

(See also Harrison's Principles of Internal Medicine, 17th Edition, Chapter 387)

Definition

- Alcoholism and alcohol abuse
 - Regular and excessive use of alcohol with concomitant social, interpersonal, legal, occupational, and/or physical problems or
 - o Repeated use in hazardous situations such as driving
- Alcohol dependence
 - Repeated alcohol-related difficulties in at least 3 areas of functioning that cluster together over any 12-month period
 - o Regular use of alcohol has resulted in a state of physiologic tolerance.

Epidemiology

- Prevalence
 - Alcohol is consumed at some time by up to 80% of the population.
 - o Approximately 20% of patients have alcoholism.
 - o Lifetime risk for alcohol dependence in Western countries
 - ~10-15% for men and 5-8% for women; statistics are higher for alcohol abuse
- Distribution
 - o All socioeconomic strata and all racial backgrounds

Risk Factors

- Genetic factors
 - o Diminished alcoholism risk in ~50% of Asian men and women
 - Due to an inactive form of alcohol dehydrogenase, which results in higher levels of acetaldehyde following alcohol ingestion
- Family history
 - 4-fold increased risk in children of alcoholics
 - Risk increased even if adopted at birth and raised without knowledge of biologic parents
- Presence of other psychiatric disorders
- Vulnerable personality
- Male sex
- Environmental factors
 - Peer group pressure
 - Access to alcohol

Etiology

- Alcohol is a central nervous system (CNS) depressant that acts on receptors for y-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the nervous system.
- Chronic alcohol use produces physiologic and psychological dependence.

- Alcoholism is a complex, genetically influenced disorder.
 - o Genes explain about 60% of the risk.
 - o Supported by a higher risk in identical versus fraternal twins of alcoholic parents
 - o Genes affecting the intensity of the response to alcohol
 - Subgroups require higher blood alcohol concentrations to produce the effects seen at lower blood levels in other people.
- Social, psychological, and environmental factors also contribute to the development of alcohol-related disorders.

Associated Conditions

- Disorders commonly associated with alcohol dependence
 - o Many cancers of the head and neck, esophagus, and stomach
 - o Unexplained hepatitis and cirrhosis
 - Pancreatitis
 - Alcohol-induced peripheral neuropathy

Symptoms & Signs

- Most patients with alcoholism do not have dramatic physical symptoms.
 - Instead present with psychosocial difficulties
 - Marital difficulties
 - Job problems (tardiness, absenteeism)
 - Legal problems resulting from driving while intoxicated
 - o Patients may describe a host of difficulties but may deny that they have a problem with alcohol abuse.
 - o Denial is a characteristic symptom of alcoholism.
- "CAGE" questionnaire: any positive answer indicates a high probability of alcoholism
 - o Are you ...
 - Cutting down, or feel the need to?
 - Annoyed when people criticize your drinking?
 - *G*uilty about your drinking?
 - Eye-opening with a drink in the morning?
- CNS findings
 - Blackouts
 - Episode of temporary anterograde amnesia associated with alcohol use
 - Occurs in ~35% of drinkers
 - Sleep disturbances
 - Deficiency in rapid eye movement and deep sleep results in prominent and sometimes disturbing dreams later in the night.
 - Sleep apnea
 - 75% of alcoholic men over age 60
 - Relaxes muscles in the pharynx
 - o Impairment in judgment and coordination
 - At least half of patients with physical trauma have evidence of substancerelated impairment.
 - In the U.S., 40% of drinkers have at some time driven while intoxicated.
 - Peripheral neuropathy
 - Chronic high doses of alcohol; occurs in 5–15% of alcoholics
 - Cerebellar degeneration
 - ~1% of alcoholics
 - Syndrome of progressive unsteady stance and gait often accompanied by mild nystagmus

- Severe cognitive problems
 - Impairment in recent and remote memory for weeks to months after an alcoholic binge
 - Alcoholic dementia syndrome
 - Apparently irreversible cognitive changes (possibly from diverse causes) from chronic alcoholism
- Psychiatric syndromes
 - Alcohol-induced mood disorder
 - Intense sadness lasting for days to weeks in the midst of heavy drinking in 40% of alcoholics
 - Alcohol-induced anxiety disorder
 - Temporary severe anxiety in 10–30% of alcoholics
 - Often begins during alcohol withdrawal
 - Can persist for many months after cessation of drinking
 - o Alcohol-induced psychotic disorder
 - Auditory hallucinations and/or paranoid delusions with a clear sensorium
- GI findings
 - o Esophagus and stomach
 - Inflammation of the esophagus and stomach
 - Epigastric distress
 - GI bleeding
 - Pancreas and liver
 - Incidence of acute pancreatitis (~25 per 1000 per year) almost 3-fold higher than in the general population
 - Repeated exposure to ethanol leads to:
 - Fatty accumulation in the liver
 - Alcohol-induced hepatitis
 - Perivenular sclerosis
 - Cirrhosis (15–20%)
 - Chronic pancreatitis
- Cardiovascular findings
 - Chronic heavy drinking
 - Mild to moderate hypertension
 - Cardiomyopathy
 - One-third of cases of cardiomyopathy are alcohol induced.
 - Atrial or ventricular arrhythmias, especially paroxysmal tachycardia
 - Occurs after a drinking binge in individuals showing no other evidence of heart disease: "holiday heart"
- Genitourinary system changes; sexual function
 - Acutely (modest alcohol dose: blood alcohol concentrations of ≤100 mg/dL)
 - Increases sexual drive and decreases erectile capacity in men
 - o Chronic alcoholism in men
 - Irreversible testicular atrophy with concomitant shrinkage of the seminiferous tubules, decreases in ejaculate volume, lower sperm count
 - Repeated ingestion of high doses of ethanol by women
 - Amenorrhea
 - Decrease in ovarian size
 - Absence of corpora lutea with associated infertility
 - Spontaneous abortions
- Musculoskeletal findings
 - Acute alcoholic myopathy
 - Condition improves, but might not disappear with abstinence.
 - Effects of repeated heavy drinking
 - Alteration in calcium metabolism
 - Lower bone density
 - Increased risk for fractures and osteonecrosis of the femoral head

- Alcohol-withdrawal syndrome
 - Any sudden decrease in intake can produce withdrawal symptoms; many are the opposite of those produced by intoxication.
 - Tremor of the hands (shakes or jitters)
 - Agitation and anxiety
 - Autonomic nervous system overactivity including an increase in pulse, blood pressure, respiratory rate, and body temperature
 - Insomnia, possibly accompanied by bad dreams
 - GI upset
 - Seizures
 - Withdrawal symptoms generally begin within 5–10 hours of decreasing ethanol intake, peak in intensity on day 2 or 3, and improve by day 4 or 5.
 - o Anxiety, insomnia, and mild levels of autonomic dysfunction may persist to some degree for ≥6 months; may contribute to the tendency to return to drinking.

Differential Diagnosis

- Other forms of substance abuse
- Psychiatric disorders
- Alcoholism frequently accompanies substance abuse and psychiatric disorders.

Diagnostic Approach

- Clinical diagnosis of alcohol abuse or dependence is made by:
 - Careful history
 - Documentation of a pattern of difficulties associated with alcohol use
 - Diagnosis not based on the quantity and frequency of alcohol consumption
 - See DSM-IV criteria below.
 - Screening tools
 - Helpful in identifying alcohol-related disorders
 - CAGE questions (see above)
 - 10-item Alcohol Use Disorder Screening Test

Alcohol dependence (from DSM-IV)

- A maladaptive pattern of alcohol use, leading to clinically significant impairment or distress
- Manifested by 3 or more of the following occurring at any time during the same 12-month period:
 - o Tolerance
 - Need for markedly increased amounts of alcohol to achieve intoxication, or
 - Reduced effect with continued use of the same amount of alcohol
 - Withdrawal
 - The characteristic withdrawal syndrome for alcohol, or
 - Alcohol or a closely related substance is taken to relieve or avoid withdrawal symptoms
 - o Impaired control
 - Persistent desire or at least 1 unsuccessful effort to cut down or control drinking
 - Drinking in larger amounts or over a longer period than the person intended
 - Neglect of activities
 - Important social, occupational, or recreational activities given up or reduced because of drinking
 - Time spent drinking
 - A great deal of time spent in activities necessary to obtain alcohol, to drink alcohol, or to recover from its effects

- Drinking despite problems
 - Continued drinking despite knowledge of having a persistent or recurrent physical or psychological problem
- Either one of the symptoms of tolerance or withdrawal defines "physiological dependence" in DSM-IV

Alcohol abuse (after DSM-IV)

- A maladaptive pattern of alcohol use leading to clinically significant impairment or distress
- Manifested by one or more of the following, occurring within a 12-month period:
 - Recurrent drinking resulting in a failure to fulfill major role obligations at work, school, or home
 - o Recurrent drinking in situations in which it is physically hazardous
 - o Recurrent alcohol-related legal problems
 - o Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol
- The symptoms have never met the criteria for alcohol dependence.

Laboratory Tests

- No well-established laboratory test for the diagnosis
 - $_{\odot}$ Elevated γ-glutamyl transferase (>30 U) and carbohydrate-deficient transferrin (>20 U/L)
 - May be useful in monitoring abstinence
 - Return toward normal within several weeks of the cessation of drinking
 - High mean corpuscular volume
 - o High serum uric acid
 - Other liver function tests abnormal

Imaging

- Brain CT or MRI
 - o Increased size of the brain ventricles and cerebral sulci are seen in ≥50% of chronic alcoholics.
 - o Atrophy of the cerebellar vermis is seen in cerebellar degeneration.

Diagnostic Procedures

There are no diagnostic procedures to confirm the diagnosis of alcoholism.

Treatment Approach

- Treat associated medical or psychiatric syndromes.
- Oversee detoxification.
 - o Refer patient to rehabilitation program.
- Provide counseling.
- Select appropriate medication (if any).
- Rehabilitation
 - o Counselina
 - o Education
 - Cognitive approaches
 - Medications

Specific Treatments

Acute intoxication

- Initially
 - Verify vital signs are stable without evidence of respiratory depression, cardiac arrhythmia, or potentially dangerous changes in blood pressure.
 - o Consider possibility of intoxication with other drugs.
 - Screen for opioids or other CNS depressants in urine or serum.
 - o Evaluate patient for hypoglycemia, hepatic failure, or diabetic ketoacidosis.
- When medically stable
 - Place in quiet environment.
 - o Position patient on his or her side to minimize aspiration risk.
 - Violent or potentially violent behavior
 - Follow hospital procedures.
 - Reassure patient in a nonthreatening way.
 - Continued aggressive behavior
 - Low doses of a short-acting benzodiazepine such as lorazepam (e.g., 1 mg orally)
 - Repeat as needed; monitor vital signs for worsening confusion.
 - Alternatively, antipsychotic medication (e.g., 5 mg of haloperidol)
 - Potential danger of lowering the seizure threshold
 - If aggression escalates:
 - Short-term admission to a locked ward for safe medication administration and closely monitored vital signs

Withdrawal

- Check for evidence of liver failure, GI bleeding, cardiac arrhythmia, and glucose or electrolyte imbalance.
- Adequate nutrition and rest
 - Oral multiple B vitamins, including 50 to 100 mg of thiamine daily for a week or more
 - When Wernicke-Korsakoff's syndrome suspected, intravenous route must be used, because intestinal absorption is unreliable.
 - Medications can usually be administered orally.
- Withdrawal symptoms
 - Administer CNS depressant and then wean; gradually decrease the levels over 3–5 days.
 - Benzodiazepines: highest margin of safety and lowest cost; preferred class of drugs
 - Short half-lives (e.g., oxazepam, lorazepam)
 - Especially useful for patients with serious liver impairment or preexisting encephalopathy or brain damage
 - Must be given repeatedly to avoid abrupt fluctuations in blood levels that may increase the risk for seizures
 - Fairly steady blood levels of drug; wide dose range
 - Average patient requires 25–50 mg of chlordiazepoxide or 10 mg of diazepam orally every 4–6 hours on the first day.
 - Administer enough drug on day 1 to alleviate most symptoms of withdrawal (e.g., tremor and elevated pulse).
 - Decrease the dose by 20% on successive days over a period of 3–5 days.
 - Dose may be increased if signs of withdrawal escalate or withheld if the patient is sleeping or shows signs of increasing orthostatic hypotension.

- Generalized withdrawal seizures
 - Rarely require aggressive pharmacologic intervention beyond normal withdrawal therapy
 - Little evidence that anticonvulsants (e.g., phenytoin) are effective in drug-withdrawal seizures; risk of seizures has usually passed by the time therapeutic levels are reached
 - Status epilepticus (occurs rarely) must be treated aggressively.
- Outpatient detoxification
 - Candidates for this approach are in good physical condition, demonstrate mild signs
 of withdrawal despite low blood alcohol concentrations, and have no prior history of
 delirium tremens (DTs) or withdrawal seizures.
 - Requires careful physical examination, evaluation of blood tests, and vitamin supplementation
 - Benzodiazepines given in a 1–2-day supply; administered by a spouse or other family member 4 times a day
 - o Patient returns daily for evaluation of vital signs and is instructed to go to the emergency room if signs and symptoms of withdrawal escalate.

DTs

- Life-threatening complication of alcohol withdrawal
- Likely to run a course of 3–5 days regardless of therapy employed
- Focus of care: identify medical problems and correct them; control behavior and prevent injuries
 - Evidence of infection or trauma that may be masked by prominent withdrawal symptoms
 - o Monitor fluid and electrolyte status and blood glucose levels.
 - Cardiovascular and hemodynamic monitoring are crucial; hemodynamic collapse and cardiac arrhythmia are not uncommon.
- High doses of a benzodiazepine may be needed.
- Antipsychotic medications: haloperidol, 20 mg or more per day
 - o Less likely to exacerbate confusion but may increase the risk of seizures

Rehabilitation

- Helps the patient achieve and maintain a high level of motivation toward abstinence
 - Education about alcoholism; instruct family and/or friends to stop protecting patient from problems caused by alcohol
- Helps the patient readjust to life without alcohol; reestablish a functional lifestyle
 - Counseling
 - Vocational rehabilitation
 - Self-help groups (e.g., Alcoholics Anonymous [AA])
- Relapse prevention
 - o Identify situations in which a return to drinking is likely.
 - Formulate ways to manage these risks.
 - Develop coping strategies that increase the chances of return to abstinence if a slip occurs.
- Setting
 - No convincing evidence that inpatient rehabilitation is more effective than outpatient care
 - More intensive interventions work better than less intensive measures; some alcoholics do not respond to outpatient approaches.
 - Decision to hospitalize or place into residential care
 - Medical problems that are difficult to treat outside a hospital
 - Depression, confusion, or psychosis interferes with outpatient care.

- Severe life crisis that makes it difficult to work in an outpatient setting.
- Previous outpatient treatment has failed.
- Patient lives far from the treatment center.
- Pharmacotherapy
 - Continuing sleep problems or anxiety
 - Do not use hypnotics or antianxiety drugs after acute withdrawal.
 - Reassure patient that sleep difficulty is normal and will improve over the subsequent weeks and months.
 - Advise rigid bedtime and awakening schedule and to avoid naps or use of caffeine in the evenings.
 - Anxiety
 - Develop strategies to achieve relaxation; use forms of cognitive therapy.
 - Decrease the probability of relapse
 - Naltrexone: 50–150 mg/d
 - A long-acting monthly injectable has been shown to be effective.
 - Acamprosate (Campral): 2 g/d
 - Disulfiram: 250 mg/d
 - Unpleasant (and potentially dangerous) reaction in the presence of alcohol
 - Especially dangerous for patients with heart disease, stroke, diabetes mellitus, and hypertension
 - Good for patients with a history of longer-term abstinence associated with prior use of disulfiram
 - Requires supervision by another individual (such as a spouse), especially during discrete periods identified as representing high-risk drinking situations (e.g., holidays)
 - Topiramate (Topamax): escalating dose of 25 to 300 mg/d
 - Effective in a randomized trial, but not yet approved by the FDA for this indication
- Self-help groups (e.g., AA)
 - o Provide additional support for alcoholics, their relatives, and their friends
 - Offer an effective model of abstinence
 - Provide a sober peer group
 - o Make crisis intervention available when the urge to drink escalates
 - Optimize chances for recovery

Monitoring

- Acute withdrawal period
 - If monitored as outpatient, daily visits to check vital signs and absence of escalating symptoms
- After rehabilitation
 - Outpatient contact maintained for a minimum of 6 months; preferably a full year after abstinence is achieved
 - Counseling with an individual physician or through groups:
 - Focuses on day-to-day living—emphasizing areas of improved functioning in the absence of alcohol (i.e., why it is a good idea to continue to abstain)
 - Helps the patient to manage free time without alcohol
 - Helps the patient develop a nondrinking peer group
 - Helps the patient to handle stresses on the job
- Family may benefit from counseling or referral to self-help groups.
 - o Al-Anon (the AA group for family members)
 - Alateen (for teenage children of alcoholics)

Complications

- Withdrawal seizures
 - o Affect 2–5% of alcoholics, often within 48 hours of stopping drinking
 - Usually involve a single generalized seizure; electroencephalographic abnormalities generally return to normal within several days
 - Treatment is with benzodiazepines, not anticonvulsants.
- DTs
 - Delirium (mental confusion, agitation, and fluctuating levels of consciousness) associated with tremors and autonomic overactivity (e.g., marked increases in pulse, blood pressure, and respirations)
 - o Serious and potentially life-threatening complication of alcohol withdrawal
 - \circ Seen in <5% of alcohol-dependent individuals; chance of DTs during any single withdrawal is <1%
- Wernicke-Korsakoff's syndrome
 - Seen in <10% of alcoholics
 - o Result of thiamine deficiency, especially in persons with transketolase deficiency
 - Wernicke's encephalopathy
 - Characterized by ataxia, ophthalmoplegia, and confusion, often with associated nystagmus, peripheral neuropathy, cerebellar signs, and hypotension
 - Korsakoff's syndrome
 - Follows as the encephalopathy and ocular findings resolve
 - Characterized by anterograde and retrograde amnesia and confabulation
- Fetal alcohol syndrome, caused by heavy drinking during pregnancy
 - Facial changes with epicanthal eye folds, poorly formed concha, and small teeth with faulty enamel
 - o Cardiac atrial or ventricular septal defects
 - Aberrant palmar crease and limitation in joint movement
 - Microcephaly with mental retardation

Prognosis

- Many have exacerbations and remissions.
 - o After alcoholic rehabilitation, 60% or more of alcoholics maintain abstinence for at least a year; many achieve lifetime abstinence.
 - There is a 20% chance of long-term abstinence even without formal treatment or self-help groups.
 - Best predictors of continued abstinence
 - Evidence of higher levels of life stability (e.g., supportive family and friends)
 - Higher levels of functioning (e.g., job skills, higher levels of education, and absence of crimes unrelated to alcohol)
- If patient continues to drink, life span is shortened by an average of 10 years.
 - Leading causes of death in decreasing order
 - Heart disease
 - Cancer
 - Accidents
 - Alcohol is associated with half of all traffic fatalities and half of all homicides.
 - Suicide
- In patients who have dependence with a physiologic component
 - More severe clinical course
- DTs
 - Mortality is 5–15%

Prevention

Abstinence is the only way to prevent recurrence in identified alcoholics.

ICD-9-CM

- 303.__ Alcohol dependence syndrome, (specific type specified by fourth digit, duration specified by fifth digit.)
- 303.90 Other and unspecified alcohol dependence, unspecified (includes chronic alcoholism)

See Also

- Alcoholic Liver Disease
- Anxiety, Including Obsessive-Compulsive Disorder
- Approach to Weight Loss
- Chronic Pancreatitis
- · Cocaine and Other Commonly Abused Drugs
- Confusion, Delirium, and Coma
- Depression
- Health Care Screening and Disease Prevention
- Thiamine Deficiency (Beriberi)

Internet Sites

- Professionals
 - Homepage
 National Institute on Alcohol Abuse and Alcoholism
- Patients
 - Alcoholism
 MedlinePlus
 - FAQs for the General Public
 - National Institute on Alcohol Abuse and Alcoholism
 - Substance Abuse--Alcoholism
 National Mental Health Association

General Bibliography

- Elder NC, Hickner J: Missing clinical information: the system is down. *JAMA* 293:617, 2005 [PMID:15687319]
- Fleming MF et al: Brief physician advice for problem drinkers: long-term efficacy and benefit-cost analysis. *Alcohol Clin Exp Res* 26:36, 2002 [PMID:11821652]
- Johnson BA et al: Oral topiramate for treatment of alcohol dependence: a randomised controlled trial. *Lancet* 361:1677, 2003 [PMID:12767733]
- Kiefer F et al: Comparing and combining naltrexone and acamprosate in relapse prevention of alcoholism: a double-blind, placebo-controlled study. Arch Gen Psychiatry 60:92, 2003 [PMID:12511176]
- Schuckit MA: Vulnerability factors for alcoholism, in *Neuropsychopharmacology: The Fifth Generation of Progress*, K Davis (ed). Baltimore, Lippincott Williams & Wilkins, 2002
- Schuckit MA et al: A 5-year prospective evaluation of DSM-IV alcohol dependence with and without a physiological component. *Alcohol Clin Exp Res* 27:818, 2003 [PMID:12766627]

PEARLS

• Alcoholism is common in the general population; it is a complex, genetically influenced disorder.

- Alcohol withdrawal can be a life-threatening condition complicated by seizures and DTs; a weaning course of benzodiazepines is the treatment of choice.
- Benzodiazepines, rather than anticonvulsants, are the treatment for alcohol withdrawal-related seizures.
- Alcohol-related seizures are treated with benzodiazepines, rather than anticonvulsants.
- Pharmacologic interventions for alcohol rehabilitation include acamprosate, disulfiram, and naltrexone. Naltrexone recently has been shown to be effective when administered in a once-monthly injectable preparation.