

Thomas A. Grieger, MD, Deborah L. Warden, MD, and Cynthia Shappell, MD  
DEPARTMENT OF PSYCHIATRY AND CLINICAL RESEARCH DIVISION, DEPARTMENT OF NEUROLOGY, UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES, BETHESDA, MARYLAND, AND DEPARTMENT OF PSYCHIATRY, WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC, U.S.A.

## Substance Abuse Update

### Abstract

Alcohol abuse or dependence is present in 13.6% of the general population and more than half of these individuals have another psychiatric disorder. Psychiatrists are increasingly involved in the management of alcohol withdrawal/detoxification. Although generally a safe procedure, patients must be carefully evaluated for comorbid conditions and for medical complications of prolonged alcohol use. Individuals who experience withdrawal symptoms require close medical monitoring during the course of alcohol detoxification. Detoxification from alcohol, traditionally done in an inpatient setting, is now routinely performed as an outpatient procedure, and a major consideration is whether patients should be managed on an inpatient or an outpatient basis. Potential complications during detoxification, as well as social support networks and likelihood of adherence to the treatment plan are key factors in making that decision. Complications arising during detoxification include seizures and delirium tremens; both require prompt and thorough evaluation and treatment. Past history of withdrawal seizures is a strong predictor of new seizures and the occurrence of new seizures is often a harbinger of delirium tremens. Patients should be carefully monitored during the detoxification procedure using readily quantifiable instruments. The selection and dosage of medications should be individually determined to provide maximum safety without unnecessary side effects or risk of complications. MEDICAL UPDATE FOR PSYCHIATRISTS 1;4:139-143, 1996.

### Introduction

The estimated lifetime prevalence of alcohol abuse or dependence is 13.6% of the general population (1). One study found that 53% of individuals with an alcohol disorder had a comorbid mental disorder (2). It is therefore likely that most psychiatrists have patients with alcohol problems and a significant portion will require detoxification from alcohol as part of their treatment. Treatment of alcohol withdrawal has been shared among psychiatrists, internists, and neurologists. Patients may be admitted to general medicine units for detoxification and subsequently transferred to dual diagnosis or rehabilitation units following completion of withdrawal protocols. In other institutions detoxification occurs in psychiatric units or in medical units under the supervision of psychiatrists. Consultation psychiatrists may also be called upon to provide withdrawal management recommendations to medical and surgical teams (3). A review of multiple studies found ambulatory detoxification to be safe and effective for mild-to-moderate detoxification and indicated that less than 10% of patients with alcohol withdrawal symptoms required admission to an inpatient unit (4). Increasing cost consciousness by third party payers has also limited the availability of inpatient hospitalization for detoxification. Ambulatory treatment also allows patients to function in their home environment and remain at work. Accordingly, there has been an increasing tendency to perform detoxification on an outpatient basis.

### Sequelae of Untreated Withdrawal

The onset of alcohol withdrawal is marked by hyperautonomic responses that occur several hours after the last

drink. In heavily-dependent individuals, withdrawal symptoms may begin when the patient is still intoxicated. The signs and symptoms include sweating, tremor, tachycardia, nausea, insomnia, elevated blood pressure, elevated temperature, and anxiety or irritability. In cases of mild withdrawal, these may be the only symptoms experienced, and will usually subside within 24 hours. In advanced cases or in otherwise vulnerable patients, the autonomic symptoms may be followed by a generalized seizure, or series of seizures. The greatest risk of seizures is 24 to 72 hours from the last drink, but they may occur for up to a week. A recent study found that 1.1% of patients treated with a three-day course of benzodiazepines went on to develop late onset seizures with a mean occurrence time five days after admission (5). Half of these patients had a history of prior withdrawal seizures.

Alcohol withdrawal seizures rarely progress to status epilepticus. Of greater concern is the development of delirium tremens, which occurs in 30% in patients who have withdrawal seizures (6). Delirium tremens is manifested by gross tremors, agitation, hallucinations, disorientation, confusion, and unstable vital signs. It generally occurs 72 to 96 hours after the last drink and may last for several days to weeks. Delirium tremens may occur in the absence of seizures. If not treated, it may progress to coma or death; when treated aggressively it is rarely fatal.

### Other Associated Disorders

Wernicke's encephalopathy due to thiamine deficiency is manifested by confusion, ophthalmoplegia, and ataxia. Korsakoff's psychosis, also due to thiamine deficiency, is a chronic amnesic disorder with poor rates of recovery, but general stabilization upon abstinence. Alcoholic hallucinosis is manifested by hallucinations without loss of orientation or presence of autonomic instability.

Address reprint requests to: Dr. Thomas A. Grieger, Assistant Professor of Psychiatry, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814.

**Table 1.** Signs of Suspected Long-Term Heavy Alcohol Use

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Chronic depressive symptoms not responsive to appropriate therapy
Episodic non-compliance with scheduled appointments
A history of multiple falls or accidents
History of GI bleeds, gastritis, reflux, pancreatitis
Hypertension
Poor nutritional state
Muscle wasting or cardiomyopathy
Ascites, spider angiomas, or abdominal venous dilation
Peripheral neuropathy (decreased distal pin prick, vibratory, proprioceptive testing)
Cerebellar dysfunction (finger nose/heel shin/Romberg/tandem walk)
Nystagmus
Difficulty with cognitive function—short-term memory loss with relatively spared long-term memory
Anemia (microcytic, macrocytic, or mixed)
Macrocytosis
Elevated hepatic transaminases
Prolonged PTT
Elevated amylase

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### Assessment

For most patients detoxification from alcohol is a safe and well-tolerated procedure. The initial step is a careful history concerning substance use patterns and past withdrawal symptoms. Daily usage over an extended period of time and use of alcohol to alleviate withdrawal symptoms are indicators of the need to initiate pharmacological treatment. Patients seeking detoxification have often recently attempted to stop using alcohol. They seek professional assistance when their attempts to quit are met with tremulousness, tachycardia, sweating, nausea, anxiety, and insomnia. A few patients will have histories of past complicated withdrawal symptoms that include seizures, hallucinations, and delirium tremens. Age greater than forty years, other medical conditions, and poor nutritional state are indicators of possible difficulty with withdrawal. Obtaining a history of other drug usage is also important because some patients may use multiple drugs and not appreciate the dangers of withdrawal from benzodiazepines and barbiturates.

A careful physical examination, with emphasis on the neurologic and mental status examinations, will assist in assessing severity and chronicity of usage. Basic laboratory studies may also be helpful in both assessment and management of medical problems. Table 1 lists a number of historical, physical examination, and laboratory findings consistent with long-term sequelae of excessive alcohol use.

### Inpatient Versus Outpatient Detoxification

There are no absolute criteria for determining inpatient versus outpatient detoxification. The tendency in the past 15 years has been to shift to the outpatient setting, and third party payers often have set criteria for reimbursement of hospitalization costs. The decision involves multiple factors as outlined in table 2 (7-9).

The American Society of Addiction Medicine guidelines for treatment enumerate six dimensional criteria that are used to select from four levels of care: outpatient, intensive outpatient/partial hospitalization, medically monitored inpatient, and medically intensive inpatient (9). These criteria are often the basis for insurance company reimbursement guidelines. They are outlined in Table 3.

Although the least objective of the criteria, the most important factor in ensuring successful outpatient detoxifica-

tion is the degree of social supports and ability to adhere to the treatment plan. Patients must be seen on a daily basis for physiologic monitoring and mental status examination. Because they will be taking sedating medications and may experience initial cognitive declines, they must have a means of transportation to the office other than driving themselves. Support and monitoring by family and friends is also vital to ensure continued abstinence from alcohol and other drugs during the period of detoxification and initial recovery.

If outpatient detoxification is prescribed, the patient should be seen on a daily basis and monitored for CIWA-Ar Scores (see below), vital signs, and mental status examination with careful attention to cognitive impairments and hallucinations. Family members or other social support networks should be called upon to report adherence to treatment and to monitor for signs of difficulty during withdrawal. If a return to drinking alcohol is suspected, a breathalyzer test or blood alcohol level should be obtained. If possible, patients should be given medications on a day-to-day basis to ensure compliance with appointments. This is also a period of education and initiation of addiction treatment or referral to providers who specialize in addiction. Some clinicians will also initiate treatment with disulfiram or naltrexone during detoxification to assist patients with early maintenance of abstinence. Disulfiram causes a severe reaction when patients ingest alcohol while using it. It should never be administered to a patient who is acutely intoxicated. A negative breathalyzer test or a 24-hour period of abstinence are recommended prior to initiating treatment. For a review of the efficacy of a monitored disulfiram treatment program see references (10,11). Naltrexone, an opioid antagonist, has also been useful in reducing

**Table 2.** Factors Supporting Inpatient Detoxification

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Significant medical or neurological problems requiring evaluation and treatment
Comorbid psychiatric conditions requiring stabilization
Acute intoxication with associated dangerous behavior or suicidal tendencies
History of prior withdrawal seizures or delirium tremens
Heavy daily usage
Age greater than forty
High tolerance (BAL > 250 with limited evidence of intoxication)
Repeated failures of outpatient detoxification attempts
Limited social supports or inability to adhere to outpatient appointments
Cognitive impairments that limit the ability to adhere to outpatient treatment

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**Table 3.** ASAM Dimensional Guidelines for Levels of Care

Severity of drug withdrawal (or anticipated withdrawal)
Coexistence of biomedical conditions or complications
Psychiatric comorbidity
Treatment acceptance/resistance
Recovery/abstinence skills
Recovery environment

future frequency and amount of alcohol consumption (12).

### Pharmacological Treatment of Withdrawal

The cornerstone of treatment of withdrawal are the benzodiazepines. In most patients a drug from this class may be the only medication needed to manage withdrawal from alcohol. These drugs are well tolerated, have few side effects and are extremely safe. There have been studies where anticonvulsants, such as carbamazepine (13), and barbiturates, such as phenobarbital (7,14), have been successful in treating alcohol withdrawal. Side effects, drug interactions, and potentially serious toxic reactions point away from these agents for most uncomplicated cases of detoxification from alcohol.

All benzodiazepines are active at the gamma-amino-butyric acid (GABA) receptor site, and all could be used for detoxification. Major differences among drugs within this class are mode of administration, rate and degree of bioavailability, elimination half life, and elimination pathway. Chlordiazepoxide (Librium) was the first commercially available benzodiazepine and has been safely used for alcohol detoxification for many years. It is available in oral and injectable forms. Librium and its active metabolites have an elimination half life ranging between 24 and 48 hours. Its two less desirable characteristics are the need for oxidative hepatic metabolism and slow and less predictable absorption. Oxidative metabolism is slower in patients with impaired hepatic function as is often found in patients with alcohol dependence. Diazepam (Valium) is a longer acting benzodiazepine and is also metabolized through oxidation. Both the parent drug and its active metabolite have elimination half lives of greater

than 20 hours. In older individuals or patients with hepatic impairment, the half life may extend to several days. Diazepam is available for oral and intravenous, but not intramuscular use. Lorazepam has a half life ranging from 6 to 20 hours and is metabolized by glucuronidation, a process less impaired in patients with liver disease. It may be administered orally, intramuscularly, or intravenously.

### Long-Acting Versus Short-Acting Agents

There are two general approaches to using benzodiazepines for alcohol detoxification (3,7). The first is to use a long-acting agent such as diazepam. In this approach the patient is given multiple doses of diazepam (usually 20 milligrams per hour) until they no longer feel anxious and are slightly drowsy. The long half life of diazepam allows for a "self taper" over the course of the next week. The advantages to this approach are ease of use and ensured protection against seizures. It may therefore be the preferred approach in treating patients with a history of withdrawal seizures. Problems arise when patients develop withdrawal symptoms while still intoxicated. Diazepam must then be reloaded following metabolism of the remaining alcohol. Excessive sedation and cognitive impairment may also be evident during the first few days. This may be troublesome for patients with ongoing occupational or social demands. It may also interfere with efforts to treat the underlying addictive process. An additional concern is that patients may resort to using alcohol while still sedated with diazepam. They would be at risk for the additive CNS depressant effects. Unless a patient has an extremely supportive environment, diazepam loading is not generally advised for outpatient detoxification.

A second approach to detoxification is the use of a benzodiazepine with an intermediate half life. Lorazepam has been widely used in this approach. Patients are placed on a standing dosage of lorazepam, which is then tapered over the next few days. A typical regimen would be 2 mg four times per day on the first day, 2 mg three times per day for the second day, 2 mg twice per day on the third day, and 2 mg at bedtime on the fourth and fifth day. Be-

cause the initial dosing interval is shorter than the elimination half life, this actually amounts to a slow loading over the first two days and a combined dosage and metabolic taper over the next three days. Patients and family members are advised to reduce the dosage if excessive sedation develops or to take additional lorazepam if withdrawal symptoms develop. Patients are monitored at least three times per day in an inpatient setting or once per day in an outpatient setting. Advantages to this approach include closer monitoring of symptoms, less likelihood of oversedation and cognitive impairment, and more rapid clearance of drug in the event that the patient elects to start drinking.

### Monitoring Withdrawal Symptoms

Although many centers continue to use fixed-schedule dosing of benzodiazepines (15), systematic monitoring of withdrawal symptoms allows for better titration of medication and greater assurance against seizures and delirium. An easily used and well established clinical tool is the Revised Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWA-Ar) (16,17). The CIWA-Ar measures 10 items: sweating, anxiety, tremor, auditory disturbances, visual disturbances, agitation, nausea, tactile disturbances, headache, and orientation. Examples of likely symptoms are listed for scoring each category. Each category is rated 0-7 (except orientation, which is rated 0-4). The ratings are then totaled. A score greater than 10 indicates moderate withdrawal and is an indication to increase medication (usually a one time dose of 1-2 mg of lorazepam). A score greater than 20 would indicate significant symptoms, heightened clinical concern, and the need to re-evaluate the taper schedule. One should also consider possible withdrawal or intoxication from other drugs. Nursing staff can quickly become familiar with the use of this instrument, but its use should be carefully monitored when the instrument is introduced to an inexperienced staff to ensure inter-rater reliability.

All patients treated for withdrawal should also receive thiamine 100 mg per day for the month following the last

drink. If the withdrawal is severe enough to warrant hospitalization, the first two doses should be administered intravenously or intramuscularly, because intestinal absorption is initially poor in chronic alcoholics. Hospitalized patients should also receive magnesium sulfate 1 g intramuscularly every six hours for the first two days. Magnesium, even in patients with normal plasma magnesium levels, reduces the risk of seizure and decreases the degree of tremor.

Antihypertensive medications reduce some of the discomfort arising from the autonomic symptoms of withdrawal. They do not provide protection against withdrawal seizures and may mask symptoms of pending delirium tremens. They should only be used after patients have been appropriately treated with benzodiazepines. If isolated hypertension or tachycardia persist, clonidine 0.2 mg three times per day or atenolol 50 mg once per day may be helpful.

### Treatment of Complications

Alcohol withdrawal seizures are usually self limited, although they may recur. If they occur, the dosage of benzodiazepine should be increased and consideration given to loading the patient with diazepam. In view of the increasing risk of delirium tremens, hospitalization should be strongly considered. Management as an outpatient should not be attempted if strong social supports are not available or if there is limited access to emergency facilities. If the seizures are focal rather than generalized, do not quickly respond to benzodiazepines, or occur more than five days from the last drink, a neurology consultation should be obtained to evaluate for the presence of an underlying seizure disorder. It is always necessary to consider other treatable conditions for convulsions, such as meningitis, hypoglycemia, hyponatremia, other drug ingestion, and occult head trauma (18). A careful physical examination with detailed neurologic examination should be performed. A complete blood count, serum electrolytes, serum glucose, and urine screen for drugs should be obtained. A computerized tomographic (CT) scan or a magnetic resonance imaging test (MRI) should be considered, as should lumbar puncture.

Delirium tremens is best managed in an intensive care setting where one-to-one nursing care is available, and where vital signs can be carefully monitored. The differential diagnosis includes alcoholic hypoglycemia, overdose with anticholinergic agents, and intoxication with amphetamines, cocaine, and PCP. Meningoencephalitis, thyrotoxicosis, and withdrawal from other drugs must also be considered (18). In treating delirium tremens the benzodiazepine dosage is titrated upward to the point of sedation or comfort. Intermediate duration agents like lorazepam provide for easier titration than do the short-acting agents (such as midazolam) or long-acting agents (such as diazepam). There should be ongoing assessment for other etiologies of delirium and patients should be well hydrated. Vital signs should be monitored and stabilized pharmacologically if necessary. Hallucinations, delusions, and disorientation that persist despite adequate treatment with benzodiazepines should be treated with haloperidol 2–5 mg twice per day. Neuroleptics should be used only after benzodiazepine treatment has been optimized.

Alcoholic hallucinosis often occurs in patients who have only mild withdrawal symptoms. It occurs days to weeks following the last drink and is distinct from delirium tremens in that level of consciousness and orientation remain intact. The usual treatment is reassurance that the symptoms will spontaneously resolve. Some patients benefit from a low dose neuroleptic.

### Pregnant Patients

Although the benzodiazepines are generally safe for short-term use in pregnancy, many obstetricians are more familiar with the use of phenobarbital in alcohol detoxification. A standard regimen is 30 to 60 mg administered orally or intramuscularly every 6 to 8 hours over 3 to 4 days (19). Diazepam loading may be used in the event of withdrawal seizures or delirium tremens.

### Conclusions

Heavy alcohol use is a common problem in our culture and brings with it a heavy load of biological, psychological, and social problems. Psychiatrists will encounter a significant number of patients who

need detoxification from alcohol. In most instances a careful evaluation, detailed treatment plan, and appropriate monitoring will result in a comfortable and safe procedure that can often be accomplished on an outpatient basis.

### References

1. Myers JK, Weissman MM, Tischler GL, et al. Six month prevalence of psychiatric disorders in three communities: 1960–1962. *Arch Gen Psychiatry* 1984;41:959–967.
2. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse: Results from the Epidemiologic Catchment Area study. *JAMA* 1990;264:2511–2518.
3. Franklin JE, Francis RJ. Substance related disorders. In *Textbook of Consultation Liaison Psychiatry*. Rundell JR and Wise MG eds. American Psychiatric Press, Inc. Washington DC, 1996.
4. Abbot PJ, Quinn D, Knox L. Ambulatory medical detoxification for alcohol. *Am J Drug Alcohol Abuse* 1995;21(4):549–563.
5. Mayo-Smith MF, Bernard D. Late-onset seizures in alcohol withdrawal. *Alcohol Clin Exp Res* 1995;19(3):656–659.
6. Adams RD, Victor M. *Principles of Neurology*. New York: McGraw-Hill, 1981.
7. Gallant D. Alcohol. In *Textbook of Substance Abuse Treatment*. Galanter M, Kleber HD, eds. American Psychiatric Press Inc., Washington DC, 1994.
8. Benzer DC. Management of alcohol withdrawal and intoxication. In *Principles of Addiction Medicine*. Chevy Chase MD: American Society of Addiction Medicine, 1994.
9. Hoffman NG, Halikas JA, Mee-Lee D, et al. ASAM Patient Placement Criteria for the Treatment of Psychoactive Substance Use Disorders. American Society of Addiction Medicine, Washington, DC, 1997.
10. Gerrein JR, Rosenberg C, Manohar V. D. Sulfiram maintenance in outpatient treatment of alcoholism. *Arch Gen Psychiatry* 1973;28:798–802.
11. Sereny G, Sharma V, Holt J et al. Mandatory supervised antiabuse therapy in an outpatient alcoholism program: A pilot study. *Alcohol Clin Exp Res* 1986;10:290–292.
12. Volpicelli JR, Alterman AI, Hyashida N, et al. Naltrexone in the treatment of alcohol dependence. *Arch Gen Psychiatry* 1992;49:876–880.
13. Malcolm R, Ballenger JC, Sturgis ET, et al. Double-blind controlled trial comparing carbamazepine to oxazepam treatment of alcohol withdrawal. *Am J Psychiatry* 1989;146:617–621.
14. Smith DE, Wesson DR. Phenobarbitol

- technique for treatment of barbiturate dependence. *Arch Gen Psychiatry* 1971; 24:56-60.
15. Saitz R, Friedman LS, Mayo-Smith MF. alcohol withdrawal: A nationwide survey of inpatient treatment practices. *J Gen Intern Med* 1995; 10(9):479-487.
  16. Sullivan JT, Sykora K, Schneiderman J, et al. Assessment of alcohol withdrawal: The revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *Brit J Addiction* 1989; 84:1353-1357.
  17. Sullivan JT, Swift RM, Lewis DC. Benzodiazepine requirements during alcohol withdrawal syndrome: Clinical implications of using a standardized withdrawal scale. *J Clin Psychopharmacol* 1991; 11:291-295.
  18. Daily RH, Diamond I. Alcohol Intoxication and Withdrawal, in *Current therapy in Neurologic Disease*, 3rd Edition. Johnson, RT ed., B.C. Decker Inc., Philadelphia, 1990.
  19. Thorp JM. Management of drug dependency, overdose, and withdrawal in the obstetric patient. *Obstet Gynecol Clin North Am* 1995; 22(1):131-142.