4 or 5 days, these patients should return daily for evaluation of vital signs and can be hospitalized if signs and symptoms of withdrawal escalate.

Treatment of patient with DTs can be challenging, and the condition is likely to run a course of 3–5 days regardless of the therapy used. The focus of care is to identify and correct medical problems and to control behavior and prevent injuries. Many clinicians recommend the use of high doses of a benzodiazepine (as much as 800 mg/d of chlordiazepoxide has been reported), a treatment that will decrease agitation and raise the seizure threshold but probably does little to improve the confusion. Other clinicians recommend the use of antipsychotic medications, such as haloperidol or olanzapine as discussed above, although these drugs have not been directly evaluated for DTs. Antipsychotics are less likely to exacerbate confusion but may increase the risk of seizures; they have no place in the treatment of mild withdrawal symptoms.

Generalized withdrawal seizures rarely require more than giving an adequate dose of benzodiazepines. There is little evidence that anticonvulsants such as phenytoin or gabapentin are more effective in drug-withdrawal seizures, and the risk of seizures has usually passed by the time effective drug levels are reached. The rare patient with status epilepticus must be treated aggressively (Chap. 445).

REHABILITATION OF ALCOHOLICS

An Overview After completing alcoholic rehabilitation, ≥60% of alcoholics, especially middle-class patients, maintain abstinence for at least a year, and many achieve lifetime sobriety. The core of treatment uses cognitive-behavioral approaches to help patients recognize the need to change, while working with them to alter their behaviors to enhance compliance. A key step is to optimize motivation toward abstinence through education about alcoholism and instructions to family members to stop protecting the patient from problems caused by alcohol. After years of heavy drinking, many patients also need counseling, some require vocational or avocational help to structure their days, and all should try self-help groups such as Alcoholics Anonymous (AA) to help them develop a sober peer group and learn how to deal with life's stresses while sober. A third component, *relapse prevention*, helps the patient identify situations in which a return to drinking is likely, formulate ways of managing these risks, and develop coping strategies that increase the chances of a return to abstinence if a slip occurs.

Although many can be treated as outpatients, more intense interventions are more effective, and some alcoholics do not respond to AA or outpatient groups. Whatever the setting, subsequent contact with outpatient treatment staff should be maintained for at least 6 months and preferably a year after abstinence. Counseling focuses on areas of improved functioning in the absence of alcohol (i.e., why it is a good idea to continue abstinence) and helping the patient to manage free time without alcohol, develop a nondrinking peer group, and handle stresses.

The physician serves an important role in identifying the alcoholic, diagnosing and treating associated medical and psychiatric syndromes, overseeing detoxification, referring the patient to rehabilitation programs, providing counseling, and, if appropriate, selecting which (if any) medication might be needed. For insomnia, patients should be reassured that troubled sleep is normal after alcohol withdrawal and will improve over subsequent weeks. They should be taught the elements of "sleep hygiene" including maintaining consistent schedules for bedtime and awakening. Sleep medications have the danger of being misused and of rebound insomnia when stopped. Sedating antidepressants (e.g., trazodone) should not be used because they interfere with cognitive functioning the next morning and disturb the normal sleep architecture, but occasional use of over-the-counter sleeping medications (sedating antihistamines) can be considered. Anxiety can be addressed by increasing the patient's insight into the temporary nature of the symptoms and helping the patient to develop strategies to achieve relaxation by using forms of cognitive therapy.

Medications for Rehabilitation Several medications have modest benefits when used for the first 6 months of recovery. The opioid antagonist, naltrexone, 50–150 mg/d orally, may shorten subsequent relapses, whether used in the oral form or as a once-per-month 380-mg injection, especially in individuals with the G allele of the AII8G polymorphism of the μ opioid receptor. By blocking opioid receptors, naltrexone decreases activity in the dopamine-rich ventral tegmental reward system and decreases the feeling of pleasure if alcohol is imbibed. A second medication, acamprosate (Campral) at ~2 g/d divided into three oral doses, has similar modest effects; acamprosate inhibits NMDA receptors, decreasing mild symptoms of protracted withdrawal. Several trials of combined naltrexone and acamprosate have reported that the combination may be superior to either drug alone, although not all studies agree.

It is more difficult to establish the asset-to-liability ratio of a third drug, disulfiram, an ALDH inhibitor, used at doses of 250 mg/d. This drug produces vomiting and autonomic nervous system instability in the presence of alcohol as a result of rapidly rising blood levels of acetaldehyde. This reaction can be dangerous, especially for patients with heart disease, stroke, diabetes mellitus, or hypertension. The drug itself carries potential risks of depression, psychotic symptoms, peripheral neuropathy, and liver damage. Disulfiram is best given under supervision by someone (such as a spouse), especially during high-risk drinking situations (such as the Christmas holiday). Other drugs under investigation include another opioid antagonist nalmefene, the nicotinic receptor agonist varenicline, the serotonin antagonist ondansetron, the α-adrenergic agonist prazosin, the $GABA_B$ receptor agonist baclofen, the anticonvulsant topiramate, and cannabinol receptor antagonists. At present, there are insufficient data to determine the asset-to-liability ratio for these medications in treating alcoholism and, therefore, no data to offer solid support for their use in routine clinical settings.

GLOBAL CONSIDERATIONS

As described above, rates of alcohol use disorders differ across sex, age, ethnicity, and country. There are also differences across countries regarding the definition of a standard drink (e.g., 10–12 g of ethanol in the United States and 8 g in the United Kingdom) and the definition of being legally drunk. The preferred alcoholic beverage also varies across groups, even within countries. That said, regardless of sex, ethnicity, or country, the actual drug in the drink is still ethanol, and the risks for problems, course of alcohol use disorders, and approaches to treatment are similar across the world.

468e Opioid-Related Disorders

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This is a digital-only chapter. It is available on the DVD that accompanies this book, as well as on Access Medicine/Harrison's Online, and the eBook and "app" editions of HPIM 19e.

Opiate analgesics have been abused since at least 300 B.C. Nepenthe (Greek "free from sorrow") helped the hero of the *Odyssey*, but widespread opium smoking in China and the Near East has caused harm for centuries. Since the first chemical isolation of opium and codeine 200 years ago, a wide range of synthetic opioids have been developed, and opioid receptors were cloned in the 1990s. Two of the most important adverse effects of all these agents are the development of opioid use disorder and overdose. The 0.1% annual prevalence of heroin dependence in the United States is only about one-third the rate of prescription opiate use and is substantially lower than the 2% rate of morphine users in Southeast and Southwest Asia.