7

Care of the Alcoholic Patient

Gerald M. Cross, Kenneth A. Hirsch, and John P. Allen

The abuse of alcohol is one of the major health problems in our society. Individuals with alcohol problems are disproportionately represented in the primary care population. In that setting, 11% to 20% of patients meet diagnostic criteria for alcohol dependence or abuse.[1] The family physician's role in the care of patients with alcohol problems may include screening, brief intervention, identification of affected family members, pharmacotherapy, detoxification, treatment of associated medical problems, and referral for consultation and rehabilitation.[2]

Background

Prevalence

Misuse of alcohol has a dramatic impact on many facets of life. The economic burden to society of alcohol abuse exceeds that of either illicit drugs or tobacco. The annual cost to U.S. society associated with alcohol abuse has been estimated as $184.6 billion for 1998. The major economic impact of alcohol abuse is on productivity losses due to alcohol-related illness and premature death. Over $26 billion of the total cost of alcohol abuse derives from treatment and prevention.[3] Annually, more than 100,000 deaths are believed to be alcohol-related.

Table 7.1. **Definitions**

Adult children of alcoholics (ACOA): This group has an increased risk for alcohol problems and may have personality traits such as perfectionistic attitude with low self-esteem.
Alcohol: Refers to ethanol.
Alcohol abuse: *Diagnostic and Statistical Manual of Mental Disorders* (DSM) category for individuals who suffer adverse consequences of drinking that are not sufficient to meet the definition for alcohol dependence.
Alcohol dependence: A group of cognitive, behavioral, and physiologic symptoms defined by the DSM. It encompasses individuals who are unable to control their drinking despite the adverse consequences of drinking.
Alcoholic: Used as the equivalent of the DSM diagnosis of alcohol dependence.
Binge drinking: Five or more drinks at a single setting.
Blackout: Anterograde amnesia associated with drinking.
Co-dependent: Usually a nonalcoholic family member who suffers as a result of the alcoholic's behavior and who attempts to control that behavior.
Cross-tolerance: Tolerance often carries over to other drugs of the same class.
Enabler: A spouse, friend, coworker, physician, or other individual who makes excuses for the alcoholic's behavior so the alcoholic does not have to face the consequences of his or her drinking.
Heavy drinking: Fourteen or more drinks per week.
Kindling: Phenomenon of progressively increased neuroexcitation during repeated withdrawals.
One drink: Equivalent to 12 ounces regular beer, 5–6 ounces wine, or 1.5 ounces "hard liquor."
Tolerance: The individual requires larger amounts of alcohol to produce the same effect. It is partially due to accelerated liver metabolism of alcohol and cellular resistance to alcohol's effects.

Approximately 7.4% of Americans meet the diagnostic criteria for alcohol abuse or alcoholism (Table 7.1).[2] Their medical care costs up to three times more than that of the general population.[4] Fifty percent of all alcohol is consumed by 10% of the drinking population. More people drink heavily in the 21- to 34-year age group, and the fewest people drink heavily in the over 65 age group.[5]

Specific Populations

Ethnicity

Employment status, ethnicity, age, and gender influence the severity of alcohol abuse and treatment outcome. African-American men have

only a slightly higher incidence of drug and alcohol disorders than do Caucasian men.[6] Among these two groups employment status was a better predictor of the severity of alcohol problems than was race.[7] American-Hispanic teenagers drink more heavily than either their African-American or Caucasian age peers, and Hispanic men suffer more alcohol-related problems than either African-American or Caucasian men. Alcohol abuse is a particularly serious problem for Native Americans. Although drinking behavior varies widely from tribe to tribe, most Native-American families are affected by alcoholism. Accidents, liver disease, homicide, and suicide, all of which may be alcohol related, rank among the top 10 causes of Native-American mortality.[6] Asian Americans have the lowest level of alcohol consumption and the lowest frequency of alcohol-related problems of any ethnic group in the United States. Within this group, drinking seems to be more socially controlled. Genetic factors may also diminish the risk of alcohol problems in this group.

Age

Overall, the earlier the age when drinking begins, the greater the long-term risk of alcohol abuse. Those who begin drinking during pre- and early adolescence are more likely to develop an alcohol disorder.[8] Many children and adolescents fall into this group. Among high school seniors, 80% report that they have already used alcohol, and 33% report having been drunk in the past 30 days.[3] Compared to parental influence, peer group norms more strongly influence the adolescent's drinking behavior. An adolescent's involvement with alcohol and tobacco serves as a predictor of subsequent experimentation with other illicit drugs.[9] Alcohol-associated violence and vehicular accidents have become the leading cause of death for America's youth.[9] Suicide victims often have a positive blood alcohol concentration (BAC). Unlike older patients, adolescents usually present psychosocial rather than physical signs of alcohol abuse. Elderly people typically drink less alcohol than do young people. Reduced consumption among older individuals may be due to health problems, decreased income, or changes in metabolism and the distribution of alcohol (higher BAC for equivalent amount of alcohol consumed). The combined use of medications and alcohol is a particular risk for elderly patients. Alcohol interacts with medications and can alter the effects of medication, especially in this age group (Table 7.2).

Gender

Men and women have differences in the way they absorb and metabolize alcohol. After consuming the same amount of alcohol,

Table 7.2. **Selected Alcohol–Drug and Alcohol–Herbal Interactions**

Anesthetics	
Propofol (Diprivan)	Increased dose required to produce unconsciousness in chronic drinkers
Enflurane (Ethrane)	Greater risk of liver damage in chronic drinkers
Halothane (Fluothane)	Greater risk of liver damage in chronic drinkers
Antibiotics	
Furazolidone (Furoxone)	Increased risk of nausea, vomiting, headache, and convulsions with acute alcohol consumption
Griseofulvin (Grisactin)	Increased risk of nausea, vomiting, headache, and convulsions with acute alcohol consumption
Metronidazole (Flagyl)	Disulfiram-like reaction; increased risk of nausea, vomiting, headache, and convulsions with acute alcohol consumption
Isoniazid	Decreased availability in the bloodstream with acute alcohol consumption
Rifampin	Decreased availability in the bloodstream with chronic alcohol consumption
Anticoagulants	
Warfarin (Coumadin)	Increased risk of hemorrhages due to increased warfarin availability with acute alcohol consumption; chronic alcohol consumption decreases warfarin availability
Antidepressants	
Amitriptyline (Elavil)	Alcohol increases sedative effect
Monoamine oxidase (MAO) inhibitors	Tyramine found in some beers and wine may produce a dangerous rise in blood pressure
Antidiabetic	
Tolbutamide (Orinase)	Increased availability with acute alcohol consumption and decreased availability with chronic consumption
Antihistamines	
Diphenhydramine (Benadryl)	Increased sedation with acute alcohol consumption

(*continued*)

Table 7.2 (Continued).

Antipsychotic	
Chlorpromazine (Thorazine)	Increased sedation with acute alcohol consumption; possible liver damage with chronic alcohol consumption
Antiseizure	
Phenytoin (Dilantin)	Increased availability with acute alcohol consumption; chronic drinking decreases availability
Cardiovascular	
Nitroglycerin	Vasodilation; acute alcohol consumption may cause fainting upon standing up
Propranolol (Inderal)	Chronic alcohol consumption decreases availability
Disulfiram	Aldehyde dehydrogenase inhibition produces nausea, vomiting, and potentially shock in the presence of alcohol
Humulus lupulus (Hops)	May potentiate other sedative medications
Narcotics	Increased sedative effect with alcohol
Nonnarcotic pain relievers	
Aspirin	Increased risk of gastric bleeding with alcohol; aspirin may heighten the effects of alcohol
Acetaminophen (Tylenol)	Chronic alcohol consumption increases the risk of liver damage
Oenotherabiennis (evening primrose oil)	Caution if used in patients taking drugs that may lower seizure threshold
Piper methysticum (Kava-Kava)	May potentiate benzodiazepines, alcohol and other central nervous system depressants.
Sedative/hypnotics	
Benzodiazepines	Increased sedation with alcohol; increased risk of accidents, especially in older patients
Barbiturates	Acute alcohol consumption prolongs sedative effects; chronic alcohol use decreases availability of barbiturates due to enzyme activation
Valerian officinalis (Valerian)	May potentiate sedatives and barbiturates

women reach a higher blood alcohol concentration, probably due to their smaller amount of body water and due to a lower activity of the enzyme alcohol dehydrogenase (ADH). These differences make women more susceptible to alcohol-induced liver and heart damage.[10] Women also experience a modest dose-response relationship between breast cancer and alcohol consumption.[3] Alcohol metabolism alters the balance of reproductive hormones, decreasing testosterone levels in men and increasing estradiol levels in women.

Throughout all age groups, men are two to five times more likely to be "problem drinkers" than are women. Although women drink less alcohol than men, they and their children are often the victims of family members who abuse alcohol.[6] Women who enter the labor force tend to drink somewhat more alcohol than other women.[11]

Etiology

Several models have been proposed to explain alcoholism.[12] Historically, the moral model has influenced Western culture. This model views alcoholism as a character weakness and recommends willpower as the solution for alcohol problems. Some proponents of this model remain, and the United States Supreme Court once labeled alcoholism "willful misconduct." The learning model provides another view of alcoholism, describing it as a maladaptive habit. The model contends that new learning can reverse the habit. Although this model is generally consistent with a goal of complete abstinence, it raises the unfortunate belief that the alcohol-dependent patient can someday resume drinking safely.

Today a modified or developmental disease model provides a widely accepted explanation of alcoholism.[13] Alcoholism is viewed as a complex disorder influenced by environmental and genetic influences. The goal of treatment is complete abstinence. Although not without criticism, the disease model has the advantage that it avoids blame and supports treatment. As with other diseases, biopsychosocial factors (ethnicity, age, gender, environment, genetics) and personal choices can affect the onset and outcome of alcoholism. Related to this is the concept of problematic alcohol use developing as a consequence of depression, e.g., self-medication. To the extent that this is valid for a given patient, treatment for depression as an independent disease entity becomes crucial.

Evidence that a significant portion of our vulnerability to alcoholism is genetic has greatly influenced the direction of alcohol research and established a biologic basis of alcoholism.[3] Twin and adoption studies suggest a genetic predisposition to alcoholism and

pattern of alcohol consumption. A study of Finnish twins[14] revealed that the quantity of alcohol consumed over a period of 6 years was influenced more by heredity than by environmental factors. The genetic predisposition to alcohol abuse may also be related to alcohol sensitivity due to genetic variants in metabolism of acetaldehyde, as is found in the Chinese Han people. A variant form of the enzyme aldehyde dehydrogenase-2 (ALDH2) has a dominant inheritance pattern and results in slower clearing of acetaldehyde.[13] This sensitivity to alcohol results in rapid flushing, which may protect against heavy or frequent use.[15] Attention has focused on serotonin (5-hydroxytryptamine, 5-HT) dysfunction as part of the biologic basis of alcoholism. 5-HT modulates impulse control and mood. Substantial evidence points to defects in 5-HT neurotransmission in alcoholics, generally indicating that alcoholics have decreased 5-HT neurotransmission.[16] Predisposition toward alcoholism is clearly not predestination for alcoholism, but a family history of alcoholism does increase the vulnerability to developing it. As with atherosclerosis and other diseases, individuals with a positive family history for alcoholism can modify their behavior to decrease their risk of alcohol dependence. Early tolerance may be a marker for a genetically related increased risk of alcoholism.[17]

Physiology

Alcohol is absorbed through the gastrointestinal tract, largely metabolized in the liver, and goes on to affect every organ system. Alcohol absorption is increased when concentrated drinks are taken on an empty stomach. Food (especially fat) in the stomach slows alcohol absorption by dilution and by delayed emptying into the small intestine where absorption is faster. Alcohol passes through the liver before it reaches the circulatory system. High concentrations of alcohol exceed the metabolic capacity of the liver, allowing more alcohol to reach the blood and brain. Typically, after one standard drink (12 ounces of beer, 5 ounces of wine, or 1.5 ounces of 80-proof distilled spirit), the BAC will peak within 30 to 45 minutes.

Alcohol metabolism proceeds at a constant rate (zero-order kinetics). Alcohol is first metabolized to acetaldehyde. The ADH enzyme carries out most of this metabolic step, but there are genetic variations in its activity. With chronic exposure to alcohol, the microsomal ethanol-oxidizing system (MEOS), another metabolic pathway for alcohol, may accelerate the rate of metabolism. Although individuals vary greatly in their ability to metabolize alcohol, an average man can metabolize about 10 mL of absolute alcohol (or one drink) per hour.

Acetaldehyde is subsequently metabolized to acetate owing to the action of aldehyde dehydrogenase. Disulfiram (Antabuse) inhibits several enzymes that metabolize acetalde-hyde. In the presence of alcohol, disulfiram causes acetaldehyde to accumulate, leading to flushing, tachycardia, nausea, vomiting, and later a drop in blood pressure. These signs and symptoms are referred to as the disulfiram-ethanol reaction.

About 5% to 10% of alcohol is released unchanged in breath and urine. Alcohol in alveolar air correlates directly with the arterial BAC, whereas levels in urine correlate with the current level of intoxication only if the bladder is emptied and the subsequent urine is tested.

Alcohol interacts with both water and lipids, allowing it to penetrate and disorder cell membranes. There is no blood–brain barrier to alcohol. Because of the brain's vascularity, the concentration of alcohol in the brain may in fact exceed the level in the venous peripheral blood until the alcohol equilibrates in total body water. Until this balance is reached, the blood alcohol concentration may be less than the cerebrospinal fluid (CSF) concentration.[18] The placenta is unable to protect the fetus from exposure to alcohol in the mother's blood. Similarly, breast milk conveys some of the alcohol in the mother's blood to the infant.

Clinical Presentation

Mental Status

In the emergency room, intoxicated patients often present with a history of recent drinking and demonstrate socially inappropriate behavior, impaired judgment, and altered consciousness. Hospitalized patients who show mental status impairment combined with sympathetic signs should be evaluated for withdrawal from alcohol, other sedative-hypnotics, or both. These patients may have anterograde amnesia, referred to as a blackout. Head trauma should be ruled out by both examination and by the patient's own report. Serial mental status examinations using a standardized format such as the Mini-Mental Status Examination are needed until substantial cognitive clearing is demonstrated. Alcoholics may present with frank delirium (altered consciousness, impaired attention, sleep–wake cycle disturbance, cognitive disorganization, dysperceptions), dementia (intellectual decline and personality changes resulting in social impairment), or both. Fluctuation in the patient's level of functioning argues for delirium, which should be considered a medical emergency until the etiology is clearly identified. To differentiate between

delirium and a psychotic disorder, a generally valid guideline is that the predominance of visual or tactile hallucinations suggests an organic etiology (e.g., delirium), whereas predominantly auditory hallucinations are more suggestive of a psychotic disorder.

Many alcoholics appear anxious or depressed, conditions that often resolve after detoxification. Sometimes clinical depression coexists with or underlies alcoholism. If depression does not diminish within several weeks of drinking cessation, treatment with an antidepressant is recommended. Treatment of primary depression may reduce the risk of a return to drinking because of continued depression, and if treatment is with a serotonergic agent, craving for alcohol (and other drugs) may be reduced, further promoting abstinence.

Brain

Chronic alcoholics lose both gray and white matter volumes. Neuronal damage may result from increased levels of reactive oxygen species and lipid peroxidation products, exceeding the capacity of the body's normal nucleotide excision repair of damaged DNA.[19] Organic brain syndromes among alcohol-dependent patients can usually be categorized as Wernicke-Korsakoff syndrome or alcoholic dementia. Wernicke's disease includes a triad of signs: confusion, ocular disturbances, and ataxia, caused by thiamine deficiency. Korsakoff's psychosis may be the chronic phase of Wernicke's disease. It includes impaired recent memory and the inability to learn new information. Confabulation, or making up details to fill in gaps in memory, has been associated with Korsakoff's psychosis. Alcoholic dementia includes total intellectual decline with dysphasia, apraxia, and cerebral atrophy. This condition may be difficult to distinguish from Alzheimer's disease. The long-term effect of alcohol on the brain, even after prolonged abstinence, is demonstrated by the extreme rapidity with which tolerance is redeveloped if the patient returns to drinking.

Neurotransmitter function constitutes an important area of alcohol research. Broadly summarized, it appears that withdrawal phenomena are mediated by dopaminergic pathways, pleasure from alcohol and drugs (and other stimuli) by opioid pathways, and craving by serotonergic pathways. This hypothesis has given rise to potential treatment options (discussed under Management, below).

Liver

Alcohol is hepatotoxic even in the presence of adequate nutrition. A single weekend of heavy drinking may be all that is necessary to pro-

duce a fatty liver. This may represent a stress reaction, as the adrenals contribute to the mobilization of fatty acids while the liver is occupied metabolizing alcohol. Continued drinking may produce alcoholic hepatitis. Whereas the fatty liver is asymptomatic, alcoholic hepatitis produces jaundice, fever, and loss of appetite. The size of the liver may increase, and enzyme levels may be elevated. Liver biopsy may reveal polymorphonuclear leukocytes and necrosis near the central vein. A typical, but nonspecific, feature of hepatocytes damaged by alcohol is the Mallory body, a hyaline inclusion. These effects on the liver may be due to the combination of a hepatic hypermetabolic state following alcohol exposure and inadequate oxygenation. Necrosis appears where the oxygen tension is lowest. Whereas fatty liver and alcoholic hepatitis are reversible, cirrhosis is not. It develops after continued necrosis and scar formation. The cirrhotic liver tends to be small and hard. Histologic findings of fatty liver, alcoholic hepatitis, and cirrhosis can be found concurrently in the same patient.[20] Although the risk of cirrhosis is a function of the amount of alcohol consumed, individual susceptibility also plays a role, and only about 10% of heavy drinkers develop clinically apparent cirrhosis.

The high prevalence of hepatitis C in the substance abusing population complicates the medical status of patients, their efforts at abstinence, and their psychiatric status (the latter adversely impacted by interferon treatment).

Pancreas

Acute pancreatitis seems to occur randomly among heavily drinking men.[21] The combination of heavy alcohol consumption, increased amylase, upper abdominal pain, nausea, and vomiting suggest the diagnosis, but it can be confirmed only at laparotomy or autopsy. The absence of an elevated amylase level does not rule out the diagnosis. Some alcoholics have an increased amylase level in the absence of pancreatitis due to amylase from the salivary glands. Radiographic findings may include a sentinel loop. Acute hemorrhagic pancreatitis can be fatal. Acute pancreatitis may be a separate entity or the early stage of chronic alcoholic pancreatitis. Seventy-five percent of cases of chronic pancreatitis in the United States are related to alcohol abuse.[21] Deep epigastric pain radiating to the back following alcohol ingestion or a heavy meal is the characteristic presentation. There may be few physical findings. Amylase levels may be normal. Ultrasonography, computed tomography, and endoscopic retrograde pancreatography are useful tests for confirming the diagnosis. Relief

of pain and abstinence from alcohol are the foundation for the treatment of chronic alcoholic pancreatitis. Abstinence may allow the patient to avoid more severe disease but does not necessarily normalize pancreatic function.

Prenatal Effects

Alcohol consumption during the first trimester is associated with multiple fetal anomalies. Exposure during the second and third trimesters is associated with growth retardation and neurobehavioral changes such as sleep disturbances and decreased attentiveness. Moderate to heavy drinking pregnant women experience a two- to fourfold increase in the incidence of second trimester spontaneous abortions. Fetal alcohol syndrome (FAS) describes a set of fetal abnormalities associated with alcohol consumption during pregnancy. The prevalence of FAS in the United States ranges from 0.5 to 3.0 per 1000 live births, and higher in some populations.[3] Criteria for FAS are prenatal or postnatal growth retardation (or both), central nervous system (CNS) involvement, and specific craniofacial dysmorphic features (microcephaly, hypoplastic maxilla, thinned upper lip, short upturned nose, and short palpebral fissure). Facial features associated with FAS tend to disappear during adulthood. Until recently, infants of alcoholic mothers who partially meet the criteria were diagnosed as having fetal alcohol effect (FAE). The Institute of Medicine of the National Academy of Sciences has classified prenatal alcohol exposure into five categories. Three categories represent children who have all or some of the FAS facial features. The other two categories do not have FAS facial features: alcohol-related neurodevelopmental disorder (ARND) and alcohol-related birth defects (ARBDs). Magnetic resonance imaging (MRI) scans of children with FAS show proportionally reduced basal ganglia, a smaller corpus callosum and cerebellum. The peak BAC contributes more to the development of FAS than does the amount consumed.[6] The more severe morphologic defects occur with more extreme levels of alcohol consumption. There is substantial individual variation in susceptibility to alcohol's effect on the fetus. Not all women who drink heavily deliver FAS infants, but no ethnic or racial group is invulnerable to the teratogenic effect of alcohol.[22] In light of the severity of the risk of FAS, it is not yet possible to recommend that any level of alcohol consumption is safe for a pregnant woman.

Cardiac Effects: Risk Versus Benefit

Advice to patients should include a discussion of the potential risks and benefits associated with alcohol consumption. Caucasian-

American men who report drinking fewer than three drinks per day were found to be less likely to die over a 12-year follow-up period than men who reported complete abstinence. Meta-analysis found that the lowest overall mortality for men was associated with an alcohol consumption of 10 g (less than one drink) per day for men and less for women. At 20 g of alcohol per day (between one and two drinks) women had an overall mortality significantly higher than abstainers.[3] The improved outcome is primarily associated with reduced coronary artery disease. Some risks of alcohol consumption may occur at moderate levels of consumption, including hemorrhagic stroke, vehicular accidents, harmful interactions with more than 100 medications and alternative medications, a 50% increase in breast cancer among women drinking three to nine drinks per week, and decreased intelligence quotient (IQ) of children born to mothers reporting as few as two drinks per day while pregnant. Heavy alcohol consumption over a period of years is associated with heart failure secondary to cardiomyopathy and susceptibility to a variety of other illnesses including tuberculosis (TB) and human immunodeficiency virus (HIV). Binge drinking has been associated with cardiac dysrhythmias, especially atrial fibrillation.

Physicians should inform their patients about these known tradeoffs. Individuals who have a very low risk of heart disease are unlikely to experience reduced mortality from moderate drinking. The reverse appears to be true for those with a high risk of heart disease. Individuals with a family history of alcoholism should be frankly discouraged from drinking. The National Institute of Alcohol Abuse and Alcoholism recommends that people 65 and older limit their alcohol consumption to one drink per day.

Diagnosis

Alcoholics may be difficult to identify, and collateral information is often critical for evaluating the patient's history. Alcoholics often minimize alcohol's impact on their life, but collateral information from family and friends typically reveals personal and marital problems related to drinking. During any routine medical examination all adolescents and adults should be asked about alcohol use. No single symptom or test can diagnose alcoholism, although the screening tests described below[23,24] are useful. Screening may itself be beneficial by drawing the patient's attention to problems related to drinking, and it may promote self-monitoring and behavioral change.[25] The diagnostic criteria in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV)[26] (Table 7.3). defines alcohol abuse

Table 7.3. **Diagnosis of Alcohol Use Disorders**

Alcohol abuse

For a diagnosis of alcohol abuse the patient must show one or more of the following, related to alcohol, on a recurrent basis:

1. Failure to fulfill major role obligations
2. Use in physically hazardous situations
3. Legal problems
4. Continued use despite having persistent or recurrent social or interpersonal problems related to alcohol use

Alcohol dependence

For a diagnosis of alcohol dependence at least three of these seven criteria must be met:

1. Clinically significant tolerance[a]
2. Clinically significant withdrawal
3. Recurrent failure of intent
4. Recurrent failure of control
5. Preoccupation with alcohol
6. Predominance of alcohol-related activities
7. Continued alcohol use despite knowledge that the drinking contributes to a psychological, physical, social, or other problem

[a]It is noteworthy that tolerance to some effects of alcohol (e.g., gait, coordination) does not necessarily suggest tolerance to all effects. Certain effects, especially impaired social judgment, may demonstrate little or no tolerance.

Source: American Psychiatric Association,[5] with permission.

as recurrent problems in one or more of the four areas of functioning; dependence is defined by the presence of at least three of seven specific areas of dysfunction.

Screening

A variety of self-report instruments are available to screen for alcohol problems.[27] Administration times generally range from less than a minute to about 5 minutes. Perhaps the most common measure is the CAGE, an acronym for the key word in each of four questions related to drinking[28]:

1. Have you ever felt you should *C*ut down on your drinking?
2. Have people *A*nnoyed you by criticizing your drinking?
3. Have you ever felt *G*uilty about your drinking?
4. Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (*E*ye-opener)?

Despite its popularity and brevity, the CAGE has certain limitations. In particular, it focuses on emotional reactions to drinking and asks about lifetime occurrence of symptoms rather than recent events.

The Michigan Alcoholism Screening Test (MAST)[29] and variants are also commonly used in primary care settings. This family of instruments has been criticized for focusing too heavily on late-stage symptoms such as liver pathology and delirium tremens. Furthermore, as with the CAGE, the questions on the MAST do not specify when the symptoms occurred, thus causing individuals with earlier, resolved problems to still score positively. Nevertheless, the CAGE, the MAST, and similar scales have fairly high validity.

A newer measure, the Alcohol Use Disorders Identification Test (AUDIT)[30] merits particular attention from primary care physicians (Table 7.4). Its advantages are brevity (approximately 2 minutes), focus on the preceding year, and item sampling from several domains

Table 7.4. **Alcohol Use Disorders Identification Test (AUDIT) Questionnaire**

1. How often do you have a drink containing alcohol?
   (0) Never
   (1) Monthly or less
   (2) Two to four times a month
   (3) Two or three times a week
   (4) Four or more times a week
2. How many drinks containing alcohol do you have on a typical day when you are drinking?
   (0) 1 or 2
   (1) 3 or 4
   (2) 5 or 6
   (3) 7 or 9
   (4) 10 or more
3. How often do you have six or more drinks on one occasion?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily
4. How often during the last year have you found that you were not able to stop drinking once you had started?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

(*continued*)

Table 7.4 (Continued).

5. How often during the last year have you failed to do what was normally expected from you because of drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily
7. How often during the last year have you had a feeling of guilt or remorse after drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily
9. Have you or someone else been injured as a result of your drinking?
   (0) No
   (2) Yes, but not in the last year
   (4) Yes, during the last year
10. Has a relative, friend, doctor, or other health worker been concerned about your drinking or suggested that you should cut down?
    (0) No
    (2) Yes, but not in the last year
    (4) Yes, during the last year

Numbers in parentheses are scoring weights. The usual cutoff for the AUDIT to be scored as positive is 8 points.

(intake, level of dependence, and adverse consequences of drinking). The AUDIT can be embedded in a general health risk appraisal survey dealing with other medical concerns such as smoking, diet, and nutrition. In a recent review contrasting it with other self-report alcohol screening measures, the AUDIT tended to perform best. A cutoff score of 6 points for females may be preferable to the more common research cutoff of 8.[31]

History

The history should include what the patient drinks, how much, how often, when alcohol was last drunk, and if the patient has used any other drugs or medications. Patients in denial minimize their drinking history. It is therefore important to review the history with the patient's family members or friends. The focus should not be on whether the individual has a problem with alcohol, but rather on the consequences of drinking (e.g., legal, financial, medical, social difficulties). Asking if others believe the patient has a problem or that drinking contributes to a social problem may be more effective than direct questions about the patient's drinking. It is important to inquire about previous withdrawal history, as successive withdrawals tend to become more severe.

Laboratory Tests

Laboratory tests can be used for screening and to support the diagnosis. Such tests might include measuring the BAC, a urine drug screen, bilirubin assay, prothrombin time, assays of liver-associated enzymes, electrolytes, and a complete blood count. Elevation of the bilirubin, liver-associated enzymes, and prothrombin time suggests the presence of liver dysfunction. Increased mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) and a decreased red blood cell (RBC) count suggest that the patient has been drinking heavily for weeks or months. MCV changes may persist for months.

The half-life of γ-glutamyltransferase (GGT) is approximately 26 days, and an elevated GGT level may be one of the most sensitive laboratory screening tests for alcoholism. An elevated carbohydrate-deficient transferrin (CDT) level is the most sensitive indicator of relapse to drinking in a purportedly abstinent patient.[23] Unlike the other biochemical markers, a rise in CDT does not seem to reflect organ damage, but rather recent heavy (five drinks or more per day) consumption of alcohol. (CDT was recently approved by the Food and

Drug Administration as an indicator of excessive drinking, the first alcohol biomarker so approved.) An elevated aspartate transferase/alanine transferase (AST/ALT) ratio (e.g., 2:1 or higher) has been interpreted as evidence of liver disease secondary to drinking alcohol, whereas a reversed ratio (e.g. 1:2) has been seen as evidence of hepatitis due to other causes. This "rule" may not hold true for all populations. The simultaneous use of CDT and GGT assays to screen for excessive alcohol consumption seems reasonably sensitive (75%) and specific (85%). Ultimately, the diagnosis of alcohol dependence must meet the criteria established by the DSM-IV.[26]

Management

Intervention

The physician should give clear directions to the patient to reduce alcohol consumption, usually in the context of health, social, or family problems.[2] The goal is to present information about the illness in a manner that can be understood and accepted by the alcoholic. A more formal intervention may include gathering friends, family members, and even the employer to firmly confront the alcoholic's behavior. The goal of this type of intervention is to obtain the alcoholic's agreement to enter treatment that same day. To be successful, this procedure often requires hours of preparation before the intervention takes place. Some treatment programs assist the physician and family in preparing the intervention. The intervention is a powerful tool that often succeeds in getting the alcoholic patient into treatment. Patients entering treatment as a result of intervention often do as well as those who enter voluntarily.

Comprehensive Assessment

The American Society of Addiction Medicine (ASAM) has released the second version of the patient placement criteria (PPC-II), a tool to help the clinician utilize the data from a comprehensive assessment to determine the appropriate level of care for a particular patient. Although alcoholism is a primary illness, it is often accompanied by a variety of medical problems (Table 7.5).

Supportive Therapy During Withdrawal

Alcohol withdrawal produces adrenergic arousal. To compensate, the patient's room should be quiet and evenly lit to allow constant re-

Table 7.5. **Summary of Alcohol Effects**

Organ	Acute effect (up to months)	Chronic effects (years)
Breast	Portion of blood alcohol content in breast milk	?Increased risk of breast cancer Male breast enlargement
Cardiovascular system	Moderate blood pressure increase "Holiday heart" syndrome[a]	Hypertension
Central nervous system (CNS)	Impaired motor coordination Sleep apnea	Depression Dementia Peripheral neuropathy Widening of frontal cortical sulci Distal symmetric polyneuropathy Hemorrhagic stroke
Endocrine system	Increased plasma corticosteroids Increased plasma catecholamines	Low testosterone Testicular atrophy Amenorrhea, anovulation
Fetal development	Fetal alcohol syndrome	
Gastrointestinal system	Delayed gastric emptying Gastroesophageal reflux Injures the gastric mucosa Loss of enzymes (disaccharidases) Worsen preexisting peptic ulcers	Esophageal carcinoma Chronic atrophic gastritis ?Gastric carcinoma[b] Esophageal inflammation
Hematopoietic system		Megaloblastic anemia Decreased platelet function

(*continued*)

Table 7.5 (Continued).

Organ	Acute effect (up to months)	Chronic effects (years)
Immune system		Increased risk of infections Decreased production of polymorphonuclear leukocytes Decreased cell-mediated immunity Decreased T lymphocytes Impaired phagocytosis
Liver	Fat deposition Liver enlargement Alcoholic hepatitis	Cirrhosis Hepatocellular carcinoma[c]
Muscular system	Increased chance of muscle injury Sudden muscle necrosis	Chronic alcoholic myopathy
Nutritional system	Interferes with vitamin metabolism Inhibits gluconeogenesis Indirect loss of calcium and potassium Loss of magnesium, zinc, and phosphorus Thiamine deficiency	Folate deficiency Thiamine deficiency Alcoholic ketoacidosis Decreased serum calcium Wernicke-Korsakoff syndrome
Other malignancies		Squamous cell carcinoma of the head and neck
Pancreas	Acute pancreatitis	Chronic pancreatitis Pseudocyst formation
Pulmonary system	Increased cough and sputum production	Pneumonia

[a]Holiday heart syndrome refers to atrial or ventricular dysrhythmias following days of heavy drinking.

[b]Smoking may also contribute to the development of gastrointestinal carcinoma.

[c]May be secondary to hepatitis B virus.

orientation to surroundings. Dimming the room lights at night mimics diurnal variation and supports orientation. Staff members should present a pleasant, nonthreatening attitude. Restraints are rarely necessary with proper sedation. Patients may be allowed to eat and drink when they feel ready. Intravenous fluids are usually not necessary for uncomplicated alcohol withdrawal. The medical staff can promote long-term recovery by directing the patient to a rehabilitation program immediately following detoxification. Indeed, some aspects of rehabilitation can be started on the detoxification unit by providing books and tapes, an introduction to an Alcoholics Anonymous (AA) sponsor, and attendance at an AA meeting as soon as the patient is physically able.

Detoxification

Monitored detoxification safely transports the patient through withdrawal. Rehabilitation is the goal; detoxification is a step toward that goal. Detoxification may be done on an inpatient or outpatient basis depending on the clinical presentation and history of the patient. In the context of managed care pressures, outpatient or ambulatory detoxification is becoming more commonplace and appears to work well for many patients.[32] Once detoxified, an alcoholic may still not function well cognitively for days, weeks, or months.

Withdrawal Syndrome

Alcohol withdrawal consists of signs and symptoms ranging from hangover to delirium tremens. The severity depends on the patient's age, physical condition, prior withdrawals, and amount of alcohol consumed. Withdrawal begins as the blood alcohol level falls and includes anxiety, restlessness, insomnia, and nausea. About 24 hours after the last drink (sometimes days longer) the patient may have increased blood pressure and pulse, a low-grade fever, and tremors that increase with the withdrawal severity. Hand tremors may be the most reliable early sign of alcohol withdrawal unless the tremors are reduced by beta-blockers or other medication. Patients in withdrawal may also have tachycardia and dry mouth, which may be misinterpreted as volume depletion. During withdrawal, total body water is more likely to be normal, and plasma volume is likely to be increased.[33] Transient hallucinations may occur that involve any sense, but visual hallucinations are more common. Typically, 2 days after the last drink (but occasionally up to 10 days after the last drink) one or more grand mal seizures occur. Seizures occur in about 5% of untreated withdrawal patients; 30% to 40% of patients with seizures

proceed to delirium tremens, typically during the third to fifth day of withdrawal, if adequate treatment is not provided. Delirium tremens is characterized by severe autonomic hyperactivity (e.g., tachycardia, hypertension, fever, diaphoresis, tremor), electrolyte disturbances, hyperreflexia, confusion, disorientation, and clouding of consciousness. Dysperceptions, especially visual and tactile hallucinations, are common, usually without the insight that accompanies hallucinations of milder withdrawal. Delusions are likewise common. Psychomotor activity may fluctuate widely during the course of the delirium, and the patient frequently demonstrates affective lability. Delirium tremens typically persist for 3 to 5 days. Medical management is directed at patient safety, as pharmacologic intervention has not been demonstrated to shorten the duration of the delirium. The physician should be aware that in a debilitated or elderly patient a delirium of any etiology may persist for weeks beyond resolution of the cause of the delirium. Delirium tremens may be fatal, especially in debilitated or elderly patients.

Adolescents often do not develop the classic signs of physical withdrawal seen in adults. They do exhibit the usual behavioral and emotional aspects of dependence. Elderly patients usually have more severe withdrawal than young patients. The rehabilitation progress of elderly patients may be delayed owing to the slower metabolism of medications used to control their alcohol withdrawal.

Pharmacotherapy

The physician should assess the patient's risk of withdrawal before treatment begins. The Clinical Institute Withdrawal Assessment (CIWA)-Ar scale may be used as an adjunct to assess the patient's risk for severe withdrawal.[34] A decision to allow the patient to go through withdrawal without the benefit of medication should be carried out only with informed consent.

Oral multivitamin supplementation, including thiamine, folic acid, and pyridoxine, should be given when the patient can tolerate oral fluids. If intravenous fluids containing dextrose are needed, 100 mg thiamine should be added to each liter of intravenous fluid administered to the patient. A normal magnesium level does not necessarily mean that magnesium supplementation is unnecessary. Serum magnesium levels do not correlate with CSF magnesium levels. Adequate levels of magnesium help prevent cardiac dysrhythmia and seizures. If the clinical history and examination suggest that the patient is at risk for serious withdrawal or is nutritionally compromised, $MgSO_4$ 2 g IM (deep) up to every 8 hours for 2 to 3 days may be administered.

The pharmacologic basis for detoxification traditionally has been the use of cross-tolerant medication to control alcohol withdrawal. Usually the agent chosen is a benzodiazepine or a barbiturate with a longer biologic half-life than alcohol. Residual symptoms are treated with adjunctive medications (e.g., antiemetic for nausea). Pharmacotherapy is justified to prevent or treat signs and symptoms of withdrawal and possibly to curb alcoholic dementia and kindling.[35] The "kindling" hypothesis suggests that repeated subthreshold (for seizures) stimulation of the CNS during withdrawal increases the risk of subsequent withdrawal seizures. All protocols for the treatment of withdrawal should be modified according to patient needs. Individuals with physical dependence on more than one drug should first be withdrawn from the drug that produces the most dangerous withdrawal. In practice, it may mean withdrawing the patient from sedative-hypnotics (e.g., alcohol) first while medically delaying withdrawal from opiates.

An appropriate benzodiazepine for the treatment of alcohol withdrawal can be selected based on the patient's age and hepatic function. Diazepam is preferred if the patient is under 55 years of age and has a well-functioning liver. Oxazepam is appropriate for older patients and those with liver dysfunction. Diazepam is administered 10 to 20 mg po every hour until the patient's symptoms are relieved and the patient is sedated. Further doses may be unnecessary. Total dosage should not exceed 60 mg without further evaluation by the physician, but doses in excess of 120 mg within 24 hours are not uncommon in the heavy drinker. Patients who are tolerant of alcohol are similarly tolerant of other sedative-hypnotics. Intramuscular chlordiazepoxide is less desirable because of erratic uptake, prolonged metabolism, and delayed onset. Patients requiring high-dose withdrawal pharmacotherapy should be in a monitored bed.

Oxazepam (15–30 mg) may also be given orally every hour until the patient's symptoms are relieved or the patient becomes drowsy. Unlike the diazepam regimen, the cumulative dose of oxazepam necessary to initially relieve the patient's symptoms is repeated every 6 to 8 hours for the remainder of the first day of treatment. The dose is then reduced by 25% on each subsequent day. Most patients complete the regimen by the fifth day.

Phenobarbital remains a reliable, effective medication for the treatment of alcohol withdrawal, for mixed sedative-hypnotic withdrawal, and for seizure prophylaxis when used by experienced clinicians as part of an established protocol. It is easily absorbed. Phenobarbital's effectiveness has been reported to be superior to that of diazepam for delirium tremens.[36] Nervousness or nausea may be treated with

promethazine (Phenergan) or hydroxyzine (Atarax, Vistaril). Until recently there was scant literature supporting the use of anticonvulsants in withdrawal treatment, except in the case of an independent seizure disorder. Research supports the clinical efficacy of some agents.[37] For delirious, hallucinating, and combative patients, haloperidol is the agent of choice, in combination with the above withdrawal agents. Haloperidol is safe in oral, intramuscular, and intravenous doses of 70 to 80 mg/day for monitored patients; higher doses are not uncommon. Usually, a dose of just 5 mg orally or intramuscularly two to four times a day is sufficient. The potential of haloperidol to lower seizure threshold is controlled by concomitant administration of an anticonvulsant.

Complications

Seizures are one of the most common complications of alcohol withdrawal. If a seizure occurs, diazepam 5 to 10 mg IV is given until the seizures are controlled or the patient is drowsy but responsive. Causes other than withdrawal should be determined if seizures are associated with head trauma, are not preceded by tremulousness, are focal in nature, or a residual neurologic defect is present.

The combination of liver dysfunction and poor vitamin K absorption can contribute to systemic bleeding. In these circumstances, minor head trauma can lead to a subdural hematoma. This diagnosis should be considered if the patient does not recover as expected.[37] The differential diagnosis for seizures also includes infection and metabolic disturbances.

Keeping the patient in the program during withdrawal is one of the most difficult challenges facing the clinician. Alcoholic patients often have a strong but unrecognized compulsion to leave treatment and return to drinking. Patients who receive adequate medication for withdrawal are less likely to leave "against medical advice." From the first day of treatment, the detoxification unit staff should repeatedly educate the patient that rehabilitation is the treatment goal, not just detoxification. Patients whose urge to leave treatment persists can often be encouraged by concerned family members to persevere.

Rehabilitation

Treatment approaches involving the family tend to be more effective than individual-focused treatment for alcoholics. The family can be used to motivate the patient to enter and stay in treatment. The family can set a common goal, participate in education, and reduce emotional distress. Rehabilitation can be accomplished on an inpatient or

outpatient basis or in a partial hospitalization program. Inpatient rehabilitation is preferred for patients who require nursing care or continuous observation, and for those who need an opportunity to progress in an environment that is free of violence and drugs. The severity of alcohol dependence and the absence of an adequate social support system may also justify inpatient treatment. Patients without convenient and reliable transportation may have a better chance of success in an inpatient program. Patients should be individually assessed and given the appropriate level of treatment from the start. The ASAM PPC-II[23] is currently being validated, and it may be used to guide the family physician to select the most appropriate level of treatment for a specific patient. The "first fail" philosophy, which requires patients to fail the least intensive treatment program before they can receive more intensive treatment, may not be cost-effective and is not consistent with quality medical care.

Physical evaluation, psychological assessment, and education of the patient and the patient's family are the foundation of rehabilitation programs. Typically, it is accomplished with group and individual therapy, classes, a family program, and a relapse prevention program. Many programs ascribe to the 12 steps of Alcoholics Anonymous as the philosophic basis of their programs. The long-term success of patients treated in such programs varies,[38] but when there is employer and family support the results can be outstanding.[39]

Continuing Care

An aftercare plan specific to the patient's needs should be created. The family physician should be familiar with this and encourage compliance with the plan. Physicians should generally avoid giving aftercare patients mood-altering medications, as these drugs may increase the chance of relapse. As previously indicated, antidepressants and the opioid antagonists may constitute an exception to this general recommendation. Alcoholism is sometimes associated with a wide range of psychiatric disorders; most notable are mood or affective disorders, anxiety disorders (especially posttraumatic stress disorder), mania, and schizophrenia. When coexisting with another psychiatric disorder, both that disorder and the alcoholism may be exacerbated; both must be treated. Potentially addictive medications should be avoided when treating coexisting psychiatric disorders in alcoholic patients, but rapidly acting benzodiazepines should be specifically avoided. In the event that hospitalization is needed for a condition requiring pain medication or anesthesia, the patient is given medications as necessary, but mood-altering medications are discontinued while the patient is still in the hospital.

Current evidence indicates that serotonin reuptake inhibitors can reduce drinking by heavy drinkers whether or not they are depressed, but the magnitude of the decrease is not dramatic. Placebo-controlled trials showed that naltrexone (ReVia) 50 mg/day could benefit alcoholics in terms of relapse prevention. Naltrexone reduced the number of drinking days and craving for alcohol. Compared to the serotonergic drugs, the opioid antagonists seem to produce more consistent reductions in alcohol consumption.[16] Some aftercare plans include disulfiram in an effort to prevent relapse. If disulfiram is prescribed, specific procedures to ensure compliance are needed. The family physician should educate the patient about food, medications, and cosmetics that contain alcohol and might produce a disulfiram-alcohol reaction. Relapses do occur, and the physician should use such occasions to refocus the continuing care plan for the patient and family.

Prevention

Physicians can play a major role in the prevention and treatment of alcohol-related problems. Training for this role should begin in medical school. Interested faculty members should be offered fellowship training in the study of addiction. Curricula and tests ought to include alcohol-related topics. Medical students and residents should play an integral role on the team that cares for patients in addiction treatment centers. This kind of physician training can support community initiatives for education and social policy changes to prevent alcohol abuse.

Of all the proposed methods to prevent alcohol abuse, education is the least controversial. The most effective educational efforts probably occur during or before adolescence. After that, peer influence becomes more important than parental influence. The physician can support parental norms by teaching adolescents to be comfortable standing up for what they believe. Counseling that delays the onset of drinking until age 15 or later may reduce alcohol related problems.[8] Such "anticipatory guidance" teaches adolescents respect for their own beliefs. The physician can also identify adolescent patients at particularly high risk for alcoholism due to their family backgrounds, peer associations, difficulties in school, or problems with impulse control. These adolescents need specific education concerning the risks of drinking alcohol during pregnancy or while driving.

Social policy changes can support education in preventing alcohol abuse. Several decades ago the price of a beer was a quarter while

the price of a soft drink was a nickel. This 5:1 ratio of alcoholic beverage cost to soft drink cost has been lost. The main reason for the change is that taxation on alcoholic beverages has not kept pace with inflation. Today there is near parity in price for these beverages. Social policies that restrict the consumption of alcohol-containing beverages seem to reduce per-capita consumption of alcohol.[40]

Family and Community Issues+

Alcohol-related motor vehicle accidents cause more than 20,000 deaths each year. This toll disproportionately affects young Americans. Nearly half of the violent deaths (accidents, suicide, homicide) among males under age 34 are alcohol-related.[6]

Risks of an automobile accident increase sharply as the BAC rises. Heightened risk begins near 0.04% BAC, and the risk of an accident is doubled at 0.06% BAC. A driver with a BAC of 0.08%, a common legal limit, is six times as likely to have an accident than a sober driver.[18] Raising the drinking age from 18 to 21 years results in decreased alcohol use among high school seniors and an overall decrease in alcohol-related traffic accidents.[41] Raising the legal drinking age has been associated with decreased death rates from automobile accidents, unintentional injuries, and suicide among adolescents and young adults.[42] The single most important deterrent that enhances traffic safety is license suspension.[43] For those convicted of a driving under the influence (DUI) offense, an education program successfully completed may be beneficial; however, the repeat offender also benefits from treatment, including involvement with AA.[44]

Ethical Issues and Physician Responsibilities

Households in which chemicals are abused are at substantially greater risk for both physical and sexual abuse. Neither the victim nor the perpetrator of abuse is likely to speak freely. The victim may experience fear of more severe abuse or even death, abandonment by the abuser, or the shame of being discovered to be a victim. The abuser is fearful of being caught and punished; losing family, job, and freedom; and being publicly humiliated. Honest disclosure by the patient and honest reporting by the physician are also limited by a frequently overlooked factor: in the managed care environment, it is not unusual that payment for services may be denied if the injury has resulted from intoxication. The likelihood of honest disclosure is increased if the physician offers support, hope, and understanding.

There are legal guidelines that govern the physician's actions in the event of threatened suicide or assault, but danger to others may also take the form of an intoxicated patient planning to drive home from the emergency room. Ordinarily, intoxicated patients cannot be legally restrained unless they can be committed under state law, except by police. If a patient is thought to be impaired, it becomes the provider's duty to persuade the patient not to drive, to use a taxi, to call a friend, and as a last resort to contact the police and inform them of the situation. Public safety may take precedence over the patient's right to confidentiality, and failure to notify appropriate authorities of a threat to public safety exposes the physician to liability. This caution may apply especially for employees of the U.S. Department of Transportation. Legal counsel is recommended before notification, as this area is in flux.

Ethical guidelines for physicians and other health care professionals clearly stipulate the responsibility to report an impaired health care provider. The treatment success rate for impaired physicians is among the highest of any patient group. Utilizing intervention services through the licensure board or impaired provider programs allows the impaired provider to maintain professional status, employment, and self-respect by receiving treatment. It also protects the public.

References

1. Bradley K. The primary care practitioner's role in the prevention and management of alcohol problems. Alcohol Health Res World 1994; 18(2):97–104.
2. Barry K, Fleming M. The family physician. Alcohol Health Res World 1994;18(2):105–9.
3. U.S. Department of Health and Human Services. The tenth special report to the U.S. Congress on alcohol and health. Rockville, MD: Public Health Service, National Institutes of Health, National Institute on Alcohol Abuse and Alcoholism, 2000;xiii, 14–17,30,273,283–295,364, 365.
4. Blose J, Holder H. Injury-related medical care utilization in a problem drinking population. Am J Public Health 1991;81:1571–5.
5. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3rd rev. ed. Washington, DC: American Psychiatric Press, 1987;173.
6. U.S. Department of Health and Human Services. The seventh special report to the U.S. Congress on alcohol and health. Rockville, MD: Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, 1990:ix,xv,xxii,xxiv,26,27,33–36,46,119,123,141.

7. Conigliaro J, Maisto SA, McNeil M, et al. Does race make a difference among primary care patients with alcohol problems who agree to enroll in a study of brief interventions? Am J Addict 2000;9(4):321–30.
8. DeWit DJ, Adlaf EA, Offord DR, et al. Age at first alcohol use: a risk factor for the development of alcohol disorders. Am J Psychiatry 2000;157:745–50.
9. Smith D. Social and economic consequences of addiction in America. Commonwealth 1996;90(5):1–4.
10. National Institute on Alcohol Abuse and Alcoholism. Publication no. 35 PH371, January, 1997.
11. Parker DA, Harford TC. Gender-role attitudes, job competition and alcohol consumption among women and men. Alcohol Clin Exp Res 1992;16:159–65.
12. Brower K, Blow F, Beresford T. Treatment implications of chemical dependency models: an integrative approach. J Subst Abuse Treat 1989;6: 147–57.
13. Devor E. A developmental-genetic model of alcoholism: implications for genetic research. J Consult Clin Psychol 1994;62:1108–15.
14. Kaprio J, Viken R, Koskenvuo M, Romanov K, Rose R. Consistency and change in patterns of social drinking: a 6-year follow-up of the Finnish Twin Cohort. Alcohol Clin Exp Res 1992;16:234–40.
15. Wall T, Ehlers C. Acute effects of alcohol on P300 in Asians with different ALDH2 genotypes. Alcohol Clin Exp Res 1995;19:617–22.
16. Kranzler H, Anton R. Implications of recent neuropsychopharmacologic research for understanding the etiology and development of alcoholism. J Consult Clin Psychol 1994;62:1116–26.
17. Schuckit MA, Edenberg HJ, Kalmijn J, et al. A genome-wide search for genes that relate to a low level of response to alcohol. Alcohol Clin Exp Res 2001;25(3):323–9.
18. Goldstein DB. Pharmacology of alcohol. New York: Oxford University Press, 1983;80.
19. Brooks PJ. Brain atrophy and neuronal loss in alcoholism: a role for DNA damage? Neurochem Int 2000;37(5–6):403–12.
20. Maddrey W. Alcoholic hepatitis: clinico-pathologic features and therapy. Semin Liver Dis 1988;8:91–102.
21. Geokas M. Ethanol and the pancreas. Med Clin North Am 1984;68:60–7.
22. Day N, Richardson G. Prenatal alcohol exposure: a continuum of effects. Semin Perinatol 1991;15:272–9.
23. Allen JP, Litten RZ. The role of laboratory tests in alcoholism treatment. J Subst Abuse Treat 2001;81:85.
24. Alexander D, Gwyther R. Alcoholism in adolescents and their families. Pediatr Clin North Am 1995;42:217–30.
25. Allen J, Maisto S, Connors G. Self-report screening tests for alcohol problems in primary care. Arch Intern Med 1995;155:1726–30.
26. Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC: American Psychiatric Association, 1994;176–83.
27. Connors GJ. Screening for alcohol problems. In: Assessing alcohol problems: a guide for clinicians and researchers. Washington, DC: DHHS, 1995;17–29.

28. Ewing JA. Detecting alcoholism, the CAGE questionnaire. JAMA 1984;252:1905–7.
29. Selzer ML. The Michigan alcoholism screening test: the quest for a new diagnostic instrument. Am J Psychiatry 1971;127:1653–8.
30. U.S. Department of Health and Human Services. Assessing alcohol problem. Rockville, MD: DHHS, 1995: series 4:11, 22, 260. NIH publ. no. 95-3745.
31. Allen JP, Litten RZ, Fertig JB, Babor T. A review of research on the Alcohol Use Disorders Identification Test (AUDIT). Alcohol Clin Exp Res 1997;21(4):613–19.
32. Soyka M, Horak M. Ambulatory detoxification of alcoholic patients—evaluation of a model project (article in German). Gesundheitswesen 2000 Jan;62(1):15–20.
33. Mander A, Young A, Merrick M, et al. Fluid balance, vasopressin and withdrawal symptoms during detoxification from alcohol. Drug Alcohol Depend 1987;24:233–7.
34. Foy A, March S, Drinkwater V. Use of an objective clinical scale in the assessment and management of alcohol withdrawal in a large general hospital. Alcohol Clin Exp Res 1988;12:360–4.
35. Nutt D, Glue P. Neuropharmacological and clinical aspects of alcohol withdrawal. Ann Med 1990;22:275–81.
36. Kramp P, Rafaelsen O. Delirium tremens: a double blind comparison of diazepam and barbital treatment. Acta Psychiatr Scand 1978;58:174–90.
37. Koranyi E, Ravindran A, Seguin J. Alcohol withdrawal concealing symptoms of subdural hematoma—a caveat. Psychiatr J Univ Ottawa 1990;15:15–17.
38. Vaillant G. A summing up: the natural history of alcoholism. Cambridge: Harvard University Press, 1983;307–16.
39. Cross G, Morgan C, Mooney A, Martin C, Rafter J. Alcoholism treatment: a ten-year follow-up study. Alcohol Clin Exp Res 1990;14:169–73.
40. Hoadley J, Fuch B, Holder H. The effect of alcohol beverage restrictions on consumption: a 25 year longitudinal analysis. Am J Drug Alcohol Abuse 1984;10:375–401.
41. O'Malley P, Wagenaar A. Effects of minimum drinking age laws on alcohol use, related behaviors and traffic crash involvement among American youth: 1976–1987. J Stud Alcohol 1991;52:478–91.
42. Jones N, Pieper C, Robertson L. The effect of legal drinking age on fatal injuries of adolescents and young adults. Am J Public Health 1992;82:112–15.
43. Mann R, Vingilis E, Gavin D, Adlaf E, Anglin L. Sentence severity and the drinking driver: relationships with traffic safety outcome. Accid Anal Prev 1991;23:483–91.
44. Green R, French J, Haberman P, Holland P. The effects of combining sanction and rehabilitation for driving under the influence: an evaluation of the New Jersey Countermeasures Program. Accid Anal Prev 1991;23:543–55.