levels, which can remain elevated during heavy drinking; inhibition of vasopressin secretion at rising blood alcohol concentrations and enhanced secretion at falling blood alcohol concentrations (with the final result that most alcoholics are likely to be slightly overhydrated); a modest and reversible decrease in serum thyroxine (T_4); and a more marked decrease in serum triiodothyronine (T_3). Hormone irregularities should be reevaluated because they may disappear after a month of abstinence.

ALCOHOLISM (ALCOHOL USE DISORDER)

Because many drinkers occasionally imbibe to excess, temporary alcohol-related problems are common in nonalcoholics, especially in the late teens to the late twenties. However, repeated problems in multiple life areas can indicate an alcohol use disorder as defined in DSM-5.

DEFINITIONS AND EPIDEMIOLOGY

An *alcohol use disorder* is defined as repeated alcohol-related difficulties in at least 2 of 11 life areas that cluster together in the same 12-month period (Table 467-2). Ten of the 11 items were taken directly from the 7 dependence and 4 abuse criteria in DSM-IV, after deleting legal problems and adding craving. Severity of an alcohol use disorder is based on the number of items endorsed: mild is two or three items; moderate is four or five; and severe is six or more of the criterion items. The new diagnostic approach is similar enough to DSM-IV that the following descriptions of associated phenomena are still accurate.

The lifetime risk for an alcohol use disorder in most Western countries is about 10–15% for men and 5–8% for women. Rates are similar in the United States, Canada, Germany, Australia, and the United Kingdom, tend to be lower in most Mediterranean countries, such as Italy, Greece, and Israel, and may be higher in Ireland, France, and Scandinavia. An even higher lifetime prevalence has been reported for most native cultures, including American Indians, Eskimos, Maori groups, and aboriginal tribes of Australia. These differences reflect both cultural and genetic influences, as described below. In Western countries, the typical alcoholic is more often a blue- or white-collar worker or homemaker. The lifetime risk for alcoholism among physicians is similar to that of the general population.

GENETICS

Approximately 60% of the risk for alcohol use disorders is attributed to genes, as indicated by the fourfold higher risk in children of alcoholics (even if adopted early in life and raised by nonalcoholics) and a higher risk in identical twins compared to fraternal twins of alcoholics. The genetic variations operate primarily through intermediate characteristics that subsequently combine with environmental influences to alter the risk for heavy drinking and alcohol problems. These include genes relating to a high risk for all substance use disorders that operate through impulsivity, schizophrenia, and bipolar disorder. Another characteristic, an intense flushing response when drinking, decreases the risk for only alcohol use disorders through gene variations for several alcohol-metabolizing enzymes, especially aldehyde dehydrogenase (a mutation only seen in Asians), and to a lesser extent, variations in ADH.

An additional genetically influenced characteristic, a low sensitivity to alcohol, affects the risk for heavy drinking and may operate, in part, through variations in genes relating to calcium and potassium channels, GABA, nicotinic, and serotonin systems. A low response per drink is observed early in the drinking career and before alcohol use disorders develop. All follow-up studies have demonstrated that this need for higher doses of alcohol to achieve effects predicts future heavy drinking, alcohol problems, and alcohol use disorders. The impact of a low response to alcohol on adverse drinking outcomes is partially mediated by a range of environmental influences, including the selection of heavier-drinking friends, more positive expectations of the effects of high doses of alcohol, and suboptimal ways of coping with stress.

TABLE 467-2 ***DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS*, FIFTH EDITION, CLASSIFICATION OF ALCOHOL USE DISORDER (AUD)**

Criteria
Two or more of the following items occurring in the same 12-month period must be endorsed for the diagnosis of an alcohol use disorder[a]:
Drinking resulting in recurrent failure to fulfill role obligations
Recurrent drinking in hazardous situations
Continued drinking despite alcohol-related social or interpersonal problems
Tolerance
Withdrawal, or substance use for relief/avoidance of withdrawal
Drinking in larger amounts or for longer than intended
Persistent desire/unsuccessful attempts to stop or reduce drinking
Great deal of time spent obtaining, using, or recovering from alcohol
Important activities given up/reduced because of drinking
Continued drinking despite knowledge of physical or psychological problems caused by alcohol
Alcohol craving

[a]*Mild AUD:* 2–3 criteria required; *Moderate AUD:* 4–5 items endorsed; *severe AUD:* 6 or more items endorsed.

NATURAL HISTORY

Although the age of the first drink (~15 years) is similar in most alcoholics and nonalcoholics, a slightly earlier onset of regular drinking and drunkenness, especially in the context of conduct problems, is associated with a higher risk for later alcohol use disorders. By the mid-twenties, most nonalcoholic men and women moderate their drinking (perhaps learning from problems), whereas alcoholics are likely to escalate their patterns of drinking despite difficulties. The first major life problem from alcohol often appears in the late teens to early twenties, and a pattern of multiple alcohol difficulties by the midtwenties. Once established, the course of alcoholism is likely to include exacerbations and remissions, with little difficulty in temporarily stopping or controlling alcohol use when problems develop, but without help, desistance usually gives way to escalations in alcohol intake and subsequent problems. Following treatment, between half and two-thirds of alcoholics maintain abstinence for years, and often permanently. Even without formal treatment or self-help groups, there is at least a 20% chance of spontaneous remission with long-term abstinence. However, should the alcoholic continue to drink heavily, the life span is shortened by ~10 years on average, with the leading causes of death being heart disease, cancer, accidents, and suicide.

TREATMENT

The approach to treating alcohol-related conditions is relatively straightforward: (1) recognize that at least 20% of all patients have an alcohol use disorder; (2) learn how to identify and treat acute alcohol-related conditions; (3) know how to help patients begin to address their alcohol problems; and (4) know enough about treating alcoholism to appropriately refer patients for additional help.

IDENTIFICATION OF THE ALCOHOLIC

Even in affluent locales, ~20% of patients have an alcohol use disorder. These men and women can be identified by asking questions about *alcohol problems* and noting laboratory test results that can reflect regular consumption of six to eight or more drinks per day. The two blood tests with ≥60% sensitivity and specificity for heavy alcohol consumption are γ-glutamyl transferase (GGT) (>35 U) and carbohydrate-deficient transferrin (CDT) (>20 U/L or >2.6%); the combination of the two is likely to be more accurate than either alone. The values for these serologic markers are likely to return toward normal within several weeks of abstinence. Other useful blood tests include high-normal MCVs (≥91 μm^3) and serum uric acid (>416 mol/L, or 7 mg/dL).

The diagnosis of an alcohol use disorder ultimately rests on the documentation of a pattern of repeated difficulties associated with alcohol (Table 467-2). Thus, in screening, it is important to probe for marital or job problems, legal difficulties, histories of accidents, medical problems, evidence of tolerance, and so on, and then attempt to tie in use