CHAPTER 142

Alcohol-Related Disease

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As eloquently stated by Paracelsus in the 16th century, "all substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy."

PRINCIPLES OF TOXICITY

Alcohol is the most common recreational drug taken by Americans, and per capita consumption is increasing. Alcohol is the third leading cause of preventable death in the United States; alcoholism permeates all levels of society and is a preventable cause of morbidity and mortality.[1] The widespread incidence and disastrous effects of alcoholism are well known to the emergency clinician. Almost all societies that consume alcohol have related health and social problems. The tragic effects of alcohol not only affect the individual drinker but also have far-reaching implications for the family, community, and workplace.

Alcohol consumption is responsible for 3.8% of global mortality, 4.6% of every disability-adjusted life-year (DALY) lost due to premature death, and is projected to take on increasing importance over time.[2] Alcohol use and misuse also have social and financial costs, with estimates of the annual economic costs (eg, the costs of health care and lost productivity) to be over $800/person for the entire US population.[3] Alcohol contributes to 79,000 deaths and $223.5 billion in societal costs annually in the United States.[4] Harmful consequences and risk of disability exist on a continuum (Fig. 142.1).[4]

At-risk drinking is defined as heavy or problematic alcohol use that may lead to an array of negative consequences, including social, physical, psychological, legal, and financial problems. Across the United States, at least 24% to 31% of emergency department (ED) patients meet National Institute Alcohol Abuse and Alcoholism (NIAAA) criteria for at-risk drinking.[3] At-risk drinking is defined as an average of 15 or more standard drinks/week or 5 or more per occasion for men and 8 or more drinks weekly or 4 or more per occasion for women and people older than 65 years.[4]

The lifetime prevalence of alcohol use disorder (AUD) in the general population is nearly 20% and of dependence is 13%.[5] AUD consist of alcohol dependence, alcohol abuse, and dependence or harmful use. These disorders are common in all developed countries and are more prevalent in men than in women, with lower but still substantial rates in developing countries. However, most people with AUD are difficult to identify because they are likely to have jobs and families and to present with general complaints, such as malaise, insomnia, anxiety, sadness, or a range of medical problems. The prevalence of AUD is higher in specialized populations, affecting about 40% of patients presenting to the ED and 59% to 67% of trauma patients.[5] In response to the high prevalence of this disease, the American Medical Association has recommended screening patients for alcohol use problems in medical and surgical settings and EDs.[3]

Alcohol is a central nervous system depressant. Like benzodiazepines, barbiturates, and drugs that have similar action, it rapidly increases the release of γ-aminobutyric acid (GABA) in the brain, and it inhibits postsynaptic N-methyl-D-aspartate glutamate receptor activity.[6] Chronic alcohol consumption also affects central α-adrenergic and β-adrenergic receptors and dopamine turnover.[7]

Animal studies have suggested that in alcohol withdrawal, the balance of the neurotransmitters GABA and glutamate is altered. Decreased synthesis of GABA and increased synthesis of glutamate might be related to withdrawal symptoms experienced on brutal cessation of chronic alcohol intake.[8]

About 40% to 60% of AUD cases are explained by genes and the rest by environmental association. Polymorphisms in genes for enzymes that metabolize alcohol are generally associated with a lower risk of AUDs because they increase sensitivity to alcohol. One candidate gene and gene product that has been shown to contribute to the risk of drug abuse and addiction-related phenotypes is the mu opioid receptor (MOR; *OPRM1* gene).[9]

Metabolism of Alcohol

Ethanol is rapidly absorbed from the stomach and small intestine. It is distributed uniformly to all organ systems, including the placenta. Although 2% to 10% of alcohol is excreted through the lungs, urine, and sweat, most is metabolized to acetaldehyde, primarily by alcohol dehydrogenase (ADH). The oxidation of alcohol is a complex process involving three enzyme systems, all contained in the hepatocyte. Acetaldehyde is then quickly converted to carbon dioxide and water, primarily through aldehyde dehydrogenase (ALDH). The common forms of ADH decrease the alcohol concentration in blood by about 4.5 mmol/L ethanol/hr (the equivalent of about one drink/hr):

$$\text{Ethanol ADH} \xrightarrow[\text{NAD}\rightarrow\text{NADH}]{\text{Alcohol hydrogenase}}$$

$$\text{Acetaldehyde ADH} \xrightarrow[\text{NAD}\rightarrow\text{NADH}]{\text{Alcohol dehydrogenase}}$$

$$\text{Acetyl coenzyme A} \xrightarrow[\text{Cycle}]{\text{Critical acid}} CO_2 + H_2O$$

where NAD is nicotinamide adenine dinucleotide and NADH is reduced nicotinamide adenine dinucleotide.

At least two variations of ADH genes (*ADH1B*2* and *ADH1C*1*) produce a slightly more rapid breakdown of alcohol and therefore potentially faster production of acetaldehyde, which is rapidly metabolized by *ALDH2*. However, about 40% of Asian people (Japanese, Chinese, and Koreans) have an inactive *ALDH2* mutation that results in much higher acetaldehyde levels after drinking than normal. About 10% of people who are homozygous for this gene form cannot drink alcohol without becoming sick and have almost no risk of AUD, whereas those who are heterozygous have a relatively low rate of AUD.

An alternative pathway, the microsomal ethanol-oxidizing system (MEOS), is induced by chronic alcohol exposure. The primary component of the MEOS is the molecule cytochrome P_{450}, which exists in several variants. The variant most important for alcohol metabolism is cytochrome P_{450} 2E1 (CYP2E1). Many effects of alcoholism are produced by the toxic byproducts (hydrogen, acetaldehyde), acceleration of metabolism of other drugs,

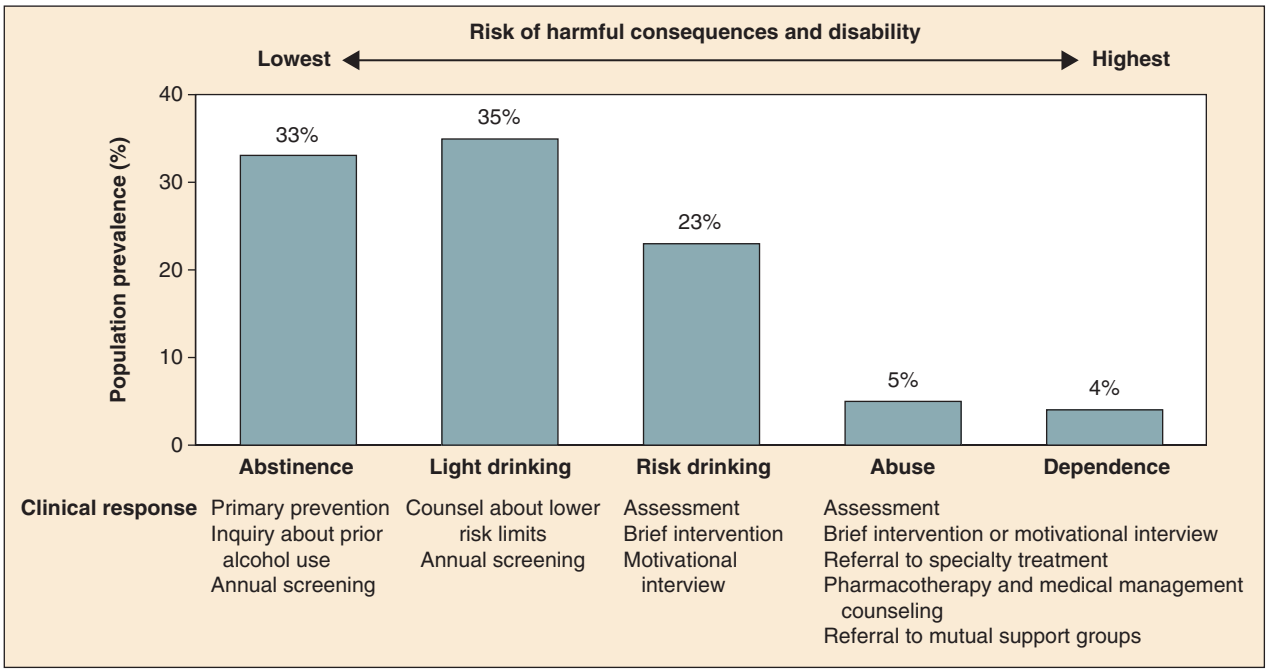

Fig. 142.1. Continuum of risk associated with alcohol use and possible clinical responses. Risk drinking is defined as an average of 15 or more standard drinks/week or 5 or more on occasion for men and 8 or more drinks weekly or 4 or more on occasion for women and people older than 65 years. Persons in remission from an alcohol use disorder remain at risk for recurrent drinking and adverse consequences.

and activation of hepatotoxic compounds by these metabolic pathways.

Although the liver is the major site of ethanol metabolism, other tissues contribute to its metabolism. ADH is found in the gastric mucosa, but the gastric metabolism of alcohol is decreased in women and those of Asian descent. This increased bioavailability of ethanol or decreased first-pass metabolism may explain the greater vulnerability of women to acute and chronic complications of alcohol.

Alcohol metabolism has two elimination rates. The alcohol elimination rate approximates zero-order kinetics (constant rate) for lower ethanol levels and first-order kinetics (amount of drug removed over time is proportional to the concentration of the drug) for higher levels, especially in chronic alcoholics; most likely, through induction of the MEOS pathway, the elimination rate is increased at higher blood levels.

The absorption and elimination rates of alcohol vary by individual and depend on many factors—diet, gender, body weight and habitus, speed of consumption, gastric motility, presence of food in the stomach, smoking history, age, whether the person is a chronic alcohol consumer with enzyme induction and high-activity MEOS, advanced cirrhosis, presence of ascites, and state of nourishment. There is enormous variation among patients in the rate of elimination of ethanol from the blood, ranging from 9 to 36 mg/dL per hour in published data. Although the clearance rate may be as high as 36 mg/dL/hr in some chronic drinkers, 20 mg/dL/hr is a reasonable rate to assume in a typical intoxicated ED patient. This holds true for adults, adolescents, and children, whether they are experienced or inexperienced drinkers.

Physiologic effects vary directly with the blood alcohol level (Table 142.1). Diminished fine motor control and impaired judgment appear with alcohol concentrations as low as 20 mg/dL (0.02 mg%), but wide individual variability exists. Chronic alcoholics can exhibit impressive tolerance. The blood alcohol concentration of a person cannot be accurately determined without quantitative testing. More than 50% of the adult population is obviously intoxicated with a level of 150 mg/dL (0.15 mg%). As the ethanol level rises, the patient's level of consciousness declines, eventually ending in coma. Death is caused by aspiration or respiratory depression.

TABLE 142.1

Physiologic Effects and Blood Alcohol Levels

BLOOD ALCOHOL CONCENTRATION (mg/dL)	EFFECTS[a]
20–50	Diminished fine motor control
50–100	Impaired judgment, impaired coordination
100–150	Difficulty with gait and balance
150–250	Lethargy, difficulty sitting upright without assistance
300	Coma in the novice drinker
400	Respiratory depression

[a]These effects are for the occasional drinker. Chronic drinkers can function at much higher alcohol concentrations because of tolerance. On the other hand, patients may become comatose with low levels of alcohol in mixed alcohol-drug overdose.

Alcohol through passive diffusion will be present anywhere there is water in the body. Hence, expired breath alcohol or saliva can be used to obtain a reliable approximation of blood alcohol concentration in a cooperative patient. This value can be used as a rapid screen for alcohol intoxication.

CLINICAL FEATURES

Alcohol Withdrawal Syndrome

The neurophysiology of alcohol withdrawal is complex and not fully understood. The hallmark of alcohol withdrawal is central

BOX 142.1

Dsm-V Criteria for Withdrawal Delirium (Delirium Tremens)

CRITERIA FOR ALCOHOL WITHDRAWAL

Cessation of or reduction in heavy and prolonged use of alcohol

At least two of eight possible symptoms after reduced use of alcohol:

- Autonomic hyperactivity
- Hand tremor
- Insomnia
- Nausea or vomiting
- Transient hallucinations or illusions
- Psychomotor agitation
- Anxiety
- Generalized tonic-clonic seizures

CRITERIA FOR DELIRIUM

Decreased attention and awareness

Disturbance in attention, awareness, memory, orientation, language, visuospatial ability, perception, or all these abilities that is a change from the normal level and fluctuates in severity during the day

No evidence of coma or other evolving neurocognitive disorders

From American Psychiatric Association: Diagnostic and statistical manual of mental disorders, ed 5 (DSM-5), Washington DC, 2013, American Psychiatric Publishing.

TABLE 142.2

Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar)

COMPONENTS OF SCALE	MOST SEVERE MANIFESTATIONS
Nine items[a]	
• Nausea or vomiting	Constant nausea with vomiting
• Tremor	Severe tremor, even with arms extended
• Paroxysmal sweats	Drenching sweats
• Anxiety	Acute panic
• Tactile disturbances (eg, itching, numbness, sensation of bugs crawling on or under the skin)	Continuous hallucinations
• Auditory disturbances (eg, sensitivity to sound, hearing things that are not there)	Continuous hallucinations
• Visual disturbances (eg, sensitivity to brightness and color, seeing things that are not there)	Continuous hallucinations
• Headache, sensation of a band around the head	Extremely severe headache
• Agitation	Pacing during most of interview with clinician or thrashing about
One item—orientation and clouding of sensorium[b]	

[a]Scored on a scale ranging from 0 (no symptoms) to 7 (most severe symptoms).
[b]Scored on a scale ranging from 0 (no symptoms) to 4 (disoriented with respect to place or person).
Adapted from Sullivan JT, Sykora K, Schneiderman, J, et al: Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). Br J Addiction 84:1353–1357, 1989.

nervous system (CNS) excitation, with increased cerebrospinal fluid, plasma, and urinary catecholamine levels.

Alcohol withdrawal syndrome (AWS) is a continuum of syndromes that begins after a decrease in the amount of intake of ethanol. AWS is often divided into three sets of symptoms. The first set consists of autonomic hyperactivity, which appears within hours of the last drink and usually peaks within 24 hours. Common presenting characteristics include trembling, sweating, nausea, vomiting, anxiety, and agitation. The second symptom set includes additional neuronal excitation, with epileptiform seizures and global confusion, usually occurring within 24 to 48 hours of abstinence. The third feature set comprises delirium tremens or alcohol withdrawal delirium (AWD), with auditory and visual hallucinations, confusion and disorientation, clouding of consciousness, impaired attention, and pronounced autonomic hyperactivity.[8] The criteria for withdrawal delirium, as described in Box 142.1, are delirium and alcohol withdrawal.[6] Emergency clinicians should be familiar with a commonly used withdrawal rating instrument known as the Clinical Institute Withdrawal Assessment of Alcohol Scale, revised (CIWA-Ar).[6] See Table 142.2.

Alcohol-Related Seizures

Among the many medical problems related to alcohol abuse, the differential diagnosis and management of seizures remain among the most challenging and controversial (Box 142.2). Patients presenting to the ED with seizures should be questioned about alcohol intake. Of seizure patients presenting to an ED, 20% to 40% will have their seizures related to alcohol use or abuse. Alcohol is a causative factor in 12% to 24% of patients with status epilepticus. In states where alcohol sales are restricted on Sundays, EDs see a spike in alcohol-related seizures on Mondays.

The primary consideration in the initial care of seizure patients who use alcohol is the recognition of treatable, life-threatening causes. These causes include but are not limited to CNS infection, metabolic disorders, and intracranial hemorrhage. Alcohol may act in one of several ways to produce seizures in patients with or without underlying foci—by its partial or absolute withdrawal after a period of chronic intake, by an acute alcohol-related metabolic disorder (eg, hypoglycemia, hyponatremia), creation of a situation leading to cerebral trauma, precipitation of seizures in patients with idiopathic or post-traumatic epilepsy, or lowering

BOX 142.2

Differential Diagnosis of Alcohol-Related Seizures

Withdrawal (alcohol or drugs)
Exacerbation of idiopathic or posttraumatic seizures
Acute intoxication (eg, amphetamines, anticholinergics, cocaine, isoniazid, organophosphates, phenothiazines, tricyclic antidepressants, salicylates, lithium)
Metabolic (eg, hypoglycemia, hyponatremia, hypernatremia, hypocalcemia, hepatic failure)
Infectious (eg, meningitis, encephalitis, brain abscess)
Trauma (eg, intracranial hemorrhage)
Cerebrovascular accident
Sleep deprivation
Noncompliance with anticonvulsants

of the seizure threshold in patients with prior existing intracerebral disease states. Moreover, alcoholics are more susceptible to other disorders associated with seizures, including neurosyphilis, acquired immunodeficiency syndrome (AIDS), brain abscess, and meningitis.

Alcohol Withdrawal Seizures

Seizures occur 6 to 48 hours after the cessation of drinking. Of patients with seizures, 90% have one to six generalized tonic-clonic seizures; 60% experience multiple seizures within a 6-hour period. The incidence of partial seizures, common with posttraumatic epilepsy, is increased in alcohol withdrawal. The term *alcohol withdrawal seizure* is reserved for seizures with these characteristics. The term *alcohol-related seizure* is used to refer to all seizures in the aggregate associated with alcohol use, including this subset of alcohol withdrawal seizure.

Cardiovascular Effects

Acute and chronic ethanol consumption can affect the mechanical function of the heart, produce dysrhythmias, and exacerbate coronary artery disease (CAD). It may alter myocardial function by direct toxic effects, by associated hypertension, or indirectly by altering specific electrolytes. Acute intoxication can decrease cardiac output in alcoholic and nonalcoholic patients with preexisting cardiac disease.

Studies have linked moderate alcohol consumption (two to four drinks/day in men and one or two/day in women) to a protective effect from CAD. Low to moderate alcohol consumption decreases platelet aggregation, raises plasma levels of endogenous tissue plasminogen activator, and lowers insulin resistance.

Studies have suggested that moderate alcohol consumption, through a reduced risk of CAD, may also protect individuals from congestive heart failure. All these beneficial effects are lost in heavy drinkers, in whom chronic alcoholism is associated with hypertension and congestive cardiomyopathy.

Heavy alcohol consumption has a detrimental effect on those with preexisting CAD. It can reduce exercise tolerance, induce coronary vasoconstriction, and raise heart rate and blood pressure. Additive cardiovascular effects of ethanol and nicotine contribute to dysrhythmias and sudden death in patients with CAD. There is an increased incidence of sudden death among heavy drinkers, regardless of concomitant CAD or smoking.

Supraventricular (usually atrial fibrillation) and ventricular (usually transitory ventricular tachycardia) dysrhythmias, labeled holiday heart, have been documented in alcoholic patients who have been drinking heavily. Tachydysrhythmias as a result of episodic drinking commonly revert to sinus rhythm with abstinence and do not require immediate intervention if the patient is hemodynamically stable.

Pulmonary Effects

Alcohol reduces the mobilization of alveolar macrophages and their bactericidal capacity. Their impairment is greatest in alcoholics with hepatic cirrhosis. There is evidence that chronic alcohol consumption decreases the level of glutathione, promoting inflammation and remodeling of the lung tissue. These effects, along with aspiration, decreased airway sensitivity, concomitant smoking, and malnutrition, probably account for the increased incidence of pneumonia, particularly lobar pneumonia, among alcoholic patients.

The high prevalence of respiratory disease in alcoholics is largely caused by smoking. Alcohol induces bronchospasm in some asthmatics and increases ventricular ectopy and sleep apnea in patients with chronic obstructive pulmonary disease.

Gastrointestinal and Hepatic Effects

Esophagus and Stomach

Alcoholic patients have a higher incidence of esophagitis, gastric cancer, and esophageal carcinoma than that in the general population. Acute alcohol ingestion also decreases lower esophageal sphincter pressure, delays gastric emptying, and disrupts the normal gastric mucosal barrier. Alcohol consumption, because of its inherent toxicity, has been shown to eliminate infection of the gastric mucosa by *Helicobacter pylori*.[5] Forceful or persistent emesis can lead to a Mallory-Weiss tear or Boerhaave's syndrome.

Gastrointestinal Bleeding

Alcohol is closely associated with gastrointestinal (GI) bleeding. Causes and contributing factors include Mallory-Weiss tears, esophagitis, esophageal varices, acute and chronic gastritis, thrombocytopenia, portal hypertensive gastropathy, qualitative and quantitative platelet disorders, and prolonged clotting times. Alcohol may exacerbate gastric mucosal damage when it is combined with nonsteroidal antiinflammatory drugs (NSAIDs), but ethanol itself is not a risk factor for peptic ulcer disease. Peptic ulcer disease is the most common cause of bleeding in alcoholic patients with upper GI hemorrhage, as well as in those who do not drink.

Liver Damage

Hepatic damage has been recognized for centuries as the hallmark of chronic alcohol abuse. The activation of the immune system with the production of cytokines such as tumor necrosis factor alpha is one of the earliest events in many types of liver injury. This cascade stimulates Kupffer cells and the production of other cytokines that together enlist inflammatory cells, kill hepatocytes, and initiate healing through fibrogenesis. There is no single test that can be used to diagnose alcoholic liver disease reliably. However, a ratio of aspartate transaminase (AST) to alanine transaminase (ALT) higher than 2 suggests that alcohol is the cause of liver injury. Alcoholic liver disease is the most common liver disorder in the West and, along with hepatitis C, is a leading cause of liver transplantation.

Alcoholic Hepatitis

Alcoholic hepatitis is more serious than fatty infiltration and develops in up to 35% of heavy drinkers. These individuals usually have right upper quadrant pain, a tender enlarged liver, fever, jaundice, leukocytosis, and altered liver function test results. AST levels are usually less than 400 IU/L, and ALT levels are typically less than half the AST level. Alcoholic hepatitis has a range of clinical manifestations, from mildly symptomatic hepatomegaly to fulminant hepatic failure. The severity of the disease can be estimated in the ED by a prolonged prothrombin time/international normalized ratio (INR) or with the use of the Maddrey discriminant factor. The ABIC (***a***ge, ***b***ilirubin, I***N***R, ***c***reatinine) score and model for end-stage liver disease (MELD) are also helpful in predicting mortality in these patients.

Alcoholic Cirrhosis

Cirrhosis is the disruption of the normal architecture of the liver by scarring and regenerating nodules of parenchyma. Alcoholism is the most common cause of cirrhosis in the United States and is responsible for approximately 50% of all cirrhotic deaths. Alcoholic cirrhosis usually requires 10 to 15 years of chronic drinking,

often punctuated by one or more episodes of acute alcoholic hepatitis. The clinical outcome is determined by the development of complications of portal hypertension and by hepatic dysfunction. It is unknown why hepatic damage develops in some alcoholic patients and not in others exposed to identical amounts of alcohol. The disorder was originally described as nutritional cirrhosis, but it has been shown that alcohol, independent of malnutrition, produces the liver damage. Alteration of the normal hepatic architecture by fibrosis and nodule formation may eventually lead to portal hypertension. Portal hypertension may be complicated by ascites and esophageal varices. Although cirrhosis is irreversible, its progression may be halted with abstinence.

No specific medical therapy exists for alcoholic liver disease other than abstinence, proper diet, and management of the subsequent hepatic decompensation (ie, ascites, encephalopathy). A decrease in the amount of alcohol consumed during 1 year is associated with a 60% decrease in mortality.

Pancreatitis and Malabsorption

The association of ethanol with acute and chronic pancreatitis is well established, but the exact pathogenesis is unclear. Hypotheses include reflux of duodenal contents and bile into the pancreatic duct, obstruction by a plug of pancreatic juice rich in proteins, and a direct toxic effect of ethanol.

The diagnosis of alcoholic pancreatitis can be difficult because asymptomatic alcoholics may have an elevated amylase level. Conversely, up to 30% of patients with acute alcoholic pancreatitis have an amylase value within normal limits. The serum lipase level rises after amylase, remains elevated longer, and is a more reliable indicator of alcoholic pancreatitis, especially when it is more than three times normal. Alcohol is the leading cause of chronic pancreatitis.

Diarrhea and impaired intestinal absorption are common problems of the chronic alcoholic. Alcohol increases small intestine transit time and decreases brush border enzyme activity. Thiamine, vitamin B_{12}, amino acids, folic acid, and glucose have impaired absorption in alcoholics. Dietary deficiencies in folic acid and protein, pancreatic insufficiency, abnormal biliary secretion, and direct toxic effects of ethanol on the GI tract contribute to malabsorption. Abstinence and adequate nutrition reverse the diarrhea and much of the malabsorption.

Neurologic Effects

Neuropathy

A symmetric sensorimotor polyneuropathy is common with chronic alcohol abuse, usually in the lower extremities. It is thought to be a combination of nutritional deficiency with thiamine or vitamin B_{12} deficit and a direct neurotoxic effect of alcohol. Burning pain and paresthesia are common complaints. Findings on physical examination include loss of light touch, decreased pinprick sensation, and reduced lower extremity deep tendon reflexes. Distal muscle weakness is a late finding. The neuropathy may lead to nonhealing ulcers on the feet. Treatment of alcoholic neuropathy is abstinence, adequate diet, and thiamine. Complete recovery is rare.

So-called Saturday night palsy or honeymooner's syndrome is a wrist drop caused by radial nerve compression. The patient usually has spent the night with his or her arm drooped over the back of a chair, bench, or companion, compressing the radial nerve against the humerus and producing a neurapraxia. Loss of function due to radial nerve neurapraxia usually returns after a few weeks to months.

Wernicke-Korsakoff Syndrome

Although they are similar pathologically and are caused by thiamine deficiency, Wernicke and Korsakoff syndromes are clinically distinct. Wernicke's encephalopathy, a medical emergency with a mortality rate of 10% to 20%, remains a clinical diagnosis and is often unrecognized. Contemporary criteria require two of these signs—dietary deficiencies, oculomotor abnormalities (nystagmus is most common), cerebellar dysfunction, and an altered mental state or mild memory impairment. Mental abnormalities include lethargy, inattentiveness, abulia, and impaired memory, progressing without treatment to coma.

Korsakoff's psychosis or amnesic state, also called alcohol-induced persisting amnestic disorder, is a disorder with recent memory impairment, inability to learn new information or recall previously learned information, apathy, and confabulation. Although it is common, confabulation is not essential for the diagnosis. Whereas 80% of patients with acute Wernicke's encephalopathy have Korsakoff's syndrome, age older than 40 years and many years of heavy alcohol use are additional risk factors.

Treatment of Wernicke-Korsakoff syndrome consists of abstinence, adequate diet, and thiamine. The ophthalmoplegia and nystagmus usually have a good response to thiamine within hours to days. The ataxia and mental changes may take days to weeks to improve and usually have a poorer prognosis. Less than 25% of patients show any real recovery, 50% show some recovery, and the remainder show no response, despite adequate thiamine replacement. Because magnesium is a cofactor for this enzyme system, its serum levels should be corrected. Patients with Wernicke's syndrome require admission and thiamine and magnesium repletion.

Movement Disorders

Alcohol withdrawal is associated with tremor, ataxia, and myoclonus. Acute alcohol consumption ameliorates essential tremor and myoclonus. Persistent tremor is occasionally seen in chronic alcoholism. This alcoholic tremor may persist up to 1 year after abstinence. Although the pathophysiologic mechanism is poorly understood, studies have confirmed that essential tremor and alcoholic tremor are distinct entities.

Alcoholic Cerebellar Degeneration

Characterized by ataxia of the extremities, cerebellar ataxia of alcoholism results in a wide-based stance and uncoordinated gait. Lower extremity involvement predominates, although the arms may rarely be involved. Pathologic changes consist of degeneration of elements in the cerebellum, especially the Purkinje cells. The diagnosis is based on history, physical examination, and findings on magnetic resonance imaging or computed tomography (CT), which shows severe cerebellar atrophy. Treatment consists of abstinence, adequate nutrition, and thiamine.

Infectious Disease

Chronic alcohol abuse causes immunosuppression. Neutropenia may be found in up to 8% of hospitalized alcoholics. Alcohol ingestion prevents the normal delivery (chemotaxis) of polymorphonuclear neutrophils to sites of bacterial infection. Chronic alcohol exposure depresses the development and expression of cell-mediated immunity. This depression may contribute to the high incidence of tuberculosis and head, neck, and upper GI cancers in alcoholics. The suppression of macrophage function by alcohol reduces the reticuloendothelial system's ability to clear particles. This may contribute to spontaneous bacteremia, spontaneous bacterial peritonitis, and pneumonia. Primary antibody

response to new antigens is also depressed. Malnutrition and liver failure also contribute to an immunocompromised state in the alcoholic.

The most common infection in alcoholism is pneumonia. Associated risk factors for pneumonia in alcoholics include smoking, decreased ciliary function, decreased surfactant production, depressed cough reflex, malnutrition, and poor oral hygiene. Although alcoholic patients may contract a variety of bacterial pneumonias, *Streptococcus pneumoniae* is still the most common organism. Periods of alcoholic stupor with incomplete glottic closure and subsequent aspiration can lead to aspiration pneumonia or lung abscess. *Klebsiella pneumoniae,* classically associated with alcoholism, is currently more common in patients with cytotoxic chemotherapy, hematologic malignant disease, and transplantation than in the chronic alcoholic. In addition, these infections now tend to be nosocomial rather than community-acquired.

Endocrine Effects

Alcohol dependence adversely affects many endocrine systems. Peripheral thyroid hormone dysfunction and central hypothalamic-pituitary-thyroid axis deregulation are seen. Male hypogonadism and feminism are seen in chronic male alcoholics. Alcohol's effects on the testes and hypothalamus decrease testosterone production in men. Alcohol may cause impotence by CNS sedation, secondary depression, or decreased testosterone production. Decreased testosterone, increased estrogen (in patients with liver disease), and increased prolactin levels can lead to decreased libido, feminization, and gynecomastia in male alcoholics and to abnormalities in lactation and menstruation in women. In female alcoholics, increased levels of testosterone and estrogen are found. Estrogen replacement therapy may increase hormonal levels threefold and thus increase the risk of cholelithiasis and breast cancer.

Metabolic Effects

Carbohydrates

Alcohol-induced hypoglycemia occurs in 1% to 4% of intoxicated ED patients. It is more frequently seen in chronic alcoholics. Coma, seizures, hemiparesis, and a variety of other neurologic signs have been described in patients presenting with alcohol-induced hypoglycemia. Starvation, depletion of liver glycogen stores, decreased plasma cortisol levels, impaired release of growth hormone, and inhibition of gluconeogenesis contribute to this phenomenon.

Hyperglycemia and diabetes may be found in chronic alcoholism. Alcohol abuse can lead to chronic pancreatitis, resulting in underproduction of insulin by the damaged pancreatic cells. Alcohol also impairs peripheral glucose utilization, causing a relative insulin resistance (similar to type 2 diabetes). In diabetic patients, alcohol can induce hypoglycemia and also mask the signs of hypoglycemia.

Lipids

A reversible hypertriglyceridemia occurs in many chronic alcoholics. Ethanol increases hepatic synthesis of triglycerides. Abstinence is necessary to reduce elevated triglyceride levels. Except for its relationship to fatty infiltration of the liver, the clinical significance of this hyperlipidemia is unknown.

Electrolytes

Ethanol has numerous effects on electrolytes and mineral metabolism, as summarized in Table 142.3. Hyponatremia and hypokalemia are common in active drinkers. Vomiting, diarrhea, magnesium depletion, malnutrition, and metabolic alkalosis contribute to these abnormalities.

TABLE 142.3

Effect of Ethanol on Mineral Metabolism

MINERAL	CAUSE OF DEPLETION	ADDITIONAL EFFECT OF COMPARTMENT SHIFTS	CONSEQUENCES
Magnesium	Alcohol diarrhea Poor intake Phosphate depletion Hyperaldosteronism	↓ Hyperventilation ↓ Free fatty acids	Pseudohypoparathyroidism Myopathy Potassium depletion Phosphate depletion Electrocardiographic abnormalities Seizures
Phosphorus	Poor intake Diarrhea Metabolic alkalosis Hypomagnesemia	↓ Metabolic alkalosis ↓ Respiratory alkalosis ↓ Glucose (refeeding) ↑ Hypoparathyroidism (secondary to hypomagnesemia) ↑ Rhabdomyolysis	Rhabdomyolysis Platelet dysfunction White blood cell dysfunction Central nervous system dysfunction Cardiac failure Renal tubular acidosis
Calcium	Poor intake Steatorrhea Hypovitaminosis K	↓ Hypoparathyroidism (secondary to hypomagnesemia) ↓ Rhabdomyolysis ↓ Hypovitaminosis D ↓ Hyperphosphatemia ↓ Pancreatitis ↓ Hypoalbuminemia ↑ Recovery from rhabdomyolysis	Tetany Seizures
Potassium	Poor intake Metabolic alkalosis Hyperaldosteronism Diarrhea	↓ Glucose (refeeding) ↓ Hyperventilation ↑ Rhabdomyolysis	Weakness Paralysis Myopathy Sudden death

↑, Into plasma; ↓, out of plasma.

Alcoholism is the most common cause of severe magnesium deficiency in adult outpatients. Magnesium deficiency is seen in 30% of alcoholics as a result of malabsorption, malnutrition, diarrhea, vomiting, and increased urinary losses. Oral magnesium supplementation in chronic alcoholics improves liver function test findings, electrolyte balance, and muscle strength. Multivitamin preparations may be considered for chronic malnutrition. Although their clinical benefit is not proved, they carry no significant risk or cost.

Hypocalcemia is common in alcoholic patients with magnesium depletion. The mechanism is related to diminished parathyroid hormone secretion, decreased tissue responsiveness to parathyroid hormone, decreased vitamin D metabolism, and decreased calcium release from bone, independent of parathyroid hormone. Correction of magnesium depletion is necessary to restore calcium to normal levels. Hypoalbuminemia, pancreatitis, or vitamin D deficiency also contribute to low serum calcium levels or low total body stores of calcium in alcoholic patients.

Hypophosphatemia is found in 30% to 50% of hospitalized patients with alcoholism. Phosphorus depletion results from malnutrition, vomiting, respiratory alkalosis, diarrhea, enhanced release of calcitonin, phosphate-binding antacids, and urinary loss (related to vitamin D deficiency and secondary hyperparathyroidism). Hypophosphatemic patients often have low magnesium levels. Rehydration, carbohydrate repletion, and parenteral alimentation further exacerbate phosphorus depletion. Glucose bolus and infusion have been shown to produce a significant fall in serum inorganic phosphate levels. Severe hypophosphatemia (<1 mg/dL) has been associated with acute respiratory failure, myocardial depression, dysfunction of erythrocytes, leukocytes, and platelets, CNS irritability, and rhabdomyolysis.

Although chronic alcoholics requiring admission often have potassium, magnesium, and phosphate depletion, empirical treatment with potassium and phosphate is discouraged. Serum levels and renal function should be determined. Unintended hyperkalemia and hyperphosphatemia can produce significant morbidity, and phosphate infusion exacerbates hypocalcemia, if present. Because most magnesium is intracellular, a normal serum magnesium level does not rule out decreased total body magnesium stores. If the serum level is normal, total body levels may still be low. As long as renal function is adequate, empirical magnesium treatment can be considered. Abstinence and a proper diet resolve electrolyte and nutritional deficiencies in the ambulatory alcoholic patient who is healthy enough to be treated as an outpatient.

Alcoholic Ketoacidosis

Alcoholic ketoacidosis occurs most frequently in severe chronic alcoholics who have had a recent binge followed 1 to 3 days later by protracted vomiting, decreased food intake, dehydration, and abstinence. Nausea, vomiting, and abdominal pain are common presenting complaints. These patients have tachypnea, dehydration, ketonuria, and little or no glucosuria. Serum glucose levels are usually less than 200 mg/dL. Normal blood pH may be found despite ketonemia because of coexisting respiratory alkalosis and metabolic alkalosis.

The exact mechanism responsible for the increase in ketone bodies is unclear. Acute starvation superimposed on chronic malnutrition, as well as release of an alcohol-induced block in ketogenesis, allowing marked ketosis, may explain the disorder. An increased ratio of NADH to NAD in the alcoholic predisposes to the accumulation of β-hydroxybutyrate and the inhibition of gluconeogenesis, which may underlie the common occurrence of hypoglycemia in alcoholic ketoacidosis.

The alcoholic patient with metabolic acidosis presents an interesting dilemma because most of these patients have an increased anion gap acidosis. Glucosuria may suggest diabetes, crystalluria can be seen in ethylene glycol poisoning, low specific gravity, proteinuria, and casts can be seen in renal failure, leukocytes and bacteria are present with urosepsis, and significant ketones in an otherwise normal urine may indicate starvation or alcoholic ketosis. Elevated levels or a very high osmolal gap (>25 mOsm/kg) is specific for methanol or ethylene glycol ingestion.

Treatment of alcoholic ketosis consists of the administration of normal saline, glucose, and thiamine and correction of hypokalemia. This can be accomplished with 5% dextrose in normal saline and 30 mEq of potassium chloride or 30 mEq of oral potassium. If no serious complicating illness is present, the ketosis is reversed in 12 to 24 hours with this treatment.

Hematologic Effects

The alcoholic presents with myriad hematologic abnormalities. The direct toxic effect of ethanol and its metabolites, secondary nutritional deficiency, and hepatic disease, individually or in combination, affect red blood cells, white blood cells, platelets, hemostasis, and the immune system. Macrocytosis is the most common hematologic manifestation of the chronic alcoholic. It may be caused by folate deficiency, reticulocytosis (the younger reticulocytes are larger), liver disease (producing an abnormal lipid coating of the red blood cell membrane), or vitamin B_{12} deficiency. The most common condition is idiopathic macrocytosis of alcoholism.

Anemia

Several mechanisms cause anemia, which is common in the alcoholic. Megaloblastic anemia resulting from folate deficiency is the most common anemia in alcoholics. The mean corpuscular volume (MCV) is typically increased but may be normal when iron deficiency coexists. Malnutrition, inability of the cirrhotic liver to store folate, excessive urinary loss, and malabsorption decrease folate stores. Alcohol accelerates the development of megaloblastic anemia in individuals with depleted folate stores (MCV > 100 fL) by a less clearly defined mechanism.

Iron deficiency anemia is common and is usually a result of blood loss from the GI tract. With iron deficiency anemia, the serum iron level is decreased, total serum iron-binding capacity is elevated, and serum ferritin level is decreased. Alcoholics frequently have chronic inflammatory diseases such as endocarditis, tuberculosis, empyema, lung abscess, malignant disease, and hepatic disease. These illnesses can produce the anemia of chronic disease, a mild microcytic or normocytic anemia in which the serum iron is low but, in contrast to iron deficiency, the total serum iron-binding capacity is low or low-normal, and the serum ferritin level is increased.

Ethanol also has a direct toxic effect on erythropoiesis. Bone marrow biopsies reveal vacuolization of erythroid precursors, resulting in decreased reticulocytosis and a reversible sideroblastic anemia. Sideroblastic anemia, which is usually seen in the presence of malnutrition with pyridoxine deficiency and folate deficiency, occurs in 25% to 30% of anemic alcoholics.

Leukocyte Abnormalities

Leukopenia is common in the alcoholic patient and has several possible causes. Sepsis, folate deficiency, and hypersplenism all lead to a decreased white blood cell count. Alcohol has a direct toxic effect on white blood cell production in the bone marrow. Granulocyte mobilization (chemotaxis) and adherence are also impaired, resulting in a decreased inflammatory response.

Platelet Disorders

Thrombocytopenia can occur with folate deficiency, marrow suppression, sepsis, disseminated intravascular coagulation, or splenic sequestration. The direct toxic effects of alcohol decrease measured survival time and impair production of platelets in the bone marrow, but marrow toxicity will rarely reduce the platelet count below 30,000/mm^3. Qualitative platelet function is also impaired. Binge drinking is associated with a reactive thrombocytosis potentially responsible for acute stroke and sudden death.

Hemostasis

Alcoholic patients have a bleeding diathesis for many reasons, including thrombocytopenia, qualitative platelet disorders, deficient production of hepatic clotting factors, GI variceal formation, and vitamin K deficiency. A complete blood count, peripheral smear, platelet count, reticulocyte count, thrombin time, prothrombin time and INR, and partial thromboplastin time help evaluate episodes of significant bleeding. Bleeding associated with coagulation abnormalities may require fresh-frozen plasma for the immediate correction of coagulation factor depletion; vitamin K (10 mg IV) takes 6 to 10 hours to reverse the vitamin K–dependent factors II, VII, IX, and X. Because of poor diet and impaired hepatobiliary function, alcoholics may have insufficient vitamin K storage and benefit from vitamin K delivery. However, alcoholic patients with profound liver failure are unable to produce the precoagulation factors II, VII, IX, X, and IV, so vitamin K therapy is futile. Platelet transfusions should be started in the ED for adult patients with active bleeding when the platelet count is less than 50,000/mm^3.

Oncologic Effects

Worldwide, 389,000 annual cases of cancer representing 3.6% of all cancers are alcohol-related.[10,11] Although alcohol itself is not carcinogenic, its metabolite, acetaldehyde, has emerged as an important contributor; it can form stable DNA adducts, trigger mutations in tumor suppressors and oncogenes, and interfere with DNA repair. Smoking certainly has an additional role as a cause of neoplasia and is difficult to isolate in these studies.

Chronic alcohol use is associated with an increased incidence of upper alimentary and respiratory tract cancers, with a clear dose-response relationship. Specifically, alcohol increases the risk of cancer of the mouth, pharynx, larynx, lung, esophagus, liver, and pancreas.[12] Chronic hepatitis B infection may sensitize the liver to alcohol, producing hepatocellular carcinoma. Women who drink two to five drinks/day have a relative risk of 1.41 for invasive breast cancer compared with nondrinkers. There is also a significant increase in endometrial cancer risk among postmenopausal women who consume more than two alcoholic drinks/day. Moderate alcohol consumption leads to an increased risk of colorectal and prostate cancer.

Hypothermia

Acute alcohol ingestion is one of the most common precipitating factors for accidental hypothermia and occurs in 33% to 73% of patients presenting with a core temperature below 35°C (95°F). Alcohol exacerbates hypothermia of other causes, with depressed hypothalamic thermoregulation, peripheral vasodilation producing heat loss, CNS depression, sepsis, inability to shiver, hypoglycemia, and increased risk of environmental exposure. Hypothermia may be the presentation of Wernicke's syndrome, possibly caused by lesions of the posterior hypothalamus, hypoglycemia, or sepsis. Intoxicated patients may have slower rewarming rates.

Psychiatric Effects

Of alcohol-dependent adults, 45% are diagnosed with one or more additional psychiatric conditions during their lifetime. Of alcoholic men admitted to a psychiatric ward, approximately 40% have another psychiatric disorder unrelated to substance abuse—in particular, antisocial personality disorder, schizophrenia, mood disorders, and anxiety disorders.

Depression and antisocial personality are the two most common psychiatric disorders that correlate with alcoholism, with a prevalence of 30% to 60% in most studies. Chronic alcohol use can produce an imbalance in the serotoninergic system. This imbalance may lead to increased anxiety, aggression, and depression. Interestingly, behavior is more strongly linked to depression than to alcohol dependence. Secondary depression may be caused by alcoholism, or the primary affective disorder may be present with secondary alcoholism. Mild depressive symptoms are also common in alcohol withdrawal. Antisocial individuals are at high risk for alcoholism and drug dependence, although an unstable, unhappy childhood environment appears to be more important than alcohol to the development of sociopathy. Alcohol increases the lifetime risk of suicide, with 17% of all alcoholics eventually dying by suicide. Alcoholism, major depression, and antisocial personality all predispose to suicide, and interaction among the three is particularly dangerous, but the acute risk on any particular day is difficult to assess.

Toxicologic Effects

Alcohol has long been known to have additive or even synergistic effects with several drugs. Acute intoxication decreases the rate of drug metabolism, which is at least partially explained by competition for the same enzymatic process in the liver. When cocaine and ethanol are taken concomitantly, the unique metabolite, cocaethylene, is a neurologically active compound that is significantly more toxic than cocaine to the heart, liver, and brain and more addicting and more lethal than cocaine alone. Cocaethylene produces a higher incidence of confusion, lower mean Glasgow Coma Scale (GCS) scores, a higher incidence of violent trauma and more often requires endotracheal intubation. Hemodynamically, these patients demonstrate an elevated heart rate (1.5–5 times normal) and higher blood pressure than with either drug alone. Sudden death is increased up to 25-fold above that associated with the use of cocaine alone. Plasma levels of cocaine in this combined group were higher than in those who used cocaine alone.

Ethanol increases aspirin-induced prolongation of bleeding time and reduces the metabolism of warfarin, leading to increased anticoagulant effects. There is an increased risk of upper GI bleeding when alcohol is combined with NSAIDs. This may be the most dangerous additive or synergistic effect of alcohol.

Disulfiram and Similar Reactions

Most patients pretreated with disulfiram (Antabuse) who then consume even small amounts of alcohol experience an extremely unpleasant reaction. These patients have a hypersensitivity to ethanol and experience a direct response within 15 minutes, lasting 30 minutes to several hours. The reaction consists of skin flushing on the head that spreads to the trunk, along with nausea, vomiting, headache, chest and abdominal discomfort, diaphoresis, vertigo, palpitations, and confusion. A severe reaction may produce hypotension, seizures, and dysrhythmias. The disulfiram-ethanol reaction is thought to occur by the accumulation of acetaldehyde secondary to inhibition of the aldehyde dehydrogenase enzyme, which may be deficient in many Asians, or another unknown toxic factor. This incapacitating reaction has been used to discourage chronic alcohol ingestion. Treatment for disulfiram

reaction is usually just observation, an antiemetic for symptoms, and intravenous (IV) fluids.

Profound hypoglycemia can occur when alcohol and oral hypoglycemic agents are combined. Patients taking metformin may have an increased risk for the development of lactic acidosis when it is combined with heavy drinking. A disulfiram-ethanol–like reaction has been described with many hypoglycemic agents.

Other Considerations

Patient Groups Affected

Adolescents. Alcohol is a common drug of abuse among adolescents and young adults. It is estimated that at least 50% of adolescents 12 to 20 years old have imbibed alcohol during any 30-day period. Alcohol is often associated with the three leading causes of death among youth—unintentional injury, homicide, and suicide.

Adolescent drinking is associated with many negative consequences, including deleterious effects on neurocognitive and hormonal development and cognitive and emotional abilities. Social conflicts, delinquency, and problems of academic adjustment are often associated with repeated episodes of heavy drinking, which also put youth at risk for the chronification of problematic substance use patterns into adulthood.[13]

Older Patients. Unhealthy drinking is found in up to 15% of older ED patients (>65 years). It has been estimated that 50% of older people drink alcohol, and 2% to 4% meet the criteria for alcohol abuse or dependence. Common screening tests (eg, the CAGE questionnaire) tend to be less sensitive in this age group. Alcohol may exacerbate underlying disease by masking anginal chest pain, worsening hypertension, and inducing dysrhythmias. However, older adults who consume low to moderate levels of alcohol may have a decreased risk for the development of dementia and heart failure. More than 90% of people aged 65 years or older use more than one prescribed medication. Aging alters GI absorption, lowers volume of distribution, diminishes homeostatic responses, and reduces renal and hepatic function. Older adults also demonstrate increased end-organ sensitivity, particularly involving the CNS, with concomitant drug use increasing their risk for alcohol and drug interactions.

Older patients are more likely to have neuropsychiatric complications of alcoholism, such as sleep problems, anxiety, depression, and dementia. Alcohol is involved in one third of suicides in older adults. Older subjects also perform less well than younger subjects on tests of perception and attention at all blood alcohol levels. This may result in an increased risk of fractures from falling and osteoporosis. However, evidence has suggested that compared with abstinence, consumption of up to one drink/day is associated with a decreased risk of osteoporotic hip fracture, and there is a beneficial effect of moderate alcohol consumption on bone density.

Pregnant Women. Many scientific reports confirm alcohol's teratogenic effects. According to the National Institute on Drug Abuse, nearly 20% of all children born in the United States have been exposed to alcohol during gestation. Pregnant women who report the use of any alcohol, binge drinking, or frequent drinking are more likely to be older than 30 years, employed, and unmarried.

Fetal alcohol syndrome is characterized by a triad of CNS defects, including mild to moderate mental retardation, dysmorphology, involving mostly facial structures, and growth deficiencies, usually consisting of short stature and microcephaly. Fetal alcohol syndrome is now considered the most common identifiable source of mental retardation. Children exposed to prenatal alcohol exhibit increased activity levels, cognitive and attention deficits, perseverative behavior, and language and motor problems, which persist into adulthood.

Ethanol rapidly diffuses across the placenta and is distributed to all fetal tissue, with a predilection for gray matter. Although infants of mothers who drink heavily have the poorest outcome, children of mothers who consume only two or three alcoholic drinks/day also display abnormalities. Even in the absence of growth retardation or congenital abnormalities, children born to women who consume excessive alcohol during pregnancy appear to be at increased risk for attention deficit disorders. These findings are referred to as fetal alcohol effects.

Whereas there is no known safe amount of alcohol consumption during pregnancy, an average of less than one drink/day in early or late pregnancy showed no measurable impact on a child's learning or cognitive functioning in a cohort study of more than 5000 patients observed for 14 years. Adverse outcomes in this study were associated with an average of more than one drink/day, binge drinking, and consumption of alcohol later in pregnancy. The American Academy of Pediatrics recommends abstinence from alcohol for women who are pregnant or who are planning a pregnancy.

Trauma

The single greatest contributor to alcohol-related mortality in the United States is unintentional injury, accounting for approximately 26,000 deaths/year. The importance of alcohol misuse as a precursor to serious injury is widely accepted enough that the American College of Surgeons Committee on Trauma requires screening for problem drinking for designation at a level I or II trauma center. In addition, level I trauma centers must provide an intervention for identified problem drinkers. Alcohol and trauma are inextricably linked. Independently, the tragic effects of each are numerous; in combination, they are staggering. Injury is a leading cause of death in those between the ages of 1 and 44 years, accounting for more than 50 million injuries/year. In the United States, alcohol is the major risk factor for virtually all categories of intentional and unintentional injury. In addition to increasing the frequency and severity of injury, alcohol significantly complicates management of the trauma victim. Alcohol intoxication often complicates the initial assessment of injury severity, resulting in an increased need for invasive diagnostic and therapeutic procedures (eg, intubation, CT, intracranial pressure monitoring).

Alcohol may diminish the patient's capacity to respond to hemorrhagic shock by altering hemodynamic effects and the acid-base balance. Volume depletion as a result of the diuretic effect of alcohol or vomiting can impair the reserve of the intoxicated trauma patient. Peripheral vasodilation caused by alcohol may contribute to hypotension and hypothermia. Although these effects may be minimal, they underscore the need for early and adequate fluid resuscitation in these patients. Intoxicated patients with severe nonneurologic trauma may have lower blood pressures and carbon dioxide levels, indicative of a compensatory hyperventilation, on hospital arrival compared with sober patients. More important, a poorly understood cardiac depressant effect also increases the depth of shock and volume requirements for resuscitation. Alcohol-induced skin vasodilation may be accompanied by an increase in skeletal muscle, mesenteric, and renal bed constriction and left ventricular stroke work. Thus, the overall effect on systemic vascular resistance and blood pressure may be balanced.

Intoxication renders the signs and symptoms of intra-abdominal and retroperitoneal injury less reliable than usual. If the risk of an intra-abdominal injury exists, further evaluation (eg, ultrasonography, CT) should be considered.

Alcohol intoxication predisposes to abdominal wall laxity and therefore less protection from blunt trauma. These patients are also likely to have full stomachs, increasing the risk of gastric injury after trauma and predisposing to vomiting and aspiration, especially during airway management. The fatty liver changes of alcoholism can result in hepatomegaly. Portal hypertension in alcoholics may produce splenomegaly. These organs can become more vulnerable to the effects of trauma because of their enlarged size, protrusion beneath the protection of the ribs, and increased intracapsular pressure.

No consensus exists on the indications for an emergency CT scan in patients with minor head injury (eg, loss of consciousness, posttraumatic amnesia, GCS score of 14–15, normal findings on neurologic examination). One disturbing prospective study has found that the GCS score and 1 hour of observation were unable to predict abnormal head CT scans in intoxicated patients with minor head trauma. Patients with signs of head trauma and focal or generalized seizures need an urgent CT scan. CT scans of the head should be performed for any patient with deteriorating mental status, focal neurologic findings, new-onset seizures, even without obvious signs of history of trauma, failure to improve over time, or mental status changes out of proportion to the degree of intoxication.

Alcohol Withdrawal Syndrome

Clinical Features

The severity of signs and symptoms of alcohol withdrawal syndrome depends on the dose and duration of ethanol consumption. The withdrawal syndrome may occur any time after the blood alcohol level starts to fall. Therefore, only a reduction, not the abrupt cessation, of ethanol intake may result in withdrawal.

Minor alcohol withdrawal occurs as early as 6 hours after cessation of or significant decrease in alcohol intake and usually peaks at 24 to 36 hours. It is characterized by mild autonomic hyperactivity—nausea, anorexia, coarse tremor, tachycardia, hypertension, hyperreflexia, sleep disturbances (eg, insomnia, vivid dreams), and anxiety.

Major alcohol withdrawal occurs after more than 24 hours and usually peaks at 50 hours after cessation of or significant decrease in alcohol intake but occasionally takes up to 5 days to be manifested after the decline or termination of drinking. The syndrome is characterized by pronounced anxiety, insomnia, irritability, tremor, anorexia, tachycardia, hyperreflexia, hypertension, fever, decreased seizure threshold, auditory and, more commonly visual hallucinations, and finally delirium.

Delirium tremens is a life-threatening manifestation of alcohol withdrawal and consists of gross tremor, frightening visual hallucinations, profound confusion, agitation, and a hyperadrenergic syndrome characterized by a temperature above 101°F (≈38.5°C), blood pressure higher than 140/90 mm Hg, and tachycardia. It seldom appears before the third postabstinence day. Only 5% of patients hospitalized for alcohol withdrawal have delirium tremens.

DIFFERENTIAL DIAGNOSES

Acute alcohol intoxication is a diagnosis of exclusion. Before it is assumed that a patient's behavior is caused only by alcohol, other conditions should be considered, particularly co-ingestants, head trauma, and infection. Hypoglycemia, hypoxia, carbon dioxide narcosis, mixed alcohol-drug overdose, ethylene glycol poisoning, isopropanol or methanol poisoning, hepatic encephalopathy, psychosis, severe vertigo, postictal state, and psychomotor seizures can be manifested in a manner similar to that of ethanol intoxication.

Alcohol withdrawal syndrome can initially be confused with acute schizophrenia, encephalitis, drug-induced psychosis, thyrotoxicosis, anticholinergic poisoning, and withdrawal from other drugs of the sedative-hypnotic type. It may be difficult to differentiate between alcohol withdrawal and alcohol-induced hypoglycemia.

Signs of alcohol withdrawal usually begin 6 to 24 hours after a decrease in the patient's usual intake of alcohol. If patients manifest withdrawal 3 to 4 days or more after their last drink, drugs with a longer half-life should be considered. Barbiturate and benzodiazepine withdrawal syndromes usually progress more slowly, with a higher frequency of seizures later (7 days vs. 2 days), and status epilepticus is more common than with alcohol withdrawal.

DIAGNOSTIC TESTING

Determination of a blood alcohol level is not routinely necessary in caring for the intoxicated patient when there is clear evidence of alcohol intake (eg, confirmation by the patient). When mental status is sufficiently altered that a good history cannot be obtained, there is evidence of head trauma, or the patient fails to improve (detoxify) as expected, determine the serum alcohol level or measure the alcohol level by breathalyzer. If the degree of obtundation is not commensurate with the measured (or breathalyzed) level, and other laboratory test results (eg, toxicology screen, electrolyte levels) do not explain the altered mental status, a head CT scan is indicated. Adequate history from paramedics, patient, and family, serial physical examinations (especially mental status), and bedside testing, such as glucose level and oximetry, can help clarify the clinical situation and guide testing.

Blood tests can be useful if the history is in doubt and can also help patients recognize that alcohol has adversely affected their health. Tests of liver function that measure AST and ALT levels can identify heavy drinking and AUDs with sensitivities of 25% to 45% and specificities as high as 90%. A ratio of AST to ALT higher than 2, especially if concentrations of these enzymes do not exceed 400 units/L, suggests alcoholic hepatitis (Table 142.4).

Laboratory Tests

In the apparently intoxicated patient with altered mental status, the serum glucose level, usually as a point of care test, should be measured to assess for hypoglycemia. In the alcoholic patient, electrolyte levels should be determined to look for hypomagnesemia, hypophosphatemia, hyponatremia, and acidemia. A complete blood count is obtained to evaluate for anemia, leukopenia, and thrombocytopenia and a serum lipase level to evaluate for pancreatitis if the patient has severe upper abdominal pain or tenderness, especially if accompanied by vomiting. Liver function tests are followed in a serial manner in cases of alcoholic hepatitis. An electrocardiogram (ECG) is indicated for tachydysrhythmias or chest pain (eg, holiday heart, acute ischemia). A CT scan of the head or cervical spine may be indicated if head trauma or seizures are suspected or confirmed or if the patient's mental status does not clear in step with the metabolism of alcohol. A chest radiograph is obtained to rule out cardiomyopathy or infectious pneumonia.

Alcohol Screening Questionnaires

Detection of risky drinking behaviors can be through clinical history or the administration of short alcohol screening tools in the ED setting, such as the Alcohol Use Disorders Identification Test (AUDIT), Fast Alcohol Screening Test (FAST), Paddington alcohol test (PAT), and CAGE questionnaires. Other questionnaires include the rapid alcohol problem screen (RAPS-4) and TWEAK (***t***olerance, ***w***orried, ***e***ye opener, ***a***mnesia, ***K*** [cut down]).

TABLE 142.4

Current Biomarkers for Alcoholism

MARKER	ABBREVIATION	HALF-LIFE ELIMINATION RATE	CLINICAL CHARACTERISTICS
Blood ethanol	EtOH	1 g/1 hr/10 kg	Levels exceeding 1.5% without evidence of intoxication or 3% at any time indicate EtOH tolerance typically found in alcohol abusers and alcohol-dependent patients; suitable for emergency clinics
γ-Glutamyltransferase	GGT	2–3 wk	Sensitive and inexpensive marker Age-dependent Specificity decreased by obesity, diabetes, nonalcoholic liver diseases, pancreatitis, hyperlipidemia, cardiac insufficiency, severe trauma, medications (eg, barbiturates, drugs for epilepsy, anticoagulants), nephrotic syndrome, renal rejection
Mean corpuscular volume of erythrocytes	MCV	2–4 mo	More sensitive in women Specificity decreased by vitamin B_{12} or folic acid deficiency, liver disease, hematologic diseases hypothyroidism, reticulocytosis, smoking
Carbohydrate-deficient transferrin (desialotransferrin)	CDT	2–3 wk	Most specific of currently available methods Specificity decreased by genetic variants of transferrin on rare occasions
GGT-CDT combination	GGT-CDT (γ-CDT)	2–3 wk	Mathematically formulated combination that is easy to manage in hospital laboratories Improves sensitivity without a loss of specificity Good correlation with t amount of recent ethanol intake Suitable for routine use
Aminotransferases—aspartate transaminase (AST); alanine transaminase (ALT)	AST, ALT	2–3 wk	AST/ALT ratio >2 suggests alcoholic cause in liver disease patients

From Niemelä O: Biomarkers in alcoholism. Clin Chim Acta 377:39–49, 2007.

The objectives of these screening tools vary; AUDIT and FAST are focused on the detection of recent hazardous or harmful alcohol consumption and associated problems, whereas CAGE is designed to detect lifetime alcohol dependence. The most sensitive screening tool appears to be FAST (93%–94%), which has a specificity of 86% to 88% and positive predicted value of 86% to 87%. Although FAST appears to be the best for accurately identifying alcohol misuse in ED patients, it was assessed as a universal screening tool and may not be feasible—in regard to time or cost—to screen all who present to this service. In contrast, PAT has been developed to be used on a select population in the ED and has already been shown to be cost-effective.[14]

As part of the initial assessment and in alignment with national recommendations, computerized screening programs could be used as an effective method for detecting at-risk alcohol use in ED patients.[15] Identification of AUD and brief advice in the ED can be an effective and cost-effective method to reduce levels of alcohol consumption and alcohol-related harm.[16]

MANAGEMENT CONSIDERATIONS

Comatose or stuporous patients may require intubation. If the bedside glucose level identifies hypoglycemia, IV glucose, as $D_{50}W$ or an infusion of D_5W, is indicated. Patients with evidence of poor nutrition should receive thiamine, 300 to 500 mg IV, before or early during administration of glucose to prevent Wernicke-Korsakoff syndrome. If an opioid overdose is suspected, IV naloxone, 0.8 mg, may be diagnostic and therapeutic. Because magnesium is a necessary cofactor for thiamine metabolism, consider administering magnesium, 2g IV. When possible, hypoglycemia should be documented before the empirical administration of glucose. With the airway maintained and respirations supported, the patient's liver eventually metabolizes the alcohol, and most patients recover.

Intoxicated patients who do not appear capable of appropriate decision making require evaluation and treatment in the ED, regardless of their willingness to cooperate. At the least, it is incumbent on the emergency clinician to establish that the patient understands the nature of the problem, whether intoxication alone or intoxication in the context of acute illness or injury, and is capable of making reasoned and responsible decisions about care. Inappropriate discharge and failure to diagnose are two common areas of liability in treatment of the alcohol-dependent patient. The theoretic liability for detention by reasonable restraint is less than the potential liability for injury sustained by the intoxicated patient or an innocent bystander after premature discharge. Discharge can be considered when a patient is clinically sober enough to be able to dress, walk, make reasonable decisions, and function independently, as judged and well documented by the treating emergency clinician. When possible, it is ideal to have another sober adult who is willing to take responsibility for and remain with the patient for the next 24 to 48 hours.

Alcohol Withdrawal Syndrome

Family, friends, bystanders, or paramedics often give more reliable historical data than the patient does. Accurate vital signs are essential; this may require a rectal temperature. Hyperthermia, hypothermia, tachypnea, or tachycardia may suggest serious disorders that often accompany the alcohol-dependent patient. These disorders should be considered during the initial assessment.

A rapid and thorough examination should be performed, with attention to the level of consciousness, signs of hepatic failure, or coagulopathy. Signs of trauma are sought, such as subcutaneous emphysema, ecchymosis, subconjunctival hemorrhage, hemotympanum, and Battle's sign, and palpation is done for occult injuries. The neurologic examination should search for focal

findings, including central facial nerve palsy, hemiparesis, and asymmetry of pupillary response.

The alcohol withdrawal syndrome should be promptly recognized and treated. The CIWA-Ar is a validated tool for symptom-based prescribing of chlordiazepoxide for alcohol withdrawal and is an alternative to traditional fixed-dose regimens, which may prolong length of stay for up to 5 days. Scores on the CIWA-Ar range from 0 to 67; scores lower than 8 indicate mild withdrawal symptoms that rarely require the use of medications, scores from 8 to 15 indicate moderate withdrawal symptoms that are likely to respond to moderate doses of benzodiazepines, and scores higher than 15 indicate severe syndromes that require close monitoring to avoid seizures and alcohol withdrawal delirium (delirium tremens).

In combination with appropriate chemical sedation, detention by reasonable restraint may be an option to prevent potential injury that patients may inflict on themselves or hospital staff. These appropriate measures need to be instituted; decision-challenged patients should not be permitted to sign an Against Medical Advice Form and be discharged.

Pharmacologic Treatment

Patients suffering from alcohol withdrawal should receive pharmacologic intervention along with supportive care. The ideal drug for alcohol withdrawal should have a rapid onset, wide margin of safety, metabolism not dependent on liver function, and limited abuse potential. Although no one drug class fits all these requirements, benzodiazepines are clearly the mainstay of treatment.

Benzodiazepines. The benzodiazepines have superior anticonvulsant activity, have the least respiratory and cardiac depressive effects of all the CNS depressants, and can be given parenterally to the uncooperative patient. By interacting with receptors linked to the GABA-associated chloride ion channel, benzodiazepines substitute for the withdrawal of the GABA-potentiating effect of alcohol and abate withdrawal signs and symptoms. Numerous benzodiazepines have been studied, but there is no evidence of the clear superiority of any one benzodiazepine.

Lorazepam has good bioavailability with the oral, intramuscular, and IV routes. It is rapidly and completely absorbed from intramuscular sites in agitated patients with no IV access. The half-life of lorazepam is intermediate (7–14 hours), and it reaches a steady state in 36 to 48 hours, without active metabolites. Excessive sedation, confusion, and ataxia are potential complications of all benzodiazepines with prolonged half-lives. Lorazepam is metabolized (conjugated) in the liver, yielding inactive products. Although the half-life of lorazepam increases in patients with cirrhosis or liver failure, it is much shorter than the increase with chlordiazepoxide. The elimination of lorazepam is only minimally altered in patients with renal failure and in older adults. Lorazepam may be given IV in a dose of 1 to 4 mg, depending on the severity of the withdrawal. Dosing can be repeated at 5- to 15-minute intervals for patients in severe withdrawal. Although it is not ideal, an intramuscular dose of 1 to 4 mg can be used every 30 to 60 minutes until the patient is calm and then every hour, as needed, for light somnolence. The oral schedule for moderate withdrawal is 6 mg/day in three divided doses, tapering the amount by 1 to 2 mg/day during 4 to 6 days.

As one dosing regimen, diazepam, 5 mg IV every 5 to 10 minutes (2.5 mg/min), can be given in major withdrawal until the patient is calm. The dose can be repeated in 5 to 10 minutes. If the second dose of 5 mg is not working, consider 10 mg for the third and fourth doses every 5 to 10 minutes. If this is not effective, consider 20 mg for the fifth and subsequent dose until adequate sedation has been obtained.

In patients who do not have a response to high doses of benzodiazepines (especially patients who are intubated), propofol may be administered (eg, 0.3 to 1.25 mg/kg of body weight, up to 4 mg/kg/hr, for up to 48 hours).[6]

Butyrophenones. Haloperidol, a dopamine antagonist, can be considered in patients with major alcohol withdrawal or delirium tremens not responding to IV benzodiazepines. Haloperidol has little effect on myocardial function or respiratory drive, and its safety and efficacy by the IV, intramuscular, or oral route in the ED have been established. Haloperidol has no anticonvulsant properties; however, extrapyramidal effects may be seen. Caution should be used in patients who may be susceptible to a prolonged QTc interval. Droperidol has effects similar to those of haloperidol. Despite the 2001 US Food and Drug Administration (FDA) black box warning for QTc interval prolongation and torsades de pointes after droperidol use, droperidol remains a relatively safe and effective treatment for agitated patients.

Other Agents. Patients being treated for major alcohol withdrawal may be given thiamine (100 mg IV) and magnesium (2 g IV). Although magnesium sulfate does not decrease the severity of withdrawal symptoms, incidence of delirium, or seizures, it carries no significant risk with adequate renal function.

If volume depletion is present, it can be corrected with normal saline. Reversal of electrolyte and metabolic disorders (eg, hypomagnesemia, hypophosphatemia, hypokalemia, acidosis) benefits the patient but does not abate the withdrawal syndrome.

Neurologic Examination

Normal Examination

New-Onset Seizures. Patients with new-onset, alcohol-related seizures should be thoroughly evaluated. This includes alcoholics who claim to have had seizures but for whom no documentation or appropriate evaluation is available. Metabolic disorders, toxic ingestion, infection, and structural abnormalities should be considered.

If the initial physical examination findings, imaging studies, and laboratory test results are within normal limits, patients who remain seizure-free and symptom-free, with no sign of withdrawal after 4 to 6 hours of observation, may be discharged. It may be unclear whether the patient has had a pure alcohol withdrawal seizure or a new-onset seizure disorder in the setting of alcohol ingestion. Long-term treatment with antiepileptic drugs is not useful in unprovoked new-onset seizures that have resolved or when a clear relation to alcohol consumption can be identified.

Optimal outpatient treatment includes follow-up and referral to a detoxification or rehabilitation program. Ideally, the help of a concerned family member or friend who is not a drinking partner and can remain with the patient for at least 1 or 2 days is helpful.

Prior History of Seizures During Withdrawal. The risk of seizure increases significantly in alcoholic patients with manifestations of alcohol withdrawal who relate a history of alcohol withdrawal seizure. Detoxification with benzodiazepines reduces the likelihood of alcohol seizure and should be initiated early because most seizures occur within the first 24 hours after alcohol withdrawal. An initial dose of 2 mg of lorazepam or 5 mg of diazepam can be given IV. These doses frequently need to be repeated.

Abnormal Neurologic Examination

New-Onset Partial Seizures. Partial seizures account for up to 50% of alcohol-related seizures. Conversely, studies have

shown that approximately 20% of patients with partial alcohol-related seizure have structural lesions—hematomas, tumors, vascular abnormalities, or stroke. These primary causes of partial alcohol-related seizure, such as prior head trauma, may be easily missed in the history taking. As a result, an emergent CT scan is indicated to evaluate new-onset partial seizures. The patient with a history of a focal alcohol-related seizure who has been previously evaluated does not require an emergency CT scan provided a return to baseline occurs promptly.

Patients Taking Phenytoin Anticonvulsant

Phenytoin has no significant benefit over placebo in the prevention of recurrence of uncomplicated alcohol withdrawal seizure. Considering the risks of phenytoin and no demonstrated benefit in the setting of alcohol withdrawal seizure, it is not indicated for the treatment of alcohol withdrawal seizures. The sudden withdrawal of phenytoin may potentiate the convulsive effects of alcohol withdrawal.

A patient currently taking antiepileptic drugs for an antecedent seizure disorder who presents with a seizure while intoxicated falls into a different category. Such an episode could be an isolated event in a usually compliant patient without a history of chronic alcohol abuse. In this patient, a seizure in the setting of a subtherapeutic antiepileptic drug level may represent the consequences of noncompliance with antiepileptic medication or sleep deprivation versus alcohol withdrawal seizure.

DISPOSITION

Most patients with acute alcohol intoxication are managed in the ED or ED observation unit and then discharged home. Patients who achieve sufficient sobriety to be ready for discharge are offered detoxification or alcohol treatment. Most alcoholics suffer from a combination of medical, psychiatric, and social problems. Hospitalization may be necessary to diagnose and treat these multiple problems. Moreover, with alcoholics who are no longer able to care for themselves, hospitalization is often dictated for this reason alone. Unfortunately, many managed care and Medicaid plans limit or do not cover inpatient detoxification. In choosing medical versus psychiatric admission, a medical illness usually takes priority. Optimal outpatient therapy for chronic alcoholics includes the involvement of concerned family or friends to ensure that the patient takes his or her medications properly, keeps follow-up appointments, abstains from alcohol, and maintains an adequate diet. Alcoholic patients who undergo outpatient treatment need close supervision; therefore, a follow-up clinic appointment within 24 to 48 hours should be considered.

Acute Intoxication

Acute intoxication alone seldom requires admission. However, a combined alcohol-drug overdose or associated medical, psychiatric, or social problems may require hospitalization. Acute alcohol intoxication is a diagnosis of exclusion reached after adequate observation to ensure that the altered mental status resolves.

Alcohol levels that may be tolerated by an adult can be lethal in children. It is prudent to admit children with acute intoxication unless close psychosocial follow-up can be ensured. Children presenting with hypoglycemia or medical complications should be admitted. Child abuse or neglect should be considered.

Alcohol Withdrawal

Outpatient treatment consists of lorazepam, 1 to 2 mg tid tapered during 3 to 6 days, chlordiazepoxide, 25 to 100 mg tid tapered during 3 to 6 days, or diazepam, 30 mg once daily tapered during 5 days, depending on the severity of symptoms. Adequate diet, abstinence, and participation in a rehabilitation program in the community are also desirable. Any patient requiring 300 mg of chlordiazepoxide or 60 mg of diazepam/day to control withdrawal should be considered for admission.

Patients with signs of major withdrawal (fever, hallucinations, confusion, extreme agitation) require admission. Patients with mild alcohol withdrawal can be observed in the ED. After 4 to 6 hours of observation and treatment, the alert oriented patient whose vital signs, physical examination findings, and results of appropriate laboratory analysis are within normal limits may be released with appropriate medications and aftercare instructions. Nevertheless, the patient requires treatment for the underlying disease of alcoholism and should be advised or referred accordingly.

Seizures

The alcoholic patient with a first-time, alcohol-related seizure may be discharged to a suitable social situation in these situations: (1) when the patient's alcohol withdrawal is mild and controlled by supportive care or low-dose benzodiazepines; (2) the diagnostic evaluation, including a head CT scan, is unremarkable; (3) the patient has had fewer than two seizures; and (4) the patient has been observed to be alert and oriented, with normal vital signs, physical examination findings, and laboratory study results during the 6 hours since the last seizure, and appropriate outpatient follow-up can be ensured.

Patients with a documented history of alcohol-related seizures can be discharged if they have had no more than two alcohol-related seizures during a 6-hour period, with a lucid interval between seizures, and are observed to be seizure-free and at baseline mental and physical status for at least 6 hours after their last alcohol-related seizure. Three to five brief, self-limited seizures may occur with alcohol withdrawal seizure. We recommend prolonged observation in the ED or ED observation unit for patients with two or more seizures because of the potential for deterioration to status epilepticus. Such patients should be observed until at least 6 hours has passed since their last seizure and they have a normal neurologic examination, including normal mental status.

Patients with partial seizures or focal neurologic findings on physical examination require admission unless these findings have been previously documented. Patients with seizures associated with head trauma or mixed alcohol-drug withdrawal are admitted. Status epilepticus or recurrent seizures during ED observation indicate a lack of seizure control and also require hospitalization.

Psychiatric and Social Problems

Alcoholic patients requiring admission with acute intoxication, alcohol-related seizure, alcohol withdrawal, or medical or surgical disorders are usually best managed in acute care units rather than by a general psychiatric service. Some psychiatric and social conditions in the alcoholic can be better handled on a general psychiatric unit—psychosis, exacerbation of schizophrenia, depression with suicidal tendencies, any patient who is a danger to self or others, or alcoholic hallucinosis with an otherwise clear sensorium.

Patients who are no longer able to care for themselves may also require admission. Although these patients' ultimate destination is a rehabilitation center or a board and care program, hospitalization may be necessary to rule out medical or psychiatric illness and treat impending withdrawal symptoms. Patients who wish to stop drinking are usually referred to a detoxification unit for treatment of impending withdrawal. Data and interest are increasing for outpatient drug therapy for alcohol dependence. The FDA has

approved disulfiram, naltrexone, acamprosate, and topiramate for the treatment of alcohol dependence. There is growing evidence that patients with alcohol dependence who carry a particular variant of an opioid receptor gene are more likely to respond to naltrexone, raising the possibility that genetic tests may one day guide medication selection. Naltrexone, ondansetron, acamprosate, and acamprosate plus naltrexone have had mixed results facilitating abstinence. The role of medications in combination with behavioral therapy is being actively investigated.

Several other medications are under active study and are sometimes prescribed for alcoholism treatment on an unapproved or off-label basis. Baclofen, because of its anticraving action and safety, could have an important role for the treatment of alcohol-dependent patients with advanced liver disease. Gabapentin is used as monotherapy or as add-on pharmacotherapy in outpatient settings in the control of alcohol consumption and craving and in helping patients achieve abstinence. Ondansetron may show benefit in early-onset but not in late-onset alcoholics.

Brief intervention and screening (SBIRT—***s***creening, ***b***rief ***i***ntervention, and ***r***eferral to ***t***reatment) is valuable and is now recommended in the ED.[17,18] Internet-based interventions show promise for reducing alcohol consumption, especially among those meeting criteria for hazardous or harmful drinking. Telephone contact after the ED visit may be another effective tool to screen injured patients for hazardous drinking and offer a brief intervention while avoiding interruptions to patient flow. Most communities have an Alcoholics Anonymous (AA) chapter or treatment center for anyone who desires help with alcohol. In smaller communities, clergy or social workers can usually arrange rehabilitation.

KEY CONCEPTS

- Moderate alcohol consumption is defined as one or two drinks/day for men and one drink/day for women.
- Benzodiazepines are the main treatment of alcohol withdrawal and alcohol withdrawal seizures. Minor alcohol withdrawal occurs as early as 6 hours and usually peaks at 24 to 36 hours after the cessation of or significant decrease in alcohol intake.
- Major alcohol withdrawal occurs after 24 hours and usually peaks at 50 hours (but occasionally takes up to 5 days) after the decrease or termination of drinking.
- Delirium tremens is the extreme end of the alcohol withdrawal spectrum; it consists of gross tremors, profound confusion, fever, incontinence, and frightening visual hallucinations.
- Alcohol withdrawal seizures occur 6 to 48 hours after the cessation of drinking, with 60% of patients experiencing multiple seizures within a 6-hour period.
- Alcohol withdrawal should be assessed and managed using a validated scale, such as the CIWA-Ar scale.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.

REFERENCES

1. Jonas DE, et al: Behavioral counseling after screening for alcohol misuse in primary care: a systematic review and meta-analysis for the U.S. Preventive Services Task Force. Ann Intern Med 157:645–654, 2012.
2. Zhang M, et al: The presence of hepatitis B core antibody is associated with more advanced liver disease in alcoholic patients with cirrhosis. Alcohol 47:553–558, 2013.
3. Trillo AD, et al: Sex differences in alcohol misuse and estimated blood alcohol concentrations among emergency department patients: implications for brief interventions. Acad Emerg Med 19:924–933, 2012.
4. Friedmann PD: Clinical practice. Alcohol use in adults. N Engl J Med 368:365–373, 2013.
5. Maldonado JR, et al: The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome. Alcohol 48:375–390, 2014.
6. Schuckit MA: Recognition and management of withdrawal delirium (delirium tremens). N Engl J Med 371:2109–2113, 2014.
7. McMicken D, Liss JL: Alcohol-related seizures. Emerg Med Clin North Am 29:117–124, 2011.
8. Brousse G, et al: Alteration of glutamate/GABA balance during acute alcohol withdrawal in emergency department: a prospective analysis. Alcohol Alcohol 47:501–508, 2012.
9. Thorsell A: The mu-opioid receptor and treatment response to naltrexone. Alcohol Alcohol 48:402–408, 2013.
10. Toriola AT, et al: The impact of alcohol consumption on the risk of cancer among men: a 20-year follow-up study from Finland. Eur J Cancer 46:1488–1492, 2010.
11. Watters JL, et al: Alcoholic beverages and prostate cancer in a prospective US cohort study. Am J Epidemiol 172:773–780, 2010.
12. Langhan ML: Acute alcohol intoxication in adolescents: frequency of respiratory depression. J Emerg Med 44:1063–1069, 2013.
13. Diestelkamp S, et al: Brief motivational intervention for adolescents treated in emergency departments for acute alcohol intoxication—a randomized-controlled trial. BMC Emerg Med 14:13, 2014.
14. Jones LA: Systematic review of alcohol screening tools for use in the emergency department. Emerg Med J 28:182–191, 2011.
15. Lotfipour S, et al: Increased detection of alcohol consumption and at-risk drinking with computerized alcohol screening. J Emerg Med 44:861–866, 2013.
16. Patton R, O'Hara P: Alcohol: signs of improvement. The 2nd national Emergency Department survey of alcohol identification and intervention activity. Emerg Med J 30:492–495, 2013.
17. D'Onofrio G, et al: A brief intervention reduces hazardous and harmful drinking in emergency department patients. Ann Emerg Med 60:181–192, 2012.
18. Field CA, Caetano R: The effectiveness of brief intervention among injured patients with alcohol dependence: who benefits from brief interventions? Drug Alcohol Depend 111:13–20, 2010.

CHAPTER 142: QUESTIONS & ANSWERS

142.1. A 56-year-old man presents with altered mental status. You recognize the patient as a frequent visitor to the emergency department (ED) for alcohol intoxication. He is drowsy but arousable to painful stimuli. He is confused. Vital signs are within normal limits, and there is no evidence of trauma. His blood glucose level is 30 mg/dL. Which treatment is indicated first?

A. Dextrose
B. Folate
C. Glucagon
D. Naloxone
E. Thiamine

Answer: A. Although alcohol intoxication clearly causes altered mental status (AMS), it should never be assumed that AMS is due to alcohol intoxication. Alcoholics are at risk for multiple medical and traumatic causes of AMS. Chronic alcoholics have decreased glycogen stores and frequently experience hypoglycemia. Because glucagon works by mobilizing glycogen stores, it is often not effective in alcoholics. Thiamine and folate stores are often depleted and can result in Wernicke's encephalopathy. However, hypoglycemia is much more common and can also result in permanent morbidity if untreated. Although the administration of thiamine and folate should be considered for alcoholics, their use should never delay treatment of hypoglycemia. Naloxone is an opioid antagonist and has no effect on alcohol metabolism or glucose levels.

142.2. A 62-year-old man presents with agitation, confusion, and fever. He is noted to experience visual hallucinations during your interview. His vital signs reveal hypertension, tachycardia, and fever. Physical examination is otherwise unremarkable. Diagnostic studies (including head CT and lumbar puncture) are nonspecific. Which diagnosis is most consistent with this patient's presentation?

A. Acute schizophrenia
B. Alcohol withdrawal
C. Anticholinergic poisoning
D. Opioid withdrawal
E. Thyrotoxicosis

Answer: B. Patients are often confused and agitated and exhibit autonomic instability, resulting in hypertension, tachycardia and, often, fever. Hallucinations are typically visual. Schizophrenia typically results in auditory hallucinations and, although patients are delusional, they are not typically confused. Patients with anticholinergic poisoning typically present with confusion but also have dry mouth, dry eyes, dry skin, hypoactive bowel sounds, and urinary retention. Patients with opioid withdrawal typically have gastrointestinal complaints and, although they may be agitated, they are seldom confused or febrile. Thyrotoxicosis is much more common in women, and patients can exhibit lid lag, tremor, and gastrointestinal complaints.

142.3. In addition to altered mental status (AMS), which of the following is a criterion for diagnosing Wernicke's encephalopathy?

A. Alcohol intoxication
B. Fever
C. Oculomotor abnormalities
D. Recent glucose administration
E. Seizure

Answer: C. Criteria to diagnoses Wernicke's encephalopathy require two of the following: (1) dietary deficiencies; (2) oculomotor abnormalities; (3) cerebellar dysfunction; and (4) AMS or mild memory impairment. Although it is most often diagnosed in alcoholics, alcohol consumption is not required. Treatment is with replacement of dietary deficiencies, particularly thiamine. Magnesium levels should be checked and treated if low. Magnesium is a cofactor for thiamine and is often depleted in chronic alcoholics.