlights the conditions most frequently seen in individuals who abuse substances, though it is not inclusive. Disorders of the following systems will be covered: gastrointestinal (including the gastrointestinal [GI] tract, liver, and pancreas), cardiovascular system, hematologic (blood) abnormalities, pulmonary (lung) diseases, diseases of the central and peripheral nervous system, infectious diseases, and special miscellaneous disorders. Where special considerations are needed for a patient presenting with a given disorder in a detoxification setting they are listed following the heading "Special Considerations."

Gastrointestinal Disorders

Frequently, the use of substances can present a range of gastrointestinal problems. Cocaine use, for example, can result in various gastrointestinal complications, including gastric ulcerations, retroperitoneal fibrosis, visceral infarction, intestinal ischemia, and gastrointestinal tract perforations (Linder et al. 2000). Gastrointestinal disorders may affect many different organs and organ systems (e.g., liver, pancreas), making diagnosis difficult. Since symptoms can be vague and patients are not always able to articulate the specific problem, diagnosis can be difficult. For a simple rule of thumb, urgent attention is needed if the patient is diagnosed with any of the following:

- Appendicitis
- Abdominal aortic aneurysm
- Perforated peptic ulcer
- Boerhaave's Syndrome (spontaneous esophageal rupture)
- Obstructed or strangulated bowel

- Ischemic bowel disease (a condition that results from inadequate blood supply to the intestines)
- Abcess of the pancreas or liver
- Ruptured spleen or other trauma to the abdominal area

Other possible diagnoses of abdominal pain include:

- Hepatitis
- Peptic ulcer (nonperforating)
- Peritonitis
- Acute pancreatitis
- Pelvic inflammatory disease
- Endometriosis
- Nephrolithiasis (kidney stones)
- Inflammatory bowel disease
- Ovarian cysts

Clinicians should also be aware of some deceptive causes of abdominal pain:

- Myocardial infarction
- Pulmonary emboli
- Herpes zoster (shingles)
- Acute pylonephritis (kidney infection)

Specific co-occurring gastrointestinal disorders requiring special attention in patients undergoing detoxification are discussed below.

Reflux esophagitis

Reflux esophagitis can be a result of alcohol's effect on the lower esophageal sphincter (i.e., relaxation) and a decrease in peristalsis of the distal esophagus, allowing gastric contents to come into contact with the lower esophagus. Typical symptoms include burning in the epigastric or retrosternal area (commonly called "heartburn" or "indigestion"). Esophageal bleeding can result from reflux esophagitis and esophageal varices (resulting from portal hypertension).

Special considerations

Several drugs used in typical protocols, such as beta blockers and calcium channel blockers, may decrease lower esophageal sphincter pressure and aggravate reflux (Dell'Italia 1994).

Mallory–Weiss Syndrome

Mallory–Weiss Syndrome is caused by torn mucosa of the esophagus at the gastroesophageal junction due to protracted or violent vomiting. Mallory–Weiss Syndrome is the etiology of 5 to 15 percent of all upper GI bleeds (Schuylze-Delrieu and Summers 1994).

Boerhaave's syndrome

Boerhaave's syndrome is manifested by rupture of the esophagus. Patients presenting with this condition complain of acute epigastric pain (83 percent of patients), vomiting (79 percent), and shortness of breath (39 percent) as the predominant, nonspecific symptoms. This lack of specificity can delay making the correct diagnosis (Brauer et al. 1997). Tachycardia, cyanosis, and subcutaneous emphysema also can be seen. If this condition is left untreated, the prognosis is severe.

Co-occurring medical conditions present an opportunity to engage patients in treatment for their substance use disorders.

Gastritis

Gastritis is described as the disruption of the gastric mucus lining that allows gastric acid to contact the mucosa with resultant inflammation and possible bleeding. The patient presents with nausea, vomiting, and abdominal pain (Ivey 1981). Alcohol increases gastric acid secretion and reduces the mucosal cell barrier,

allowing back-diffusion of the gastric acid into the mucosa. This frequently causes an occurrence of erosive gastritis in the individual with an alcohol use disorder (Fenster 1982).

Special considerations

Aspirin and nonsteroidal medications should be avoided in the withdrawal protocols.

Detoxification staff providing support should be familiar with the signs and symptoms of common co-occurring medical conditions.

Pancreatitis

Pancreatitis can be caused by many factors, although studies suggest that alcohol may be a factor in anywhere from 5 to 90 percent of all cases (Apte et al. 1997), with some experts suggesting about 60 percent of all cases result from excessive alcohol consumption (Yakshe 2004). The acute condition presents with abdominal pain, which is described as sharp, burning, and constant and is located in the epigastric area of the abdomen with radiation to the back. Presenting symptoms and signs can include abdominal tenderness, decreased bowel sounds, low-grade fever, tachycardia, nausea, and vomiting. Pancreatitis can proceed to a chronic condition where pancreatic calcification, diabetes mellitus, malabsorption, and chronic abdominal pain occur.

Special considerations

There may be a need to forbid oral intake of food and medications, necessitating a change of route of administration of both food and medications to intravenous forms. In alcohol withdrawal protocols, Ativan might be considered as an appropriate agent, as it can be administered intravenously or intramuscularly. Opioids may have to be used to control pain.

Liver disorders

Liver disease can range from fairly benign *fatty liver*, which presents usually as an asymptomatic enlargement of the liver associated with mild elevation of the serum liver enzymes, to a broad spectrum of viral infections and the toxic consequences of alcohol and other drug use. The end point of liver disease is liver necrosis or failure. Midway in the progression of liver disease is *acute alcoholic hepatitis*. The presentation is one of liver tenderness, jaundice, fever, ascites, and an enlarged liver. The patient is quite sick and frequently has nausea and vomiting.

Special considerations

Alcoholic hepatitis usually needs acute medical treatment to prevent electrolyte imbalance and dehydration. Protocols may have to be adapted if the patient cannot take oral agents.

Portal hypertension

Portal hypertension is a frequent consequence of liver disease. If elevation of the portal pressure goes untreated, esophageal varices develop and hemorrhage can ensue. Treatment of acute hemorrhage includes endoscopic sclerotherapy or ligation. Initial therapy should include prompt and adequate intravascular volume replacement, correction of severe anemia and coagulopathies, and adequate airway management.

Special considerations

Propranolol or isosorbide therapy is effective in the prophylaxis of variceal bleeding (Trevillyan and Carroll 1997), though beta blockers can interfere with measuring the true heart rate that determines the content of many detoxification protocols. If bleeding is

present, changeover to intravenous medication protocols is recommended, as the patient will not be able to take oral medications.

Cirrhosis

Cirrhosis, or the formation of fibrous tissue in the liver, leads to a state of increased resistance in the hepatic venous circulation. The inability of blood to flow freely gives rise to portal hypertension with ensuing esophageal varices, splenomegaly, ascites, dilatation of superficial veins, peripheral edema, and hemorrhoids.

Liver necrosis can be seen in patients who use inhalants, particularly chronic use of benzene and carbon tetrachloride. African Americans and Hispanics/Latinos have higher mortality rates from cirrhosis of the liver resulting from alcohol abuse than do Caucasians and Asians and Pacific Islanders (Sutocky et al. 1993). Liver function test abnormality and jaundice can occur in individuals who use anabolic steroids, but this usually resolves on cessation of the drugs. Studies in the elderly show that 1-year mortality was 50 percent among patients over age 60 with cirrhosis, versus 7 percent for those under age 60 (Potter and James 1987). Great care needs to be used when giving diuretics to elderly patients with cirrhosis, since their total body water may already be decreased, making them more susceptible to fluid and electrolyte depletion (Scott 1989).

Alcohol-related hepatic injury is seen in a higher proportion of women due to a possible potentiation (strengthening) of this effect by estrogen (Brady and Randall 1999).

Special considerations

For the treatment of alcohol withdrawal, lorazepam (Ativan) is well tolerated in patients with severe liver disease (D'Onofrio et al. 1999) as is oxazepam (Serax), with its short half-life of 6 to 8 hours and simple metabolism with no metabolites.

Cardiovascular Disorders

The presentation of chest pain or discomfort remains one of the most difficult differential diagnoses to sort through, as disorders of several systems can cause this single complaint. Inability to correctly diagnose this symptom can be brought about by the patient's inability to be interviewed and give succinct symptoms (the intoxicated or severely withdrawing patient), a sociocultural or educational level that does not allow for the verbal nuances necessary to making a diagnosis, or fabrication of symptoms by a patient seeking to obtain pain medications or other drugs.

A normal resting electrocardiogram does not rule out the presence of organic heart disease and the presence of nonspecific changes does not necessarily mean that heart disease is present. Final diagnoses can range from reflux to myocardial infarction brought about by underlying ischemic heart disease or the use of cocaine. Frequently, lung diseases can have as their presenting symptom chest discomfort. The consensus panel believes that this condition should never be overlooked or minimized and it is imperative that an especially prompt diagnosis be made and treatment be undertaken to ensure patient safety.

Underlying cardiac illness could be worsened by the presence of autonomic arousal (elevated blood pressure, increased pulse and sweating) as seen in alcohol, sedative, and opioid withdrawal. Thus prompt attention to these findings and aggressive withdrawal treatment is indicated. Special considerations for the treatment of specific cardiac conditions are outlined below.

Hypertension

Hypertension frequently is seen in the detoxification patient. Evaluation should include a complete history to determine if the elevated blood pressure predated the present withdrawal status. Consideration should be given to include serum electrolytes, urinalysis, BUN/creatinine, and an EKG in the detoxifi-

cation unit's initial workup. More elaborate workup can be carried out after completion of detoxification.

Propranolol (Inderal), labetalol (Trandate) and metoprolol (Lopressor) are the beta blockers of choice for treating hypertension during pregnancy (McElhatton 2001), however, the impact of using them for alcohol detoxification during pregnancy is unclear. If treating African Americans with beta blockers, clinicians should be aware that propranolol is less effective in this population than it is in Caucasians (Pi and Gray 1999). Asians require much lower doses of beta blockers than Caucasians, inasmuch as they tend to be very sensitive to the blood pressure and heart rate effects (Pi and Gray 1999).

Special considerations

The presence of a hypertensive history and poorly controlled blood pressures may have an effect on the proper evaluation of withdrawal as the examiner would have difficulty determining whether the elevated blood pressure was due to withdrawal or to the underlying hypertensive history. Thus modifications of the usual parameters and scheduling of detoxification medications should be considered. In any event, severe elevation of blood pressure should be treated concurrently with, at minimum, salt restriction and rest. If the blood pressure is still elevated in several days despite a reduction in other withdrawal parameters and symptoms, then medication is warranted.

Beta blockers and clonidine have been used in the treatment of alcohol withdrawal and clonidine also has been used in opioid protocols. These medications can help control blood pressure and also work well in the protocol. Calcium channel antagonists have also been used to ameliorate some of the symptoms of alcohol withdrawal and can be used concurrently for blood pressure control.

Ischemic heart disease

Ischemic heart disease presents as chest pain or pressure, palpitations, dizziness, and/or shortness of breath and requires immediate attention, which will dictate what setting is appropriate for the detoxification.

Cocaine use is associated with various cardiovascular complications including angina pectoris, myocardial infarction, and sudden death. It is estimated that over half of the 64,000 patients evaluated annually for cocaine-associated chest pain will be admitted to hospitals for evaluation of myocardial ischemia. Only about 6 percent of patients will demonstrate biochemical evidence of myocardial infarction (Hoffman and Hollander 1997). The typical patient with cocaine-related myocardial infarction is a male in his mid-30s with a history of chronic tobacco and repetitive cocaine use (Hollander 1995). This effect of cocaine appears to be increased because the drug causes an increase in myocardial oxygen demand and thus a decrease in oxygen supply. These two factors, which are caused by vasospasm and vasoconstriction of the coronary arteries, may lead to cardiovascular disorders.

Patients with recent cocaine use can experience persistent cardiac complications such as prolonged QT interval and vulnerability for arrhythmia and myocardial infarction (Chakko and Myerburg 1995). (QT is the Q to T interval measured on EKGs. If the interval is prolonged, it can lead to cardiac rhythm disturbances.) Amphetamines are rarely reported as the cause of myocardial infarction, though a case report shows that a patient subsequently experienced a non–Q-wave anterior wall infarction associated with amphetamine use (Waksman et al. 2001). Cocaine use and HIV infection have been associated with an increased incidence of cardiac dysfunction, but concomitant exposure may cause a synergistic effect (Soodini and Morgan 2001).

Special considerations

Beta-adrenergic blocking agents may exacerbate cocaine-induced coronary arterial vasoconstriction and thereby increase the myocardial ischemia. Nitroglycerin and verapamil reverse cocaine-induced hypertension and coronary arterial vasoconstriction and are the medications of choice in the patient who uses cocaine and presents with chest pain (Pitts et al. 1999). Cocaine may cause platelet activation leading to acute coronary events—thus more aggressive antiplatelet therapy may be indicated (Callahan et al. 2001).

Cardiomyopathy

Cardiomyopathy is caused by degenerative changes of the cardiac muscle with enlargement of the heart (cardiomegaly) and left ventricular failure. Alcoholic cardiomyopathy presents with a similar picture as cardiac failure from other etiologies, with shortness of breath on exertion, shortness of breath when the patient is lying flat, and edema of the lower extremities.

Besides alcohol as the etiology, a dilated cardiomyopathy can be seen with use of the inhalant trichlorethylene. Cardiomyopathy in the elderly patient with an already underlying ischemic or atherosclerotic heart disease can be quite debilitating. Women have shown alcohol metabolism different from that of men and distinct pathophysiologic mechanisms, which frequently lead to a higher sensitivity to alcohol-induced heart damage. The prevalence of cardiomyopathy in women is equal to that in men, despite cases in which women have consumed far less ethanol (Fernandez-Sola and Nicolas-Arfelis 2002).

Special considerations

Alcoholic cardiomyopathy may respond poorly to digitalis with increased likelihood of digitalis toxicity (Zakhari 1991).

Arrhythmias

Arrhythmias (irregular heartbeats) can be seen in the presence of ischemia and cardiomyopathy. Two specific cases of arrhythmogenic disorders are "holiday heart," where the patient who has ingested alcohol presents with supraventricular arrhythmia (Greenspon and Schaal 1983), and the individual who uses cocaine with the stimulant leading to significant atrial and ventricular arrhythmias. Consumption of anabolic steroids also has been associated with hypertension, ischemic heart disease, cardiomyopathy, and arrhythmia (Sullivan et al. 1999).

Special considerations

Treatment of arrhythmia in the person who abuses substances is similar to that for the patient who does not abuse substances, though the setting of detoxification may have to be altered to allow for cardiac monitoring (telemetry).

Cocaine use is associated with various cardiovascular complications including angina pectoris, myocardial infarction, and sudden death.

Hematologic Disorders

Hematologic (blood) disorders can be seen due to several factors, such as a direct toxic effect of the drug on the bone marrow, as seen in alcohol and benzene use, or as a result of malabsorption of essential nutrients (B12, folate), or as a general poor state of nutrition.

Anemia

Anemia can be seen due to folate deficiency, iron deficiency, B12 deficiency, acute blood loss, or more frequently as a combination of factors. *Folate deficiency* can cause a megaloblastic anemia, which is diagnosed by macroovalocytes and hypersegmented neutrophils seen on a peripheral blood smear. *Iron deficiency anemia* results from blood loss and thus subsequent iron loss. This can be seen in low-level gastrointestinal bleeding, after childbirth, and as a result of menstrual blood loss. The presentation of anemia usually is nondescript with generalized fatigue and weakness. With severe anemia, shortness of breath on exertion and an elevated heart rate can be seen. Specific to the megaloblastic anemias (B12 and folate deficiency) one can see neurologic complications such as peripheral neuropathy.

Traumatic brain injury (TBI) should always be considered in patients with neurological impairment.

White blood cell disorders

White blood cell disorders can occur due to malnutrition and liver disease. Lymphopenia may be present in the patient with HIV disease.

Platelet disorders

Platelet disorders frequently are attributable to the direct effect on the bone marrow by the substance being abused or, as seen in alcohol-related thrombocytopenia, are due to bone marrow suppression. Splenomegaly caused by portal hypertension also can cause a low platelet count (thrombocytopenia), which is due to enlargement of the spleen and abnormally high platelet storage. Thrombocytopenia also can be seen in cases of vitamin B12 and folate deficiency.

The African-American patient with sickle cell disease or trait can be severely affected (inasmuch as the patient already has an impaired oxygen delivery system) if other harm threatens the bone marrow.

Special considerations

Elevated heart rates can hinder the use of the heart rate as a parameter in various detoxification protocols.

Pulmonary Disorders (Other Than Infectious)

Pulmonary disorders are common in people who abuse substances, in part because of the high rate of nicotine use in this population (Graham et al. 2003).

Aspiration pneumonia

Alcohol or other drug ingestion may reduce a patient's gag reflex, leading to the blockage of the airways. Aspiration pneumonia occurs when oro-pharyngeal secretions and/or gastric contents enter into the lower airways. This serious condition may require prolonged hospitalization.

Asthma

Asthma, a chronic condition characterized by exacerbations of bronchial spasm manifested by wheezing, should be differentiated from bronchospasm, which is related to inhaled drugs and usually is self-limited. Treatment is similar to that provided to patients who do not use substances, with the addition of cessation of the substance use.

The patient with underlying chronic asthma can be severely compromised if the use of a smokeable drug causes exacerbation of an already impaired system.

Special considerations

Asthma medications can cause a significant increase in heart rate, which can affect the evaluation of withdrawal protocols that use heart rate as one of the parameters.

Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) (emphysema, chronic bronchitis) frequently is due to cigarette use and the resulting alterations of the pulmonary immune system, inflammation, and destruction of lung parenchyma. Presentation includes shortness of breath on exertion, a cough producing mucous, and wheezing.

African Americans who smoke cigarettes take in more nicotine, and therefore more tobacco smoke toxins per cigarette, than Caucasians (Perez-Stable et al. 1998).

Daily marijuana smoking has been shown to have adverse effects on lung function including a productive cough, wheezing, and excessive sputum production. However, the habitual marijuana-only smoker, in the absence of alpha-1-antitrypsin deficiency, would have to smoke four to five marijuana cigarettes per day for a span of at least 30 years to develop overt manifestations of COPD (Van Hoozen and Cross 1997).

Special considerations

During nicotine withdrawal and cessation treatment, different levels of nicotine absorption, as seen in some groups, will affect dosing for nicotine replacement therapies (Perez-Stable et al. 1998). The patient with COPD, especially if elderly, would be sensitive to the sedating effects of many of the detoxification protocol medications, especially the benzodiazepines, which may have to be reduced in dosage to avoid respiratory depression and worsening hypoxemia and hypercarbia (decrease in oxygen and increase in carbon dioxide). For smokers, always consider the use of the nicotine replacement agents, particularly in hospitalized patients. Evaluation for infections and the use of oxygen, steroids, and inhalers is dictated by the clinical picture. During detoxification, if nicotine use is not allowed, there can be significant effects on drug levels (see chapter 4).

Neurologic System

The neurologic system of patients with substance use disorders is affected directly in the toxic effects on cell membranes, effects on neurotransmitters, associated metabolic changes from other underlying disorders, and changes in blood flow. Researchers have found that the majority of those with an alcohol use disorder (75 percent) have some degree of cognitive impairment (Goldstein 1987). Specific disorders found in patients with substance use disorders can affect the central nervous system and the peripheral system. For example, a broad array of neuropathologic changes are seen in the brains of people who use heroin. The main findings are due to infections as a result of endocarditis or HIV infection. Other complications include hypoxic-ischemic changes with cerebral edema, ischemic neuronal damage thought to be due to heroin-induced respiratory depression, stroke due to thromboembolism, vasculitis, septic emboli, and hypotension. Myelopathy occurs as a result of possible isolated vascular accident in the spinal cord, and a distinct condition, leukoencephalopathy, has been described after the inhalation of pre-heated heroin (Buttner et al. 2000).

As a final note, traumatic brain injury (TBI) should always be considered in patients presenting with neurological impairment. People who abuse substances are at high risk of falls, motor vehicle accidents, gang violence, domestic violence, etc., which may result in head injury (Graham et al. 2003). Unrecognized TBI can affect the treatment outcome.

Wernicke-Korsakoff's Syndrome

Wernicke-Korsakoff's Syndrome is composed of Wernicke's encephalopathy and Korsakoff's psychosis. Wernicke's encephalopathy is an acute neurological disorder with a triad of

- Oculomotor dysfunction (bilateral abducens nerve palsy—eye muscle paralysis)
- Ataxia (loss of muscle coordination)
- Confusion

Weakness and nystagmus are also seen in this syndrome on examination of the eyes. Wernicke's encephalopathy is clearly related to thiamine deficiency.

Korsakoff's psychosis is a chronic neurological condition resulting from thiamine deficiency that includes retrograde and antegrade amnesia (profound deficit in new learning and remote memory) with confabulation (patients make up stories to cover memory gaps).

Special considerations

Thiamine initially is given parenterally and then oral administration is the treatment of choice. Always give thiamine prior to glucose administration.

Alcohol and sedative withdrawal seizures

Alcohol and sedative withdrawal seizures represent a significant medical challenge (Ahmed et al. 2000), since no large clinical studies have been conducted to firmly establish the best treatment practices. Up to 90 percent of alcohol withdrawal seizures occur in the first 48 hours and usually are single and nonfocal. Repeated episodes of drinking and withdrawal are thought to predispose people to seizures due to a kindling phenomenon (Post et al. 1987). Patients with a history of withdrawal seizures are at greatest risk and should receive prophylactic doses of a long-acting benzodiazepine (e.g., chlordiazepoxide 50mg every 6 hours for 24 hours) when detoxifying from alcohol.

Individuals with an alcohol use disorder show an increase in seizures due to withdrawal, metabolic insults such as hypoglycemia or electrolyte imbalance, or head trauma. In one study, researchers found that of 195 cases of seizures in those with an alcohol use disorder, 59 percent were due to alcohol withdrawal, 20 percent to head trauma, and 5 percent to vascular disorders (Earnest et al. 1988).

Special considerations

Evaluation of a first seizure should include a neurological evaluation and evaluation for head trauma. Metabolic etiologies, such as low magnesium levels, should be considered.

Mayo-Smith (1997) has shown that benzodiazepines confer protection against alcohol withdrawal seizures and thus patients with previous seizures should be treated early with this class of medications. The consensus panel suggests that anti-epileptic drug 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 a family history of seizures.

Clinicians should be aware that treatment of the first seizure with benzodiazepines does not prevent the likelihood of a second seizure (D'Onofrio et al. 1999). Slower medication tapers should be considered when this condition co-occurs with detoxification. Lorazepam, which can be used in patients with liver disease, has been suggested as appropriate, but it and other short-acting benzodiazepines may not prevent late-occurring withdrawal seizures (Shaw 1995). Dosages of anticonvulsant medications should be stabilized before sedative-hypnotic withdrawal begins. Adequate treatment with a long-acting benzodiazepine is effective in preventing withdrawal seizures (Mayo-Smith and Bernard 1995). D'Onofrio and colleagues (1999) found that a one-time dose of the rela-

tively shorter acting agent lorazepam also reduced the risk of a subsequent seizure compared to placebo. However, in D'Onofrio's study doses were small and the results were limited somewhat by use in an emergency room setting.

Older, first-generation anticonvulsants have limitations in that they have only been studied in mild to moderate withdrawal, on rare occasions they can cause serious hepatic and bone marrow toxicities, and they can interact with other classes of medication. Newer drugs, such as gabapentin (Neurontin) and oxcarbazepine (Trileptal), do not appear to have these liabilities, but sufficient studies to show this have not yet been done. There is little evidence that long-term use of phenytoin is helpful in the patient who does not have an underlying seizure disorder (Kasser et al. 2000). Medications that may lower the seizure threshold, including phenothiazines, such as prochlorperazine (Compazine), and several antidepressants, such as bupropion, should be used with great caution in the patient with a seizure history.

The use of anticonvulsants, such as valproic acid and barbiturates, has been studied in pregnant women. Valproic acid is associated with several malformations in the fetus. The use of any anticonvulsant medication should be discussed with the pregnant patient and risks and benefits explained (Robert et al. 2001).

Cerebrovascular accidents

Cerebrovascular accident (stroke) can be seen in alcohol and cocaine use, coagulation impairment, and severe uncontrolled hypertension.

Patients with recent cocaine/amphetamine use may present with headaches, which could represent subarachnoid and/or intracerebral bleed, and therefore should be appropriately evaluated (Buxton and McConachie 2000). Heavy alcohol consumption increases the risk for all major types of stroke by a variety of mechanisms (Hillbom and Numminen 1998). There is a higher than normal incidence of hemorrhagic stroke and other intracranial bleeding among patients with heavy alcohol use, and a particular association of strokes within 24 hours of a drinking binge (Altura 1986).

Special considerations

Nifedipine and verapamil have been shown to prevent alcohol-induced vasospasm, which suggests a possible therapeutic approach to hypertension and stroke in the patient with heavy alcohol use (Altura 1986).

Polyneuropathy

Polyneuropathy frequently is seen in nutritional deficiencies that occur in the patient with chronic alcohol use. Presenting signs and symptoms include lower extremity pain, distal motor loss, numbness or tingling, and loss of reflexes. Polyneuropathy can be seen in the inhalation of h-hexane, methyl-n-butyl ketone, and toluene (Geller 1998).

Treatment of the first seizure with benzodiazepines does not prevent the likelihood of a second seizure.

Hepatic encephalopathy

Hepatic encephalopathy is a toxic brain syndrome that results from the accumulation of unmetabolized nitrogenous waste products in a patient with severe liver dysfunction. Presenting signs and symptoms include an alteration in consciousness and behavior, fluctuating neurologic signs such as a flapping tremor (asterixis), and an elevated serum ammonia level. Clinicians should evaluate

patients for precipitating causes, which include the following:

- GI hemorrhage
- Electrolyte imbalance (metabolic alkalosis)
- Infections
- Excessive diuresis (dehydration)
- Use of sedatives
- Increase of dietary protein intake

Those patients who are infected with *Helicobacter pylori* may be more prone to hepatic encephalopathy (Duseja et al. 2003).

Special considerations

Clinicians should avoid the use of diuretics, identify and treat factors that may have precipitated the encephalopathy, decrease dietary protein intake, and use Lactulose to decrease nitrogenous waste products via the GI tract. Protocols that use the benzodiazepines should be adjusted to use those specific medications that are hepatically metabolized minimally or not at all.

Immunocompromised patients may not react to the tuberculin skin tests.

Infectious Diseases

The viral causes of hepatitis are multiple, though the hepatitis B and C viruses are the predominant causative agents. Hepatitis C virus infection appears to be the most common form of infectious hepatitis in patients with substance use disorders. At least 76 percent of patients who have used injection drugs for less than 7 years are positive for hepatitis C, while 25 percent of patients with alcohol use disorders and those who do not inject drugs show serologic evidence of infection (Fingerhood et al. 1993; National Institute on Drug Abuse 2000). Hepatitis B infections are likely to present more often as a chronic infection than as an acute-stage phenomenon. Testing for chronic hepatitis B and C infection is appropriate during the detoxification period.

Special considerations

Followup for hepatitis B and C should be arranged for after discharge from the detoxification setting. Vaccination is recommended for hepatitis A and B in the patient with hepatitis C. The vaccination schedule is over a 6-month period, so it needs to be done after the detoxification program. If significant liver disease is present, use of shorter-acting medication with less liver metabolism should be considered. For more on infectious disease and substance abuse, see TIP 6, *Screening for Infectious Diseases Among Substance Abusers* (CSAT 1993*c*).

Endocarditis

Endocarditis is caused by the introduction of various bacterial species into the vascular system when the protective defense mechanisms of the skin are bypassed through injection. The patient frequently will present with fever, cardiac murmur, anemia, enlargement of the spleen, petechiae, and peripheral embolic disease. The course can be subtle and indolent to fulminant, and if untreated can lead to a poor prognosis. In the patient who uses drugs intravenously, the tricuspid valve is affected in 70 percent of cases, followed by effects on the aortic valve and the mitral valve. Seventy-five percent of all cases are caused by *Staphylococcus aureus* and up to 15 percent are caused by gram negative aerobic bacilli (Aragon and Sande 1994).

Endocarditis always should be suspected in the febrile patient who uses intravenous drugs. Patients who use drugs intravenously are 300 times more likely to die suddenly from infectious endocarditis than patients who use drugs nonintravenously (Burke et al. 1997). Patients who use cocaine intravenously

may have a higher rate of endocarditis as a result of more frequent injections and the reduced need to solubilize cocaine solutions with heat (Chambers et al. 1987).

Bacterial pneumonia

Bacterial pneumonia can result from immune system dysfunction, interference with normal respiratory defense mechanisms (from alcohol or smoked drugs), direct toxicity, or aspiration.

The treating physician should be aware that the usual pathogens found in community-acquired pneumonia (i.e., *Streptococcus pneumoniae*) may not be the causative agent in pneumonias seen in patients dependent on alcohol. *Haemophilis influenzae*, *Klebsiella pneumoniae*, and other gram-negative microorganisms must be suspected and treatment given until definitive culture results are reported. Among patients who use parenteral drugs, pneumonia is the most common reason for admission to the hospital, accounting for 38 percent of all hospitalizations in this population (Marantz et al. 1987).

Special considerations

Careful use of respiratory depressants is recommended. Indications for hospitalization of the patient with pneumonia (Neu 1994) include the following:

- Old age
- Dehydration
- Vomiting and inability to take in oral fluids and medications
- Multilobar disease
- Low white blood cell count
- Respiratory acidosis
- pO2 less than 55 mm Hg
- Significant concomitant diseases
- HIV

Tuberculosis

Tuberculosis (TB) is caused by acid-fast rod (*Mycobacterium tuberculosis*). Transmission is by droplets spread through the air. The infected patient presents with complaints of cough (most common finding), bloody sputum, chest pain, fever, and weight loss. Recent immigrants from countries where TB is prevalent, socioeconomically disadvantaged populations, homeless persons, people who use illicit drugs, incarcerated people, and people who live in areas where infection with HIV is prevalent, are at increased risk for this disease and should be tested. Furthermore, new strains of multidrug-resistant TB are appearing, especially among the homeless population (Borgdorff et al. 2000; Moss et al. 2000).

TB is endemic in many areas of the world (Asia, Africa, and South and Central America) (Gupta et al. 2004). As a public health concern, testing all patients is of the utmost importance, even more so for patients from regions where TB is endemic. It is important to remember that immunocompromised patients may not react to the skin tests (anergy). Diagnosis is made with tuberculin skin testing, sputum smears and cultures, and radiographic findings. For more information on dealing with tuberculosis in detoxification and treatment settings see TIP 18, *The Tuberculosis Epidemic: Legal and Ethical Issues for Alcohol and Other Drug Abuse Treatment Providers* (CSAT 1995*i*).

Skin infections

Skin infections frequently are seen as a result of the intravenous administration of drugs. *Staphylococcus aureus* and *Streptococcus pyogenes* are frequently the infectious agents. The patient presents with tenderness, swelling, pain, erythema, and warmth in the injection area. The type and route of antibiotic is determined by the infecting organism and the extent and severity of the infection. Clinicians should remember that injection sites can be found virtually any place on the body where there is access to the venous system.

Patients who use drugs intravenously, patients with peripheral vascular disease, and

patients with diabetes (particularly with infections of the feet) should all be evaluated carefully for skin disease.

Sexually transmitted diseases

Sexually transmitted diseases can be seen in the form of urethritis, vaginitis, cervicitis, and genital lesions. These disorders are caused by a variety of microorganisms, and a complete history and physical that includes examination of the genitalia is indicated in all patients. The clinical picture and cultures frequently can guide the treatment protocols. Patients who use drugs intravenously occasionally display a false-positive serologic test for syphilis, possibly due to a nonspecific reaction to repeated exposure of injected antigens (Hook 1992).

HIV/AIDS

HIV/AIDS is a serious and prevalent medical condition among persons with substance use disorders, especially those who inject drugs and may share needles with other users. Patients with AIDS can present with a spectrum of complaints and illnesses ranging from an asymptomatic history to complaints of fever, enlargement of the lymph nodes, difficulty swallowing, diarrhea, weight loss, skin lesions, shortness of breath (due to *Pneumocystis carinii* pneumonia), headaches (due to *Toxoplasma gondii*), seizures, and dementia. As a rule of thumb, no complaint in the patient infected with HIV should be dismissed as irrelevant.

Gay men and patients who use drugs intravenously may be at higher risk for HIV/AIDS than other groups; thus, testing or referral for testing should be done and appropriate counseling offered. All such patients should be tested for HIV/AIDS or referred for testing. Some States, such as Colorado, require that a risk assessment be administered to all clients and that clients be advised of their risk and referred for testing if they are at risk for HIV/AIDS. Patients who decline HIV testing still should be educated about the risk and prevention.

Due to increased virulence of syphilis in patients who are HIV positive, as well as increased resistance to the treatments indicated in the usual treatment protocols, all such patients should be tested for syphilis and all patients who test positive for syphilis should be sent for HIV testing (McNeil et al. 2004).

Special considerations

If methadone is being used in withdrawal protocols, or maintenance is being continued, the clinician should be aware that certain HIV medications can cause an increased metabolism of methadone:

- Efavirenz (Sustiva)
- Nevirapine (Viramune)
- Lopinavir/ritonavir (Kaletra)
- Rifampin (a drug to prevent mycobacterium avium complex, a serious bacterial infection, in HIV-positive clients)
- Amprenavir (Agenerase)
- Abacavir
- Ritonavir

TIP 37, *Substance Abuse Treatment for Persons With HIV/AIDS* (CSAT 2000*e*) provides further information about substance abuse treatment for patients with HIV/AIDS.

Other Conditions

Cancer

Cancer occurrence is increased in people with substance use disorders due to the carcinogenicity of the drugs used. Cigarette smoking is linked to lung, larynx, oral cavity, esophagus, stomach, bladder, and pancreatic cancer. Heavy alcohol consumption is associated with an increased incidence of oral, pharyngeal, esophageal, laryngeal, respiratory tract, and breast cancer (Polednak 2005). Synergism is seen with alcohol and smoking being associated with even higher risks of cancer (Fagerstrom 2002). A history of weight

loss could suggest many chronic diseases, though cancer should be considered in the differential. There may be an increase in head and neck cancers in persons with heavy cannabis use (Donald 1991). Liver cancer may be seen in patients with hepatitis C and those using anabolic steroids (Socas et al. 2005). There is a particular interrelationship among alcohol intake, hepatitis C, and hepatocellular carcinoma (Yoshihara et al. 1998).

Diabetes

Patients who use drugs intravenously may experience infections that affect diabetic control, though any infection in any detoxification patient needs to be addressed both from an infectious disease and diabetic viewpoint.

Special considerations

Several medications can lead to impaired glucose tolerance and an elevated serum glucose (Garber 1994). Some examples include

- Thiazide diuretics
- Clonidine
- Glucocorticoids
- Haloperidol
- Lithium carbonate
- Phenothiazines
- Tricyclic antidepressants
- Indomethacin
- Olanzapine
- Risperdol

Antidiabetic agents in concert with alcohol may produce hypoglycemia and lactic acidosis. Diabetes mellitus also is seen in patients who present with new-onset hyperglycemia (elevated glucose) or with a history of diabetes and poor control.

Acute trauma/fractures

Acute trauma/fractures can be seen in any patient with a substance use disorder due to an altered level of consciousness or impaired gait when intoxicated. Patients with substance use disorders appear to be particularly prone to accidents of all kinds, with a spectrum of complications from head trauma to falls with fractures. Chronic pain frequently is seen in patients as a result of trauma (treated or untreated), poor health maintenance, or an inability to deal with pain without drug use. Chronic pain treatment and the issues of opioid use have to be considered for each patient on an individual basis.

The surgeon should consider drug withdrawal in the differential diagnosis of any physical or neurologic symptoms or signs that emerge during the perioperative period. There is a two- to threefold increase in postoperative morbidity in patients with alcohol use disorders, the most frequent complications being infections, bleeding, cardiopulmonary insufficiency, and withdrawal complications (Tonnesen and Kehlet 1999).

Certain HIV medications can cause an increased metabolism of methadone.

Special considerations

Opioids may be used to control pain in the initial period of trauma. Detoxification protocols should be started prior to anticipated surgery and continued throughout the perioperative period. Pain that causes an increased heart rate, as well as postoperative temperature elevation, may impact the detoxification parameters.

Due to tolerance to opioids, the daily methadone dose in a methadone-maintained individual will not serve as an analgesic for pain relief from surgical or other illnesses. Full therapeutic doses of analgesic drugs should be given to methadone-maintained

patients who have co-occurring painful conditions (CSAT 2005*d*; Ho and Dole 1979).

Since most medications for pain management are drugs with a high abuse potential, programs may need to alter their policies regarding the use of such drugs. Pain patients do not require detoxification from prescribed medications unless they meet the criteria for opioid abuse or dependence described in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Treatments for pain include physical therapy, transcutaneous electrical nerve stimulation, and therapeutic heat and cold. Trials of nonsteroidal anti-inflammatory agents or nerve block should be considered prior to the use of highly addictive and abusable medications.

The effects of drug toxicity and withdrawal often can mimic psychiatric disorders.

The use of acetaminophen in the patient with an alcohol use disorder always has been questioned, especially if there is evidence of liver disease. However, a review article of the medical literature showed that repeated ingestion of a therapeutic dose of acetaminophen over 48 hours by patients with severe alcoholism did not produce an increase in hepatic aminotransferase enzyme levels or any clinical manifestations as compared to a placebo group (Dart et al. 2000).

Treatment of Co-Occurring Psychiatric Conditions

Pharmacological agents can be used as indicated for co-occurring psychiatric conditions in patients with substance use disorders. Incidence of the co-occurrence of psychiatric conditions and substance use disorders is high; moreover, there is a higher rate of psychiatric conditions in patients dependent on alcohol than that found in the general population (Kessler et al. 2003; Modesto-Lowe and Kranzler 1999).

Comorbidity of substance use and co-occurring mental disorders serves to complicate diagnosis and treatment for patients (Salloum and Thase 2000). It is difficult to accurately access underlying psychopathology in a person undergoing detoxification. The effects of drug toxicity and withdrawal often can mimic psychiatric disorders. For this reason, it may be best to conduct psychiatric evaluations after several weeks of abstinence; however, this should be weighed against the time an individual has been in detoxification and what treatment plan is set up for him. Some patients also present to detoxification while taking medications to treat underlying psychiatric disorders, such as depression and anxiety. The risk of not treating a severe comorbid psychiatric disorder predisposes the patient to relapse; the decision needs to be weighed against the risk of prescribing medications when the clinician is not entirely certain that a comorbid condition exists. If a period of recent extended abstinence exists, the patient's mental condition when abstinent can be better evaluated.

Although it is the philosophy of some physicians to discontinue all psychiatric medications upon entering a detoxification program, this course of action is not always in the best interest of the patient. Abrupt cessation of psychotherapeutic medications may cause withdrawal symptoms or the re-emergence of the psychiatric disorder. As a general rule,

therapeutic doses of medications should be continued through any withdrawal if the patient has been taking the medication as prescribed. Decisions about discontinuing medications should be deferred until after the individual has completed detoxification. If, however, the patient has been abusing a medication or the psychiatric symptoms were clearly caused by substance abuse, then the rationale for discontinuing the medication is strengthened. Finally, practitioners should consider withholding medications that lower the seizure threshold (e.g., bupropion or conventional antipsychotics) during the acute alcohol withdrawal period, or at a minimum prescribing a loading dose or scheduled taper of benzodiazepine.

During detoxification, some patients decompensate and lapse into psychosis, depression, or severe anxiety. In such cases, careful observation of the withdrawal medication regimen is of paramount importance. If the decompensation is a result of inadequate dosing with withdrawal medication, the appropriate response is to increase the dose of medication. If it appears that the withdrawal medication is adequate, other medications may be needed. Before choosing such an alternative, it is important to take into account additional considerations, such as the side effects of the added medication and the possibility of interaction with the withdrawal medication.

A patient with psychosis may need to take neuroleptics. Medications that have a minimal effect on the seizure threshold are recommended, particularly if the patient is being withdrawn from alcohol or benzodiazepines. Small, frequent doses of Haldol, such as 1mg every 2 hours, may be used until the patient's symptoms of psychosis begin to disappear. The case for emergency use of antidepressants is weaker than for other psychiatric medications because of the 2- to 3-week lag time between initiation of medication and therapeutic response. After detoxification, the patient's need for medication should be reassessed. A trial without medications sometimes is the best way to assess the patient's need for the medication; however, it may not be the best practice or in the best interest of the patient, particularly for those with a serious mental illness. For more information on working with patients with co-occurring substance use and mental disorders, see TIP 42, *Substance Abuse Treatment for Persons With Co-Occurring Disorders* (CSAT 2005*c*).

Treatment for Co-Occurring Conditions

The treatment of substance use disorders can be difficult without adequate treatment of any co-occurring mental disorders. For instance, a patient with schizophrenia who is hallucinating and delusional, but who also abuses substances, cannot participate in substance abuse treatment without adequate control over the psychosis. Likewise, patients with mania who are euphoric and delusional, patients who are depressed, or patients with agoraphobia who also have a substance use disorder, will have difficulty cooperating with substance abuse treatment. Treatment of the substance use disorder is necessary to improve the course of both the substance abuse and co-occurring mental disorder. Psychotherapy should serve as one aspect of rehabilitation, initially focused around relapse prevention (Aviram et al. 2001). Highly effective treatment programs may include a combination of therapeutic techniques. Programs should be long-term and approach recovery in stages. Drake and colleagues (2001) suggest that treatment for co-occurring substance use and other mental disorders include skill building, illness management, cultural sensitivity, and support to patients for the pursuit of practical goals.

Limitations of pharmacological agents in persons with substance dependence

Pharmacologic agents have limitations in the population of persons with substance use dis-

orders. Medications may impair cognition and blunt feelings, sometimes subtly. Clinicians treating substance use disorders advocate that clients need clear thinking and access to emotions in order to make fundamental changes in themselves. A person recovering from a substance use disorder must take an active part in changing attitudes and abandoning a long-held belief that alcohol or other drugs can "treat" life problems and uncomfortable psychological states. Although these are potential risks, the intent of pharmacotherapy is to enhance a person's ability to sustain abstinence and benefit fully from concurrent psychosocial interventions and treatments. Still, many psychiatric disorders, if untreated, result in mood, anxiety, or thought disorders that prevent or retard the behavioral changes necessary to recover from substance use disorders.

Risks versus benefits of pharmacological agents need to be considered carefully. Untreated anxiety, mood, or thought disorders can be powerful relapse triggers, especially for people with a long-standing pattern of relying on alcohol or other drugs to manage their symptoms. In many instances, the benefits and reduced relapse risk that appropriate pharmacotherapy can provide far outweighs the risk of taking medications. Some clinicians believe that the "no pain, no gain" approach has far greater risk of interfering with recovery than of promoting it. Symptoms such as anxiety and depression in persons recovering from substance use disorders might be vital to recovery, and pharmacotherapy to treat such symptoms needs to be considered carefully in this context. Clinically, anxiety and depression can provide the motivation to change when the patient otherwise has little awareness of the need to alter behavior.

Standard of Care for Co-Occurring Psychiatric Conditions

After detoxification and stabilization with pharmacologic agents, the current treatment of choice for substance use disorders is nonpharmacologic. Further, several studies have shown that treating substance use disorders with abstinence alone results in improvement of the psychiatric syndromes associated with the substance use (Anderson and Kiefer 2004). Severe syndromes induced by alcohol that may otherwise meet criteria for major depressive and anxiety disorders are best classified as substance-induced disorders if they resolve within days to weeks with abstinence. Likewise, manic syndromes induced by cocaine resolve within hours to days, and schizophrenia-like syndromes (e.g., hallucinations and delusions) induced by cocaine and PCP often resolve within days to weeks with abstinence.

Further studies are needed to confirm the clinical experience that psychiatric symptoms (including anxiety, depression, and personality disorders) respond to specific treatment of the addiction. For example, cognitive–behavioral techniques employed in the 12-Step treatment approach have been effective in the management of anxiety and depression associated with addiction. Although challenging, treatment of both addiction and co-occurring psychiatric conditions has proven cost-effective in some studies (Goldsmith 1999).

Psychotropics for Co-Occurring Psychiatric Conditions

General aspects

Because alcohol and other drugs can induce almost any psychiatric symptom or sign or mimic any psychiatric disorder, their effects always must be considered before a co-occurring condition diagnosis is established or treated.

With an understanding of the interactions between substance use and other mental disorders, a rational approach can be applied to the use of pharmacologic therapies in co-occurring conditions. The use of medications for psychiatric symptoms should begin only after the knowledge of the natural history of the addictive disorder and other psychiatric disorders is clarified. Further, it is important to be able to identify the respective roles of substance use and other mental disorders in the generation of psychiatric symptoms.

Generally, substance-induced psychiatric symptoms resolve within days to weeks of abstinence. In many studies, the prevalence rates for anxiety and affective disorders in persons dependent on alcohol were not greater than those for persons not dependent on alcohol (Schneider et al. 2001).

A retrospective history of psychiatric symptoms often can lead to an inflated diagnosis of these conditions because of rationalizations regarding drinking and drug use by the individual. Typically, psychiatric symptoms are emphasized by both the patient and the psychiatric examiner.

Longitudinal observation frequently clarifies the role of alcohol and other drugs in the production of anxiety, affective, psychotic, or personality symptoms, particularly if objective criteria are relied on in addition to the subjective report of the person who is addicted. Also, specific treatment of substance use disorders can result in improvement of mood, psychotic behavior, and personality disturbances if related to the alcohol or other drug use. Mood lability and personality states can be a manifestation of substance use disorders, and treatment of the addictive disorder can lead to stabilization of these psychiatric symptoms.

Furthermore, treatment plans and efficacy may rely on the gender of the patient. Women with a substance use disorder appear to have higher rates of co-occurring mental disorders, such as depression and anxiety, as well as higher rates of physical and sexual abuse, panic and phobia disorders, posttraumatic stress disorder, victimization, and eating disorders. Deficits in the management of mood disturbances may be self-medicated through alcohol consumption in females. It has been proposed that the outcomes of substance abuse in women are different when compared to those of men. For these reasons, the efficacy of treatment for substance use disorders needs to be assessed independently for both genders (Becker and Walton-Moss 2001; Brady and Randall 1999).

Anxiety Disorders

General approach

Prevalence rates for the co-occurrence of anxiety and substance use disorders in the general population range from 5 to 20 percent in epidemiologic and clinical studies (Merikangas et al. 1996).

Major depressive and anxiety disorders are best classified as substance-induced disorders if they resolve within days to weeks with abstinence.

Some antianxiety agents can oversedate and dull the individual's reaction to internal and external influences. Because anxiety in recovery can be critically important for emotional growth, the individual will feel a certain amount of anxiety to motivate change in behavior, attitudes, and emotions. (The expression "emotional growth" is related to the anxiety or discomfort a recovering individual feels while undergoing the process of change to reach a more mature state.) It is important for the clinician to distinguish between anxiety that can promote growth and anxiety that can impair a person's ability to make change. Adapting behavior in response to anxiety or other emotion requires coping

skills that may not be available to persons in early recovery. A fully symptomatic anxiety disorder may significantly limit a person's capacity to learn nonpharmacological coping strategies. Medications with minimal addiction potential can be helpful and in some cases necessary if patients are to make progress in their recovery.

Depressants (e.g., alcohol) can produce anxiety during withdrawal, and stimulants (e.g., cocaine) can produce anxiety during intoxication. Because people with substance use disorders are in a relatively constant state of withdrawal (it is impossible to maintain a constant blood level), they regularly experience anxiety as the result of pharmacological withdrawal from dependence. As the substance abuse becomes more chronic, the anxiety produced by withdrawal from pharmacologic dependence can become increasingly severe. Relapse and/or periods of abstinence (sometimes prolonged—for weeks or months) should be considered (confirm abstinence with laboratory drug testing, if necessary) before the effects of depressant or stimulant drugs in inducing anxiety can be ruled out. It can take weeks or months for these effects to subside completely, although a period of only a few days to weeks often is sufficient in clinical practice.

Medication is indicated when the anxiety is preventing the patient from participating in treatment.

Treatment is indicated when the anxiety persists after adequate effort in a substance abuse treatment program, or when the clinician suspects that anxiety is preventing the patient from participating in treatment. A thorough evaluation to assess whether the individual is abstinent, involved in continuing treatment, and/or attending self-help meetings usually is necessary before a diagnosis of a co-occurring psychiatric condition can be definitely established. After such an evaluation, treatment of the anxiety disorder can proceed separately from similar symptoms arising from the addictive disorder.

Pharmacologic therapies

The ideal medication works against abnormal anxiety but not against the "normal" anxiety needed for recovery. Some of the physical symptoms of anxiety include sweating, tremors, palpitations, muscle tension, and increased urination. Psychological symptoms include nervousness, feelings of dread or impending doom, unpleasant tenseness, and many more.

The most common agents used in anxiety disorders are benzodiazepines and antidepressants. The benzodiazepines most frequently used are alprazolam and lorazepam. Diazepam and clonazepam are used less often. Because the benzodiazepines can cause significant problems in patients who are addicted as well as in patients who are not addicted, they generally are not recommended for people with substance use disorders or for long-term treatment of anxiety or depressive disorders.

Antidepressants may be considered sooner if depression is a known pre-existing condition or historical experience and collateral information suggests a comorbid depression. Again the risk of treating prematurely needs to be weighed against the risk of not treating a condition that may prevent recovery from a substance use disorder. Antidepressants such as imipramine and nortriptyline and selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine (Prozac) have a low addiction potential and can be used with relative safety. They differ in their tendency to produce sedation and anxiety and have a withdrawal

syndrome of their own. Because of its anticholinergic properties, imipramine is more sedating, but nortriptyline and the SSRIs can produce anxiousness in some individuals and sedation in others. Not all individuals react the same way to these medications.

When medications are used, a specific target symptom should be the focus. Also, medications should be tried in time-limited intervals, such as weeks to months. A "drug holiday" (i.e., a brief period where the patient stops taking medications) should then be attempted to see if the medication is still necessary.

The patient should be instructed that the medications will not "cure" the addiction, that treatment of anxiety will not control the addiction, and that treatment of the addiction will not necessarily ameliorate the anxiety disorder. In essence, the substance use disorder must be treated independently of the anxiety disorder and vice versa.

Depressive Disorders

General approach

Prevalence rates for the co-occurrence of depressive and addictive disorders range from 5 to 25 percent in epidemiologic and clinical studies. Depressive disorders include major depressive and dysthymic disorders, which can occur independently with addictive disorders, or similar depressive symptoms can be induced by substance use disorders. Major depressive disorder is more common in older individuals and in women and can be difficult to distinguish from substance-induced depression.

Depression can be viewed as protective and can be associated with "healing" in many conditions involving emotions. For example, a grief reaction is an expected experience after loss, with depression an essential emotion in this process. Recovery from a substance use disorder has been compared to a grief reaction because of losses (e.g., of the substance or relationships based on substance use) suffered by the patient with an addictive disorder. Likewise, and analogous to the role of anxiety, depression also is a part of the healing process that the patient with a substance use disorder experiences during recovery.

Depressant drugs (e.g., alcohol) can produce depression during intoxication which often resolves following abstinence. A survey of 69 adults with alcohol use disorders showed a strong correlation between the reduction in cravings for alcohol over 2 weeks of abstinence and the lifting of depressive mood. The patients' cravings were assessed with the Obsessive-Compulsive Drinking Scale (OCDS) and their depressive symptoms measured with the Self-rating Depressive Scale (SDS). Between day 1 and day 14, their cravings score dropped nearly a third, while the scores for severity of depression fell by about one fourth. The correlation between the reduction in cravings and the lifting of depression persisted after controlling for sex, age, duration and extent of alcohol abuse, and the amount of clomethiazole administered (Anderson and Kiefer 2004).

Stimulant drugs (e.g., cocaine) can produce depression during withdrawal. These effects may be prolonged with certain drugs that linger in the body (i.e., are stored in fat), such as cannabis and benzodiazepines. These drugs can produce depression or anxiety that is indistinguishable from other psychiatric causes of depression. Therefore, they must be considered causative whenever depression is present, and the possibility of addiction needs to be assessed when these drugs are identified. While depression may persist for weeks or months, it often resolves within days with abstinence from these drugs.

Pharmacologic therapies

The use of medication is recommended if the depression persists beyond a few weeks of drug withdrawal or arises during confirmed abstinence (laboratory drug testing may be necessary to confirm abstinence). The risk of suppressing normal depressive processes dur-

ing recovery versus the benefit from suppressing depression that is interfering with function should be weighed, as is the case with anxiety disorders.

Antidepressants are the main treatment for depression. The target symptoms are a sad mood, tearfulness, appetite and sleep disturbances, and other neurovegetative symptoms. Depression can be found in many conditions, including a variety of psychiatric and medical conditions. SSRIs are the drug of choice for many physicians treating depressed patients with substance use disorders. Although some are costly, they provide adequate treatment of depression with fewer side effects than other medications commonly used (Thase et al. 2001).

Depressive disorders are thought to have a significant biological component, including deficiencies in such central nervous system neurotransmitters as serotonin, norepinephrine, and dopamine. Interestingly, these neurotransmitters are also affected by substances of abuse. These agents are thought to act by increasing the activity of these neurotransmitters, ultimately alleviating depression and stabilizing mood.

Bipolar Disorders

General approach

Prevalence rates for the co-occurrence of bipolar and addictive disorders range from 30 to 60 percent, depending on the population studied, in epidemiologic and clinical studies (Chen et al. 1998; Sallom and Thase 2000; Sonne and Brady 1999; Strakowski and DelBello 2000).

Mania is a condition associated with elevated mood, grandiosity, hyperactive behavior, poor judgment, and lack of insight. The patient with mania will show excess such as spending sprees, sexual promiscuity, intrusiveness, and abnormal alcohol and drug use. A manic episode can follow, precede, or alternate with depressive moods.

Bipolar disorder may be complicated by the influence of substances (Sonne and Brady 1999). The manic state can be produced by stimulants (e.g., cocaine) during intoxication, and from depressants (e.g., alcohol) during withdrawal. A period of confirmed abstinence usually is necessary before mood-stabilizing drugs are started. Generally, a period of a week or two may be required for the role of drugs in inducing manic symptoms to be properly assessed.

Pharmacologic therapies

Mood stabilizers control bipolar disorders in patients with or without co-occurring substance use disorder. These medications can control either the manic or depressed phase, or both.

Manic episodes can occur cyclically, alternatively, and concurrently with depressive episodes. One theory of the pathogenesis of bipolar disorder involves the neurotransmitter norepinephrine (i.e., excessive in mania and deficient in depression).

Lithium is a natural salt, available in the carbonate form and slow release preparations. Its exact mechanism of action is unknown, but it can be effective in reducing or preventing the recurrence of manic and depressive episodes. Lithium carbonate must be taken daily in doses of 600 to 2,400mg to achieve plasma levels in the 0.5 to 1.5-m equiv/L range. It should be noted that studies have shown that lithium has no conclusively positive effect on rates of abstinence in either depressed or nondepressed patients.

Anticonvulsant mood stabilizers, such as divalproex sodium and carbamazepine, can be effective in controlling mania and, some evidence suggests, in co-occurring addictive conditions as well. Carbamazepine is known to be as effective as some benzodiazepines in inpatient treatment of alcohol withdrawal and, because of its anticonvulsant properties, it may be a good choice for treating those patients at high risk of withdrawal seizures

(Malcolm et al. 2001). One theoretical explanation for the mechanism of action for carbamazepine involves suppression of mood centers in the limbic system that act like seizure foci. In this context, a "kindling" model has been proposed for both mood and addictive disorders (Gelenberg and Bassuk 1997).

Psychotic Disorders

General approach

Prevalence rates for co-occurrence of schizophrenic and addictive disorders range from 40 to 80 percent, depending on the population studied, in epidemiologic and clinical studies.

Schizophrenia is a chronic illness characterized by bizarre thinking and behavior. Hallucinations and delusions are "positive" symptoms of the psychotic process, while symptoms such as social withdrawal and poverty of emotions are "negative" symptoms (or deficit syndrome). Conventional neuroleptics are more effective for positive symptoms, whereas behavioral, group, and individual psychotherapy are more effective for negative symptoms. New agents such as clozapine and risperidone may be more effective in treating both the positive and negative symptoms.

Psychosis can be caused by stimulant drug use during intoxication and depressant drug/alcohol use during withdrawal. A period of weeks or months may be necessary to assess the effects of substances of abuse, but as with anxiety, depression, or mania, medications can be started at almost any time as the psychosis is persistent and waiting is not possible. Moreover, the greater the number of psychiatric admissions, the greater the probability of a chronic mental disorder associated with the co-occurring psychiatric disorder.

High- or moderate-potency neuroleptics (e.g., haloperidol or atypical agents) generally are the agents of choice in the treatment of schizophrenia. The clinical potency correlates with the drug's ability to block the action of the neurotransmitter dopamine at its postsynaptic receptor sites.

Adverse Effects

Antianxiety agents

While benzodiazepines are useful in the short term, their efficacy wanes with long-term use, probably because of the development of pharmacologic tolerance and dependence. It should be noted that benzodiazepines can be addicting, particularly in those already addicted to other substances.

A period of confirmed abstinence usually is necessary before mood-stabilizing drugs are started.

Antipsychotic agents

Antipsychotics can produce sedation and hypotension (at times causing lightheadedness in some individuals), particularly with postural changes. Conventional neuroleptics produce acute extrapyramidal reactions, which include pseudoparkinsonism, dystonia, and akathisia. Dystonia usually responds to treatment with anticholinergic drugs such as benztropine or diphenhydramine. Akathisia is the subjective feeling of anxiety and tension, causing the patient to feel compelled to move about restlessly. This symptom usually requires beta blocker, as a decrease in the antipsychotic dose does not have the desired effect. Alternatively, switching to risperidone may accomplish the intended effect while avoiding intolerable neurologic syndromes.

Antidepressants

Antidepressants, particularly the tricyclics, can produce sedation, hypotension, syncope, and other anticholinergic effects. The SSRIs can produce anxiousness, sedation, insomnia, and gastrointestinal upset. A withdrawal syndrome also has been reported with most antidepressant medications.

The SSRIs are preferred in patients with addiction and co-occurring psychiatric conditions because of their reduced side effect profile and low risk of dangerous drug interactions; for example, there are no anticholinergic effects on the senses and no risk of lethal effects from overdose.

Cognitive State in Recovery

A person recovering from a substance use disorder must have a clear mind and a stable mood. Medications have a tendency, sometimes subtly and other times obviously, to dull the senses and thinking and blunt or disrupt the emotions. People with substance use disorders must eventually change and control feelings to remain abstinent and also to comply with psychiatric management. The ability of a person with a substance use disorder to use the 12 steps of Alcoholics Anonymous (AA) and to accept psychiatric advice will depend on clear thinking and emotional balance, which is stressed as central to the recovery process in AA. In other cases—such as patients with traumatic brain injuries—treatment venues should be adaptable to their cognitive abilities.

Accordingly, the use of medications should be conservative, taking into consideration the pros and cons of their expected positive and negative effects. Unfortunately, few psychiatric medications are totally free of mood-altering properties. However, the cognitive state of individuals who have a serious mental illness often is more distorted when not medicated appropriately. The very nature of their illness is a disruption to their cognitive processes.

Dosing

Because of inherent susceptibility to drug effects by people with substance use disorders, it is important to use the lowest effective doses possible. Also, the intervals for administration should be selected to reduce effects on cognition and feelings.

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