Current PSYCHIATRY

How to manage medical complications of the 5 most abused substances

Monitor for symptoms and lab findings that indicate risk of serious consequences

Individuals who abuse substances often have comorbid psychiatric disorders—80% of alcoholics have another axis I disorder[1]—and the reverse also is true. More than one-half of schizophrenia patients and 30% of anxiety and affective disorder patients abuse substances.[1]

In addition to worsening psychiatric illnesses and interfering with proper treatment, alcohol and other substances can lead to serious cardiac, neurologic, pulmonary, or gastrointestinal complications that can linger even after your patient stops abusing drugs. This article provides an overview of common medical complications related to using alcohol, marijuana, cocaine, methamphetamines, and opioids.

Alcohol

Because some consequences of alcohol abuse (***Table 1, page 36***) are thought to be dose-dependent, ask about your patient's alcohol consumption. Moderate drinking is defined as up to 2 drinks/day for men and 1 drink/day for women.[2] Heavy drinking is ≥5 drinks/day (or ≥15 drinks/week) for men and ≥4/day (or ≥8/week) for women.[3] A drink contains 12.5 grams of ethanol and is defined as:

- 12 oz (360 mL) of beer or wine cooler
- 5 oz (150 mL) of wine
- 1.5 oz (45 mL) of 80-proof distilled spirits.[3]

Gastrointestinal effects. Chronic heavy alcohol consumption can lead to fatty liver (steatosis), alcoholic

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Substance abuse

Clinical Point

Steatosis can occur after just a few days of heavy drinking, but can be reversed with abstinence from alcohol

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Table 1

Medical complications of alcohol abuse

Cardiovascular: Cardiomyopathy; hypertension; ischemic heart disease; acute myocardial infarction
Gastrointestinal: Alcohol hepatitis; cirrhosis of the liver; pancreatitis; cancer of the mouth, larynx, pharynx, esophagus, liver, and colon/rectum/appendix
Neurologic: Wernicke's encephalopathy; Korsakoff's syndrome; decline in cognitive abilities; decreased gray and white matter; increased ventricular and sulcal volume; peripheral neuropathy
Other: Renal dysfunction; osteoporosis; breast cancer

hepatitis, and cirrhosis. Steatosis—the first stage of alcoholic liver disease—can occur from heavy drinking for just a few days but can be reversed with abstinence from alcohol. Prolonged use can lead to alcoholic hepatitis. Symptoms include nausea, lack of appetite, vomiting, fatigue, abdominal pain and tenderness, spider-like blood vessels, and increased bleeding times.

Abstinence might not reverse liver damage from alcoholic hepatitis, and cirrhosis can still develop. Up to 70% of patients with alcoholic hepatitis will develop cirrhosis.[4,5] Common physical manifestations of cirrhosis include generalized weakness, fatigue, malaise, anorexia with signs of malnutrition, and increased bleeding.

Laboratory findings of elevated aspartate aminotransferase/alanine aminotransferase, gamma-glutamyltransferase, and carbohydrate-deficient transferrin also point to heavy alcohol use.[6]

Acute pancreatitis—the most common cause of hospitalization from alcohol-related GI complications—is seen more often than liver disease.[7]

Cardiovascular effects. Light to moderate drinking may be cardioprotective, but heavy alcohol consumption increases the risk of hypertension and ischemic heart disease.[8] Incidence of hypertension is two-fold greater in individuals who have >2 drinks/day and highest in those who have >5 drinks/day.[9]

Prolonged excessive alcohol consumption is the leading cause of nonischemic dilated cardiomyopathy. Symptoms of alcoholic cardiomyopathy include fatigue; dyspnea, including paroxysmal nocturnal dyspnea and orthopnea; loss of appetite; irregular pulse; productive cough with pink/frothy material; lower extremity edema; and nocturia.[10] Cardiac function can recover with early diagnosis and alcohol abstinence.[11]

Cognitive decline. The effects of light drinking on cognitive function are controversial, but heavy consumption—especially at ≥30 drinks/week—is known to cause impairment.[12] Alcohol-dependent individuals have been shown to have impaired verbal fluency, working memory, and frontal function as is seen in Alzheimer's disease.[13] One possible factor contributing to cognitive dysfunction is cortical volume loss in chronic alcoholics.[12]

Marijuana

Marijuana is the most commonly abused illicit substance worldwide, and data show an increasing prevalence of marijuana abuse and dependence (32% of U.S. 12th graders endorsed its use in 2007).[14]

In many populations marijuana use seems to precede use of cocaine, opioids, or other substances.[15] Although the concept of marijuana as a "gateway drug" is still debated, consider the possibility that your patients who use marijuana also are using other illicit substances. In a 2004 survey, 19% of marijuana users admitted to use of other illicit drugs.[16] Although many people consider marijuana a "safe" drug, it can cause adverse effects (*Table 2*).

Pulmonary complications. Even infrequent marijuana use can lead to burning

and stinging of the mouth and throat, usually accompanied by a heavy cough. Regular users may develop complications similar to chronic tobacco use: daily cough, chronic phlegm production, susceptibility to lung infections (such as acute bronchitis), and potential for airway obstruction.[17,18]

Marijuana use can double or triple the risk of cancer of the respiratory tract and lungs.[19] Tetrahydrocannabinol—the active chemical in marijuana—might contribute to this risk because it can augment oxidative stress, lead to mitochondrial dysfunction, and inhibit apoptosis.[19]

Cardiac complications. Acute marijuana use causes tachycardia, increases supine blood pressure, and decreases standing blood pressure, resulting in dizziness, syncope, falls, and possible injuries.[20,21] Increased cardiac output and cardiac work—coupled with a decreased capacity to carry oxygen—can lead to angina or acute coronary syndrome, especially in older adults with preexisting cardiovascular disease.[21] Growing evidence shows that marijuana use could lead to cardiac arrhythmias, such as atrial fibrillation.[20] Long-term heavy users seem to develop tolerance to some cardiovascular effects, but blood volume overall increases, heart rate slows, and circulatory responses to exercise are diminished.[18]

Cognitive impairment. Chronic marijuana users might experience cognitive impairment—particularly on memory of word lists and attention tasks[22]—but there is debate as to whether these deficits are stable or temporary. Some studies show persistent cognitive impairments in longer-term cannabis users, even after 2 years of abstinence.[22] However, most studies suggest that marijuana-associated cognitive deficits are reversible and related to recent exposure.[18]

Cocaine

Cocaine is the most frequent cause of drug-related death, particularly when combined with alcohol.[23]

Table 2

Medical complications of marijuana use

Cardiovascular: Tachycardia; increased supine blood pressure; increased risk of myocardial infarction; atrial fibrillation
Pulmonary: Stinging of mouth/throat; chronic/heavy cough; increased lung infections; obstructed airways; lung cancer
Neurologic: Decreased performance on cognitive tasks (word lists, attention); diminished reaction times
Other: Decreased serum testosterone, sperm count, and sperm motility; shorter menstrual cycles; increased prolactin; suppressed activity of macrophages and natural killer cells

Table 3

Medical complications of cocaine use

Cardiovascular: Chest pain; 24-fold increased risk of myocardial infarction; coronary vasospasm; ventricular fibrillation; tachycardia; hypertension
Pulmonary: Pleuritic chest pain; chronic cough; wheezing; hemoptysis; melanoptysis (black sputum); 'crack lung' (fever, cough, difficulty breathing, and chest pain)
Gastrointestinal: Xerostomia; bruxism; decreased gastric motility; ischemic colitis; bowel ulceration, infarction, and perforation
Neurologic: Seizures; headaches; cerebral vasoconstriction; hemorrhagic/ischemic stroke; cerebral gray matter atrophy (especially frontotemporal lobes); dystonic reactions; akathisia; choreoathetosis ('crack dancers')
Other: Acute renal failure via rhabdomyolysis; nephrosclerosis; impaired sexual function (chronic use)

Chronic nasal insufflations can cause loss of sense of smell, nosebleeds, dysphagia, hoarseness, and overall irritation of the nasal septum, which in turn can lead to chronic mucosal inflammation and rhinorrhea.[24] Intravenous users often have puncture marks or "tracks," usually on the forearms, and are predisposed to infectious diseases such as human immunodeficiency virus (HIV) and other blood-borne infections.[24,25] Regular cocaine ingestion can lead to bowel gangrene because of

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Clinical Point

Asking about how your patient ingests cocaine will guide your evaluation of possible medical complications

subjects and younger subjects, and other reported clinical experience has not identified differences in response between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

This drug is known to be substantially excreted by the kidney and clearance is decreased in patients with moderate to severe renal impairment *[see Clinical Pharmacology (12.3) in full PI]*, who should be given reduced doses. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function *[see Dosage and Administration (2.5) in full PI]*.

Renal Impairment: Dosing must be individualized according to the patient's renal function status *[see Dosage and Administration (2.5) in full PI]*.

Hepatic Impairment: No dosage adjustment is required in patients with mild to moderate hepatic impairment. INVEGA® has not been studied in patients with severe hepatic impairment.

DRUG ABUSE AND DEPENDENCE

Controlled Substance: INVEGA® (paliperidone) is not a controlled substance.

Abuse: Paliperidone has not been systematically studied in animals or humans for its potential for abuse. It is not possible to predict the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, patients should be evaluated carefully for a history of drug abuse, and such patients should be observed closely for signs of INVEGA® misuse or abuse (e.g., development of tolerance, increases in dose, drug-seeking behavior).

Dependence: Paliperidone has not been systematically studied in animals or humans for its potential for tolerance or physical dependence.

OVERDOSAGE

Human Experience: While experience with paliperidone overdose is limited, among the few cases of overdose reported in pre-marketing trials, the highest estimated ingestion of INVEGA® was 405 mg. Observed signs and symptoms included extrapyramidal symptoms and gait unsteadiness. Other potential signs and symptoms include those resulting from an exaggeration of paliperidone's known pharmacological effects, i.e., drowsiness and somnolence, tachycardia and hypotension, and QT prolongation.

Paliperidone is the major active metabolite of risperidone. Overdose experience reported with risperidone can be found in the OVERDOSAGE section of the risperidone package insert.

Management of Overdosage: There is no specific antidote to paliperidone, therefore, appropriate supportive measures should be instituted and close medical supervision and monitoring should continue until the patient recovers. Consideration should be given to the extended-release nature of the product when assessing treatment needs and recovery. Multiple drug involvement should also be considered.

In case of acute overdose, establish and maintain an airway and ensure adequate oxygenation and ventilation. Gastric lavage (after intubation if patient is unconscious) and administration of activated charcoal together with a laxative should be considered.

The possibility of obtundation, seizures, or dystonic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis.

Cardiovascular monitoring should commence immediately, including continuous electrocardiographic monitoring for possible arrhythmias. If antiarrhythmic therapy is administered, disopyramide, procainamide, and quinidine carry a theoretical hazard of additive QT-prolonging effects when administered in patients with an acute overdose of paliperidone. Similarly the alpha-blocking properties of bretylium might be additive to those of paliperidone, resulting in problematic hypotension.

Hypotension and circulatory collapse should be treated with appropriate measures, such as intravenous fluids and/or sympathomimetic agents (epinephrine and dopamine should not be used, since beta stimulation may worsen hypotension in the setting of paliperidone-induced alpha blockade). In cases of severe extrapyramidal symptoms, anticholinergic medication should be administered.

Inactive ingredients are carnauba wax, cellulose acetate, hydroxyethyl cellulose, propylene glycol, polyethylene glycol, polyethylene oxides, povidone, sodium chloride, stearic acid, butylated hydroxytoluene, hypromellose, titanium dioxide, and iron oxides. The 3 mg tablets also contain lactose monohydrate and triacetin.

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reduced blood flow and orofacial complications.[24] Asking about how your patient ingests cocaine will guide your evaluation of possible medical complications (***Table 3, page 37***).

Cardiac complications. Recent cocaine use is a common cause of chest pain. A 2002 survey reported that 25% of patients in urban hospitals and 13% in rural settings presenting with nontraumatic chest pain tested positive for cocaine use.[26] Although cocaine can lead to ventricular fibrillation, tachycardia, and increased blood pressure, its main mechanism for inducing chest pain and myocardial infarction (MI) is coronary vasospasm, especially of diseased vessels. The acute risk of MI is increased by a factor of 24 in the first 60 minutes after cocaine use.[23] Chronic use promotes thrombus formation, leading to atherosclerotic disease.[23] Recurrent chest pain in a young, otherwise healthy individual could indicate cocaine abuse.

Neurologic complications. Headache is the most common neurologic complication of cocaine use. Although usually associated with intoxication or withdrawal, headaches can become chronic with chronic use.[25] Reduced seizure threshold also has been reported with cocaine use, particularly in patients with cerebral lesions, and most seizures occur with first-time use. Isolated events might not require anticonvulsant therapy, although referral to a neurologist is recommended.[27]

Cocaine use puts individuals at higher risk for subarachnoid hemorrhage, intracerebral bleed, ischemic stroke, and transient ischemic attacks. The route of cocaine ingestion seems to influence the type of stroke: IV and intranasal use are associated with hemorrhagic stroke, and inhalation with ischemic stroke.[25]

Methamphetamine

Like many illicit substances, methamphetamine can be taken in many forms.

- "Speed," a powder form, can be snorted or injected.
- "Base" is a powder with higher purity.
- "Ice," also known as "crystal," has very high purity and can be smoked, "chased" (cooked on aluminum foil and smoked), mixed with marijuana, or injected.[28]

Evaluate meth-abusing patients for many of the same medical complications associated with cocaine and other stimulants. Acute effects include hyperten-

sion, tachycardia, and arrhythmias; chronic effects include stroke and cardiac valve sclerosis. Pulmonary hypertension can occur when the drug is smoked (***Table 4***).[28]

Dental complications. Originally believed to result from the acidity of methamphetamine, advanced tooth decay or "meth mouth" is thought to be caused by decreased production of saliva—a consequence of increased sympathetic activity—combined with overall decreased oral intake, sugar and soft drink consumption, and poor oral hygiene. Methamphetamine abusers often experience bruxism, which exacerbates tooth decay.[29]

Neurologic changes. Chronic methamphetamine use is characterized by poor cognitive functioning and emotional changes such as paranoia and depression.[28] These are believed to be caused by neuropathologic changes in the cortex, striatum, and hippocampus.

Opioids

Prescriptions of opioid analgesics for chronic pain—and their subsequent diversion—are the main conduit to nonmedical use.[30] IV heroin use is the most common cause of illicit drug overdose.[31] Opioids are used by:

- ingestion, usually of synthetic analgesics (prescription drugs)
- parenteral administration, often IV heroin
- inhalation, a pure form that is heated and burned.

Infectious complications. Injection drug use—especially with unsterilized shared needles—is an efficient vector for bloodborne infections. Needle sharing is the most common cause of new HIV and viral hepatitis infections.[32] All IV drug users should be routinely tested for these viral infections. Chronic IV drug use can cause vein sclerosis, leading to visible "track marks" and, rarely, thromboembolic events. Be alert for integumentary infections—especially in patients who "skin pop" drugs by injecting them under the skin—or systemic infectious diseases, such as skin abscesses, cellulitis, septicemia, botulism, or bacterial endocarditis (***Table 5***).[33]

Table 4

Medical complications of methamphetamine abuse

Cardiovascular: Arrhythmias; hypertensive crisis; myocardial infarction; cardiomyopathy; tachycardia
Pulmonary: Pneumomediastinum respiratory failure
Gastrointestinal: Tooth decay ('Meth mouth'); xerostomia; bruxism; hepatitis infection; hepatotoxicity
Neurologic: Cerebral infarct; seizures; blurred vision; obtundation
Other: Jaw clenching; excessive sweating; aplastic anemia; hyperthermia; muscle cramping

Table 5

Medical complications of opioid abuse

Cardiovascular: Prolonged QTc interval (methadone)
Pulmonary: Respiratory suppression
Gastrointestinal: Hepatitis C infection; hepatotoxicity; nausea; constipation
Neurologic: Drowsiness; lightheadedness; confusion; myoclonus; hyperalgesia; miosis
Other: Urinary retention; pruritus

Pulmonary complications. Overstimulation of opioid receptors in the brainstem and carotid bodies can cause slow and irregular respiration and decreased gag and coughing reflex during acute intoxication. The rate of opioid intake appears to play a role; a gradual increase in opioid blood levels leads to progressive respiratory depression by causing gradual hypercapnia, and a quick rise in receptor occupancy can lead to rapid apnea. Therefore opioids with slow receptor binding, such as buprenorphine, may be safer than those that bind more quickly, such as fentanyl. However, all opioids can cause this dangerous side effect.[34] Inhaled forms of heroin have also been shown to lead to status asthmaticus.[35]

continued

Clinical Point

In IV drug users, be alert for integumentary infections or systemic infectious diseases, such as cellulitis or septicemia

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Substance abuse

Clinical Point

Overstimulation of opioid receptors can cause slow and irregular respiration and decreased gag and coughing reflex during intoxication

Cardiac and neurologic complications. Methadone use could prolong the QTc interval, leading to dysrhythmias such as torsades de pointes. Higher doses increase the incidence of syncope.[36] Ongoing monitoring of the QTc interval is warranted for all patients on methadone.

Neurologic effects of opioids include:

- delayed leukoencephalopathy with IV overdose and inhaled preheated heroin, known as "chasing the dragon"
- widespread cortical dysfunction (abulia, lack of volition, hemineglect,[37] and deficits in executive functioning and emotional processing) leading to impaired decision-making.[38]

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Related Resources

- National Institute on Drug Abuse. www.nida.nih.gov.
- Substance Abuse and Mental Health Services Administration. www.samhsa.gov.
- National Institute on Alcohol Abuse and Alcoholism. www.niaaa.nih.gov.
- Johnston LD, O'Malley PM, Bachman JG, et al. Monitoring the Future national survey results on drug use, 1975-2008. Volume I: Secondary school students. Bethesda, MD: National Institute on Drug Abuse; 2009. NIH Publication No. 09-7402.

Drug Brand Names

Buprenorphine • Subutex
Fentanyl • Actiq, Duragesic, others
Methadone • Dolophine, Methadose

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Clinical Point

Ongoing monitoring of the QTc interval in warranted for all patients on methadone

Bottom Line

Substance abuse can lead to many medical complications. Heavy drinkers may present with liver disease, hypertension, cardiomyopathy, or cognitive dysfunction. Marijuana use can lead to lung disease, impaired memory and attention, and increased cardiac output and angina attacks. Cocaine is associated with chest pain and headaches. Methamphetamine use often leads to advanced tooth decay. Understanding and remaining vigilant for these effects will help you make appropriate referrals as necessary.