

Alcoholism Pharmacotherapy: New Approaches to an Old Disease

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In the US population, the lifetime prevalence of alcohol abuse/dependence is approximately 15%.¹⁻³ However, among individuals examined in outpatient medical clinics, the prevalence of these alcohol-use disorders may be twice as high.¹⁻³ Moreover, studies have reported that 20% to 40% of patients in general medical hospital settings meet criteria for lifetime alcohol-use disorders.^{4,5} Also, surveys of US hospital discharges have reported that over one million patients, annually, have an alcohol-related discharge diagnosis.^{4,5}

Primary care physicians are in an ideal position to (1) screen for individuals at risk for alcoholism and diagnose alcohol abuse or alcohol dependence; (2) provide effective detoxification, office-based counseling, and pharmacologic treatment of alcoholism; (3) treat coexisting medical and psychiatric conditions; and (4) appropriately refer patients to substance-abuse treatment specialists when warranted. Physicians in private practice, as well as those in general medical clinics and those in general medical hospital settings, are in a unique position to foster reduced drinking and prolonged abstinence among patients in whom they diagnose alcoholism.^{6,7}

However, many physicians are poor at diagnosing alcohol abuse and alcohol dependence and at initiating appropriate treatment or referral.^{8,9} Several recent review articles have discussed methods that may help primary care physicians to become more competent and efficient in their screening, diagnostic, office-based counseling, and referral practices pertaining to problem drinkers in their care.^{6,7}

This article describes the pharmacologic and behavioral rationale that should govern the use of medications in the treatment of patients with alcoholism. It focuses



on pharmacotherapies for acute alcohol withdrawal, as well as those that render the drinking of alcohol aversive, those that may reduce the desire to seek and consume alcohol, and those that alleviate comorbid psychiatric conditions such as depression and anxiety disorders—thereby reducing the risk of alcoholic relapses (Table 1).^{10,11} The article builds upon recent neuroscientific research that has illuminated the behavioral and neurobiological mechanisms believed central

to alcohol withdrawal, compulsive alcohol consumption, and the process of relapse among patients with alcoholism.¹²⁻¹⁴

PHARMACOTHERAPY OF ALCOHOL WITHDRAWAL

For individuals who drink heavily, an abrupt cessation in alcohol use may result in the onset of alcohol withdrawal syndrome (AWS), characterized by sleep disturbances, intention tremors, irritability, nausea, agitation, headaches, sweating, and increases in pulse and blood pressure.^{14,15} This syndrome is accompanied by increased electrical activity in the cortical, limbic, and cerebellar regions of the brain and is associated with increased excitatory activity at glutaminergic *N*-methyl-D-aspartate (NMDA) receptors and reduced inhibitory activity at γ aminobutyric acid (GABA) receptor-chloride channel complexes.^{13,14}

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Table 1. Medication Treatments for Alcoholism

Medication (Dosage)	Indications	Contraindications
Benzodiazepines Chlordiazepoxide (25–100 mg prn) Lorazepam (1–4 mg prn)	Detoxification (inpatients and reliable outpatients)	Actively drinking outpatients, polysubstance abusers, cognitive and/or psychomotor impairment (outpatients)
Disulfiram (250 mg daily)	High motivation for abstinence, contingency contracts, spouse/SO to monitor compliance, prn when facing high risk situations (eg, wedding receptions, class reunions, holidays)	Liver disease (AST/ALT levels >200 U/L), low cognitive function, poor impulse control, homelessness/limited social supports; caution should be exercised in treating those with cardiovascular disease or a seizure disorder
Naltrexone (50 mg daily)	High craving (daily or prn use), strong family history, involvement/compliance with psychosocial therapies	Liver disease (AST/ALT levels > 200 U/L), current or recent opioid use
Acamprosate (not yet FDA-approved)	Hyperarousal s/p alcohol discontinuation, concomitant opioid use, liver disease, use of multiple medications, established abstinence prior to pharmacologic therapy	Primary renal disease
Anticonvulsants* Valproic acid Carbamazepine Gabapentin	Acute and protracted alcohol or other sedative-hypnotic withdrawal; comorbid bipolar disorder, PTSD, anxiety disorders, impulsivity; seizure prophylaxis	Liver disease (VPA, CBZ), drug interactions (CBZ)
Antidepressants* SSRIs Nefazodone Mirtazepine	Depression/dysthymia, anxiety disorders (OCD, PTSD, social phobia, panic disorder) [†]	No psychiatric comorbidity
Busiprone (15–30 mg bid)	Generalized anxiety disorder [†]	No psychiatric comorbidity
Ondansetron (4 mg/kg bid)	Early onset alcoholism (< age 25, family history, antisocial behaviors)	Still under investigation

AST/ALT = aspartate aminotransferase/alanine aminotransferase; bid = twice a day; CBZ = carbamazepine; OCD = obsessive compulsive disorder; prn = as required; PTSD = posttraumatic stress disorder; SO = significant other; s/p = status post; SSRI = selective serotonin reuptake inhibitor; VPA = valproic acid.

*Dosages vary.

[†]For patients with alcoholism and anxiety disorders, antidepressants or busiprone is preferred to benzodiazepines. Benzodiazepines are contraindicated because of synergistic effects with alcohol and the potential for abuse.

Benzodiazepines, which are active at GABA receptor-chloride channel complexes, are generally recommended as the primary drugs of choice to treat AWS, based on substantial evidence that supports their safety and efficacy.^{14–17} These medications reduce the severity of withdrawal symptoms and reduce the risk for alcohol withdrawal seizures and delirium tremens. To date, no single benzodiazepine appears more effective than any other, although longer-acting agents, such as diaz-

epam and chlordiazepoxide, yield fewer breakthrough symptoms.¹⁶ For elderly patients and those with significant hepatic dysfunction, agents such as lorazepam and oxazepam are recommended; these drugs are not oxidized before hepatic conjugation and have shorter half-lives.^{15,16}

There are standardized methods for assessing the severity of AWS symptoms, such as the Clinical Institute Withdrawal Assessment for Alcohol-revised (CIWA-Ar),

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that can guide decisions regarding the initiation of pharmacotherapy and provide assistance in monitoring the therapy's efficacy.^{15–17} By using symptom-triggered dosing schedules for benzodiazepine therapy (eg, administering only to individuals who score 10 or higher on the CIWA-Ar and continuing this treatment only until scores fall below 10), effective clinical outcomes have been produced with the use of minimal benzodiazepine doses.^{15–17} When combined with supportive measures (eg, adequate fluid administration and nutrition, minimization of stimulation, and treatment with thiamine to prevent development of Wernicke's encephalopathy), benzodiazepine treatment can be remarkably efficacious in the treatment of AWS.

Because benzodiazepines and other sedatives interact synergistically with alcohol to produce increased sedation, cognitive impairment, and impulse dyscontrol, unmonitored outpatient detoxification with these medications is risky and not recommended. However, patients without a history of withdrawal seizures or delirium, concurrent sedative dependence, or debilitating medical or psychiatric illnesses can often be safely detoxified as outpatients.^{18,19} Outpatient detoxification with benzodiazepines can generally proceed safely if (1) the patient's home use of the medication can be monitored by a responsible adult who can restrict the patient's access to alcohol and monitor the patient for autonomic withdrawal symptoms and confusion and (2) the patient can be seen daily by a physician or nurse for assessments and dispensation of limited quantities of benzodiazepines. Favorable outpatient detoxification outcomes are associated with alcohol cravings of lower intensity and AWS symptoms of lesser severity.²⁰ There is also increasing evidence that some anticonvulsants may be effective for alcohol detoxification, with the added advantage of having no abuse potential or cross-reactivity with alcohol.^{21,22}

RELAPSE PREVENTION

Psychosocial Treatments for Alcoholism

Relapses are common among patients with alcoholism who are trying to abstain from drinking. Psychosocial treatments for alcoholism are often based on the theory that learning processes play an important role in the development of maladaptive behavior patterns that predispose individuals to relapse. Thus, one of the goals of relapse prevention therapies is to help the patient to identify and correct maladaptive cognitions and behaviors. Other goals include facilitating the patient's motivation to quit drinking and developing strategies to help the patient to avoid relapse. Such interventions may include helping the patient to recognize negative

consequences of alcohol use (eg, medical problems, marital discord) and to avoid the "people, places, and things" that might lead to a relapse.

Several effective individual, family, and group therapies for alcoholism have been developed during the past decade, and the largest study of individual therapies for alcoholism, Project MATCH (Matching Alcoholism Treatment to Client Heterogeneity), has yielded favorable results. The study, for example, found that Twelve-Step Facilitation, Cognitive-Behavioral Therapy, and Motivational Enhancement Therapy each produced an 85% or greater rate of abstinence, a 70% reduction in drinking intensity on drinking days, and a marked reduction in drinking problems. Of these 3 therapies, none appeared clinically superior to the others.²³ Participation in self-help groups such as Alcoholics Anonymous was also associated with successful outcomes according to this and other studies.

Medications That Reduce the Desire to Drink

The observation that both alcohol and opioids produce euphoria, sedation, and the development of tolerance and withdrawal states led researchers to suggest that alcohol's effects may be mediated by endogenous opioids and their receptors in the central nervous system.²⁴ Some researchers have proposed an opioid compensation hypothesis, which posits that patients with alcoholism have a deficiency of endogenous opioid activity that is subjectively experienced as a craving for alcohol.²⁵ Alcohol consumption might reduce the deficiency via its stimulatory effects on the endogenous opioid system.

Chronic alcohol consumption is thought to be reinforced by increasing the concentration of endorphins and enkephalins, which bind to receptors of the mesolimbic dopaminergic neurons, which in turn mediate reinforcement pathways in the brain. Cessation of chronic drinking leads to a renewal of craving and subsequent risk of relapse. Pharmacologic blockade of central opioid receptors in animals with the opioid antagonists naltrexone and naloxone appears to interrupt this system of reinforcement of drinking, thereby decreasing drinking behavior, particularly drinking following exposure to a stressor.^{24,25}

Naltrexone HCl, an antagonist primarily active at μ -opioid receptors, received FDA approval in 1994 for treatment of alcoholism, if used in conjunction with psychosocial treatments. Authors of several placebo-controlled clinical trials have reported that daily treatment with naltrexone (50 mg/day) significantly increased the percentage of days abstinent and reduced rates of relapse to heavy drinking.^{26,27} Craving for alcohol

and preoccupation with thoughts related to drinking appear to be modestly reduced in patients treated with naltrexone. Studies of naltrexone's efficacy in primary care settings also support its effectiveness.²⁸

The use of naltrexone is limited by two significant adverse effects.^{25,29} First, because it acts by blocking μ -opioid receptors, naltrexone poses a problem in patients who are addicted to opioids or who require opioid analgesia. Patients with alcoholism who are active opioid addicts or who are taking methadone or high-dose opioid analgesics typically develop an opioid withdrawal syndrome after taking naltrexone. However, the likelihood of inducing opioid withdrawal is very low if naltrexone therapy is delayed until such patients have two consecutive weeks of documented abstinence from opioids. Alternatively, a naloxone challenge can be administered to such patients before naltrexone therapy is initiated if recent opioid usage is suspected. Also, the patient in need of brief pain management for elective dental or surgical procedures may require temporary cessation of naltrexone before carefully monitored opioid analgesia. For acute pain, such patients may be effectively treated with regional analgesia, with conscious sedation with a benzodiazepine, with the use of nonopioid analgesics, or with general anesthesia. In emergency cases in which opioid blockade must be overridden by use of high-dose opioid analgesia, treatment should be monitored in a setting adequately staffed and equipped for cardiopulmonary resuscitation because of risks of respiratory depression.

The second significant adverse effect relating to naltrexone involves its being associated, although infrequently, with hepatocellular damage and enzyme level elevations when used in much higher dosages (eg, 300 mg/day) than the typical dosages used for treatment of alcoholism. Its use is contraindicated in patients who have acute hepatitis, moderate-to-severe chronic hepatitis, or hepatic failure. Its use in patients with milder forms of hepatic dysfunction must be carefully considered. The mild elevations in transaminase levels commonly seen in alcohol-dependent patients are not themselves a contraindication to naltrexone treatment, although periodic monitoring of liver enzyme levels after initiation of naltrexone treatment is recommended. In clinical trials, naltrexone-treated patients had lower serum transaminase levels after 12 weeks of treatment than did placebo-treated patients, presumably because of their lower rates of drinking.²⁵⁻²⁷

Other commonly encountered adverse effects experienced by opioid-naïve patients taking naltrexone include nausea, headache, dizziness, somnolence, and anxiety (symptoms that mimic a mild case of opioid withdrawal).

In general, however, naltrexone is fairly well tolerated, and these adverse effects occur in fewer than 20% of patients with alcoholism treated with naltrexone.²⁹

Predictors of a favorable response to naltrexone have been identified.^{30,31} They include (1) high pretreatment levels of alcohol craving; (2) a family history of alcoholism in parents, siblings, or children of the patient; (3) greater dependence on alcohol, including tolerance or withdrawal; (4) somatic distress; and (5) lower educational attainment (eg, failure to complete high school). Patients with such characteristics appear to represent a subgroup of patients with alcoholism with a substantial genetic and biological predisposition to severe alcohol problems, stress, and poor coping skills.

Nalmefene is another opioid antagonist that is structurally and pharmacologically similar to naltrexone, but with several clinical advantages. It binds with greater affinity to δ opioid receptors, which are strongly implicated in brain reinforcement pathway physiology, and has greater bioavailability and a longer half-life than does naltrexone, which may allow it to provide more sustained opioid receptor blockade. It has shown no dose-dependent hepatotoxicity in controlled clinical trials thus far and, in preliminary studies, appears to be efficacious and well tolerated.³² Its efficacy for treatment of alcoholism is currently being evaluated in a multicenter clinical trial in the United States.

Aversive Agents

Medications that produce a noxious and aversive effect if alcohol is consumed concomitantly have been available since 1948, with the introduction of disulfiram.^{10,11,33} Disulfiram irreversibly inhibits the enzyme aldehyde dehydrogenase, which converts the ethanol metabolite acetaldehyde to acetate. When an individual taking disulfiram consumes ethanol, acetaldehyde accumulates, producing vasodilatation, flushing, nausea, vomiting, headache, secondary tachycardia, and palpitations; in severe cases, shock and death can occur. Patients taking disulfiram are informed of this potentially serious reaction, and the fear of such a reaction serves as a deterrent to consumption of alcoholic beverages. Non-beverage ethanol, which is found in mouth washes, topical agents such as colognes, and industrial solvents, must also be avoided if a disulfiram-ethanol reaction is to be prevented.

Following a series of uncontrolled studies, a Veterans Administration-sponsored clinical trial tested the efficacy of disulfiram, at standard (250 mg/day) and trival (1 mg/day) dosages, against that of a treatment regimen excluding disulfiram.³⁴ Although the standard dose of disulfiram did not yield longer duration of abstinence, it

was associated with substantially less total alcohol consumption than was either of the comparison conditions. Medication compliance was strongly predictive of drinking outcomes during treatment, and compliant patients treated with disulfiram had significantly more abstinent days than did placebo-compliant patients.

Predictors of efficacy with disulfiram treatment include having high motivation in abstinence-oriented treatment, being married, and being compelled (eg, legally) to comply with alcoholism treatment.³⁵ Use of behavioral contracts has been very effective in increasing compliance with disulfiram, promoting prolonged abstinence, and reducing marital discord among married patients with alcoholism.³⁶ The spouse, a party to the behavioral contract, monitors daily disulfiram ingestion by the patient and tells the prescribing physician of any persistent disulfiram noncompliance.

In addition to daily use of disulfiram, many patients use disulfiram in a targeted manner, taking the medication for one or more days before a high-risk (eg, wedding receptions, class reunions) situation that may trigger cravings to drink or a relapse to drinking. In our experience, brief use of disulfiram is also helpful for patients who have been detoxified during an inpatient hospital admission and who are subsequently discharged to begin outpatient rehabilitation in a counseling program—a transition period when the risk of relapse is quite high.

Disulfiram is generally well tolerated by abstinent patients with alcoholism.^{10,11,33} As a thiuram, it can produce a garlic-like odor of the breath in a minority of patients. Drowsiness also occurs in a minority of patients treated with disulfiram; for these patients, bedtime daily dosing may be preferable. Prolonged treatment with disulfiram, which is metabolized to carbon disulfide, a peripheral neurotoxin, can result in peripheral small fiber neuropathy; periodic monitoring is recommended. Rarely, disulfiram produces hepatocellular injury or hepatic failure. It is prudent to monitor transaminase levels before starting disulfiram treatment and every 3 to 6 months during disulfiram treatment, but the mild elevations in liver transaminase levels associated with alcoholism are not necessarily contraindications.³⁷ The optimal duration of disulfiram treatment is unknown, but high relapse rates during the first 3 to 6 months of abstinence suggest that a 3 to 6 month treatment period is recommended.

TREATING COMORBID ALCOHOLISM AND PSYCHIATRIC DISORDERS

Comorbidity of psychiatric disorders and substance abuse or dependence is common. Approximately half

of individuals with bipolar disorder or schizophrenia and approximately one third of those with panic disorder or major depression have a lifetime substance use disorder.^{1,2,38} In general, among patients with alcoholism, nearly half have a lifetime history of coexisting mood, anxiety, and/or personality disorders.³⁸

Attempting to identify temporal relationships or to determine which illness is primary—the addiction or the psychiatric condition—is often difficult. Psychiatric conditions such as anxiety (eg, social phobia, agoraphobia) mood disorders (eg, major depression, bipolar disorder), attention-deficit/hyperactivity disorder, and some personality disorders (eg, conduct and antisocial personality disorders) are risk factors for development of substance use disorders.³⁸ Also, psychiatric disorders (eg, major depression, panic disorder) can sometimes result from heavy drinking or drug abuse or their behavioral sequelae.³⁹ Some individuals appear genetically predisposed to both psychiatric and substance use disorders.³⁹ Finally, some individuals may have been exposed to risk factors, such as severe physical threat or psychological trauma, that predispose them to develop both psychiatric and substance use disorders. Alcohol use may be a means of self-medication for some individuals, but just as often, psychiatric conditions may emerge as a result of chronic heavy drinking. Coexisting psychiatric disorders and substance use disorders tend to reduce the likelihood of successful recovery from either if both are not treated simultaneously.⁴⁰

The diagnosis and treatment of the addicted patient with a comorbid psychiatric disorder is particularly challenging for the busy clinician. Because symptoms and signs of depression and anxiety decline substantially in the month following cessation of heavy drinking, we recommend that acute detoxification be completed and that a careful history be obtained in cases in which a comorbid psychiatric diagnosis is suspected. Features such as family history of a related psychiatric disorder, onset of symptoms of the psychiatric disorder before the onset of alcoholism, or a history of the disorder being present during periods of 3 or more months of sobriety all reduce the rate of false-positive diagnoses of psychiatric disorders. However, with some psychiatric disorders, including bipolar disorder and schizophrenia, evidence clearly indicates that abstinence is beneficial, but not sufficient, to treat acute symptoms of the condition or prevent symptomatic relapses.

Most medical professionals specializing in addiction problems believe that individuals with current or recent addictions should not be routinely given psychotropic agents that are cross-reactive with alcohol, have synergistic psychomotor and disinhibiting effects, or have

abuse potential. Thus, benzodiazepines, barbiturates, and other sedative-hypnotics should be avoided if possible. They are controlled substances with abuse potential, as made evident by self-administration studies in animals and humans, and the use of benzodiazepines has been reported to lead to relapse in patients recovering from alcoholism.^{32,41} Numerous non-benzodiazepine anxiolytics, such as antidepressants, anticonvulsants, buspirone, antihypertensive agents, and low-dose atypical neuroleptics, have proven to be efficacious in the treatment of a wide range of anxiety disorders.⁴²

Serotonin abnormalities have been found in a subgroup of patients with alcoholism and among individuals with impulse control deficits, making serotonergic agents logical choices for the treatment of patients with alcoholism accompanied by depression, anxiety, or an impulse control disorder.^{43,44} The serotonergic agent buspirone, in high doses, has been found to be effective in enhancing treatment retention and in promoting abstinence and reduced drinking in anxious, recently detoxified patients with alcoholism.³³ Controlled clinical trials have demonstrated the efficacy and safety of high-dose treatment with the tricyclic antidepressants (TCAs) imipramine and desipramine in depressed patients with alcoholism, as well as the selective serotonin reuptake inhibitors (SSRIs) fluoxetine and sertraline in patients with alcohol dependence and coexisting major depression.⁴³⁻⁴⁵ Because of their more favorable safety profile, particularly in overdose situations, we recommend use of the newer serotonergic agents over TCAs in the treatment of these patients. Nefazodone may be a good choice because it may relieve insomnia and anxiety, which are often prevalent in early recovery, and may be devoid of the side effects that characterize SSRIs.

Recent studies suggest that the antiemetic, ondansetron, a 5HT₃ antagonist, may effectively decrease alcohol consumption in early onset alcoholism, presumably by ameliorating an underlying serotonergic abnormality.⁴⁶ Early onset alcoholism is characterized by presentation before age 25, a more extensive family history, increased antisocial behaviors, and a generally more serious course of illness and adverse consequences of alcoholism.

Mood lability and impulse dyscontrol are symptoms commonly encountered in patients with alcohol dependence, alcohol withdrawal, and bipolar spectrum disorders and are frequently cited as antecedents to drinking relapses. Mood stabilizing anticonvulsants such as carbamazepine, valproic acid, and gabapentin have been found to be efficacious in open and controlled clinical trials in the treatment of alcohol withdrawal and the prevention of relapse to a substance use

disorder.^{21,22,47} These agents appear to enhance inhibitory neuronal activity in the cortex and limbic structures involved in affect and selective attention, perhaps by increasing GABA-mediated inhibitory neuronal activity. Some authors have suggested that these medications may reduce spontaneous neuronal activity in limbic structures that have been "kindled" by stressful events, prior stimulant exposure, or sedative or alcohol withdrawal episodes. They appear useful in treatment of the alcoholic patient with bipolar affective disorder and may be useful for outpatient detoxification of individuals with mild or moderate alcohol withdrawal syndromes, given their low abuse potential and lack of pharmacologic interaction with alcohol, particularly compared with benzodiazepines.

Unfortunately, the treatment of comorbid psychiatric and addictive disorders is often not well integrated and has occurred historically in parallel or sequential fashion, if at all. Given the substantial comorbidity of substance use and other mental disorders, we recommend that primary care practitioners receive training in assessment and treatment of both types of disorders, and that treatment proceed in an integrated fashion.

THE FUTURE OF ALCOHOLISM PHARMACOTHERAPY

The past decade has witnessed an explosion of neurobehavioral research on the mechanisms of addiction, which has led to renewed interest in pharmacotherapy to treat withdrawal states and reduce the risk of relapse in patients with alcoholism. Although several promising medications have emerged, much remains to be learned about the neurobiology of the relapse process and effective pharmacotherapy for alcohol dependence. Several important questions remain to be answered: What neurotransmitter or other biological processes are the most suitable targets for effective alcoholism pharmacotherapies? What is the optimal dose and duration of treatment with each medication? What combinations of medications, each with a different mechanism of action, would be optimal to reduce the risk of relapse? What types of patient characteristics best predict efficacy with each medication? What psychosocial treatment is best combined with each medication to improve patient outcomes? What methods are most effective in improving compliance with particular treatment regimens?

Newer investigatory agents, including more specific opiate receptor antagonists, antagonists of the NMDA receptor, and antagonists of neurotransmitters mediating the stress response, such as antagonists of corticotrophin-releasing hormone, might help to more effectively reduce relapses. They might target both the

reward system in the brain and the related limbic regions believed to mediate stressful responses, which often precede relapses. Ideally, newer agents would not interact with ethanol in ways that might increase the risk of injury, illness, or behavioral deterioration. They should have no significant abuse potential and would be nontoxic, particularly in patients with substantial risk of hepatic dysfunction, and should have no adverse effects that would limit their extended use or reduce compliance among minimally motivated patients.

Acamprosate is a promising medication that seems to reduce the neuronal hyperexcitability that occurs after long-term alcohol use or withdrawal, perhaps by reducing glutamate receptors of the NMDA type.^{48,49} Several controlled European studies have demonstrated acamprosate's effectiveness.^{48–50} A multicenter study has recently been completed in the United States with favorable results, and FDA approval is pending. Clinically, acamprosate appears to reduce anxiety, irritability, and insomnia—nonphysical components of withdrawal that commonly emerge upon drinking cessation. It is an amino acid precursor that is eliminated by glomerular filtration, not hepatic metabolism, so it is not contraindicated in patients with hepatic dysfunction. It is well tolerated, with few adverse effects beyond mild diarrhea. To date, no drug interactions, dose-limiting toxicity, psychoactive effects, or abuse potential have been found for this medication.⁵¹

Several large studies are presently attempting to match combinations of medications and pharmacotherapy to particular characteristics of patients with alcoholism. Project Combine, a large, multicenter study of alcoholism treatment funded by the National Institute of Alcohol Abuse and Alcoholism, is examining the efficacy of naltrexone and acamprosate separately, in combination, and in conjunction with brief and more extended psychosocial treatments. The goal is to determine if medications (which might reduce cravings for alcohol, improve stress tolerance, or ameliorate unpleasant moods) might supplement and enhance outcomes provided by psychosocial treatments (which enhance motivation for abstinence, provide training in skills believed important to avoid a relapse, and enhance self-efficacy and commitment to remaining sober).

CONCLUSION

Advances in neuroscientific research and the effectiveness of new pharmacotherapies for alcoholism provide clear scientific evidence supporting the biopsychosocial model of alcoholism. Although none of the pharmacologic treatments for alcoholism represent a cure for the disease itself, current research suggests that

the combination of medication therapy and psychosocial interventions may improve treatment outcomes.

As with other chronic diseases, such as diabetes and hypertension, a combination of pharmacologic and behavioral management and treatment of co-occurring disorders appears necessary for the effective treatment of the alcohol-dependent patient. Given the high prevalence of alcoholism and its attendant personal, societal, and economic costs, all effective therapies, including pharmacotherapies, should be considered in the treatment of patients with alcoholism. As with other chronic diseases, enhancing the patient's motivation to change behaviors and to comply with prescribed treatment modalities is a key to successful clinical outcomes. **HP**

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