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Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Alcoholism

Learning objectives for this issue: **1.** Describe the medications used to treat alcoholism. **2.** Explain the treatment options for comorbid anxiety and alcoholism. **3.** Compare and contrast the different types of alcohol use disorders. **4.** Understand some of the current findings in the literature regarding psychiatric treatment.

Drugs to Treat Alcoholism

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Dr. Frenz has disclosed that he has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

Psychiatrists often take a "don't ask, don't treat" approach to alcohol use disorders, often because of the seeming futility of treatment. Why address addiction when many patients will continue to drink?

Addiction, not surprisingly, behaves like other mental disorders. No one is too shocked when a patient with a history of major depression develops a new episode. Although we shoot for full remission, many patients are left with residual symptoms. The same is true of alcoholism: it often follows a relapsing-remitting course characterized by partial remission. In longitudinal studies stretching decades, only about 40% to 50% of patients achieve stable recovery with the remainder using alcohol to varying degrees (Vaillant GE, *Arch Gen Psychiatry* 1996;53(3):243–249; Öjesjö L et al, *J Stud Alcohol* 2000;61(2):320–322).

In this article, I will focus on medication management of alcoholism, with the understanding that the best treatment combines medications with some form of psychotherapy or other therapeutic support, such as AA meetings.

Disulfiram

Disulfiram (Antabuse) inhibits a liver enzyme needed to metabolize alcohol. When alcohol is consumed, this leads to a build-up of acetaldehyde, which causes the characteristic disulfiram reaction: flushing, nausea, palpitations, and other miserable symptoms. In theory, these symptoms should serve as an extreme disincentive to drink.

Although disulfiram has been around forever (it was initially approved by the FDA in 1951), only a few decent clinical trials exist and their results are mixed. The most recent meta-analysis, which acknowledges issues with the underlying data, demonstrates that disulfiram may slightly increase abstinence in the short-term (Jørgensen CH et al, *Alcohol Clin Exp Res* 2011;May 25, online ahead of print). Studies involving supervised administration—medication compliance is a major problem—have shown more convincing benefit.

This plus-minus efficacy must be weighed against possible harms to patients. I often describe the disulfiram reaction, which involves tachycardia and hypotension, as a stress test in pill form. You need to be reasonably assured, either by history or diagnostic testing, that the patient can survive a major cardiovascular challenge before issuing a prescription. Although hepatotoxicity is rare, patients should also have at least fair liver function.

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Treating Anxiety in Alcoholics

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Dr. Balt has disclosed that he has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

Alcoholism and anxiety go hand in hand. The extent of this comorbidity is clear from the numbers: as many as 45% of patients with alcohol disorders meet diagnostic criteria for a co-occurring anxiety disorder. And alcoholic patients with a comorbid anxiety disorder—particularly panic disorder or social phobia—are three to seven times more likely to relapse than those without concurrent anxiety (Kushner MG et al, *Alcoholism: Clin Exp Res* 2005;29:1432–1443).

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Drugs to Treat Alcoholism

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Disulfiram can pose special challenges for patients with other mental disorders. It rarely causes psychosis by increasing dopamine through its effects on catecholamine production. Disulfiram can also reduce the clearance of some benzodiazepines, tricyclic antidepressants, and anticonvulsants (Fishman MJ et al, *ASAM Patient Placement Criteria: Supplement on Pharmacotherapies for Alcohol Use Disorders,* 2010:62).

In light of this, I struggle with patient selection. Patients who have previously succeeded with disulfiram can usually convince me to prescribe it. Ditto for healthy patients with the goal of abstinence who struggle with impulsive drinking. I start at 125 mg per day and eventually titrate to 250 mg to 500 mg, if tolerated. You need to counsel patients to avoid all alcohol, which is often present in things we don't think about—mouthwash, over-the-counter cough-and-cold preparations, wine used for religious purposes, and certain foods (eg, those containing vanilla extract).

Naltrexone

Naltrexone (ReVia) hit the U.S. market in 1984. As an opioid blocker (antagonist), it blunts the rewarding aspects of alcohol use. On average, it reduces heavy drinking by 17% and drinking days by 4% (Rösner S et al, Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev* 2010, Issue 12). In the United States, heavy drinking for men is generally defined as more than four drinks per day or more than 14 drinks per week; for women, the corresponding thresholds are three and seven. Although naltrexone also reduces the amount of alcohol consumed per drinking day, it does not increase abstinence.

The latest buzz with naltrexone—although it's getting to be old news by now—is the long-acting, injectable formulation (Vivitrol) that received FDA approval in 2006. Administered once a month, it reduces heavy drinking by about 25% (Garbutt JC et al, *JAMA* 2005;293(13):1617–1625). Patients who are abstinent from alcohol for seven days prior to injection ("lead-in abstinence") appear to realize the greatest benefit (80% versus 21% reduction in heavy drinking).

Although compliance with oral naltrexone can be a problem, the substantial cost of Vivitrol is part of my clinical calculus. At about $1,200 per injection versus $85 for a month of tablets, third party payers are loathe to authorize Vivitrol without a compelling rationale. As there are no clinical trials comparing the two formulations, decisions need to occur on a patient-by-patient basis. I tend to reserve Vivitrol for chronic alcohol abusers with profound psychosocial impairment and a documented history of poor compliance with the oral formulation.

I typically start oral naltrexone at 25 mg per day and titrate to a target of 50 mg to 100 mg over several weeks. The injectable dose is 380 mg per month. Chronic use of opioid analgesic medications is an absolute contraindication and patients should be off of all opioids for at least a week before starting therapy. Common side effects include nausea, anorexia, and abdominal discomfort, although these can typically be avoided with gentle introduction. Side effects unique to Vivitrol include injection site pain and sterile abscesses.

Patients with mild-to-moderate liver enzyme elevations can usually take naltrexone safely. You should consult with an addiction specialist or gastroenterologist before prescribing if clear hepatic insufficiency (decreased albumin, increased bilirubin) or cirrhosis is present. After taking baseline liver function tests, ongoing monitoring is only necessary if there are symptoms to warrant it (Rie RK et al, *Principles of Addiction Medicine,* 4th ed. Philadelphia; LW&W, 2009).

Acamprosate

Acamprosate (Campral) was being used in Europe for a long time before receiving U.S. approval in 2004. Its mechanism of action is a bit of a mystery; however, the prevailing theory is that acamprosate normalizes GABA-glutamate balance, which is especially important in early recovery when there is theoretically too much glutamate and not enough GABA.

The acamprosate literature in recent years has been inconsistent and therefore hard to interpret. The most rigorous meta-analyses still suggest that acamprosate reduces lapse/relapse by 14% compared to placebo but does not affect heavy drinking. Acamprosate has been shown to be either inferior or superior to naltrexone, depending on the trial, with no difference between the two when data are pooled (Rösner S et al, Acamprosate for alcohol dependence. *Cochrane Database Sys Rev* 2010, Issue 9).

There has been a lot of handwaving about who is most appropriate for acamprosate and when to start it. Acamprosate is likely more effective if a patient's stated goal is abstinence and there is a period of lead-in abstinence prior to initiating therapy (Chick J et al, *Alcohol* 2000;35(2):176–187). Moreover, a small open-labeled trial demonstrated that patients given acamprosate during detoxification did worse in the long run compared those who began therapy later (Kampman KM et al, *Addict Behav* 2009;34(6–7):581–586).

Although acamprosate's efficacy is modest, it scores points for safety and tolerability. Diarrhea is the most common side effect but this rarely leads to discontinuation of therapy. Acamprosate is renally excreted, which makes it a good

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choice for patients with hepatic dysfunction unless they also have chronic kidney disease (consult with an addiction specialist or nephrologist for recommendations about dose reduction). The standard regimen, 666 mg three times a day, poses some compliance problems due to dose frequency.

Topiramate

Topiramate (Topamax) was approved by the FDA in 1996 for seizure disorder, and although it does not have formal approval for alcohol use disorders, it is generally considered to be part of the standard addiction pharmacopeia.

Topiramate has a complex mechanism of action but, at minimum, appears to fiddle with the GABA-glutamate teeter-totter. It acts as an anticonvulsant by increasing GABA, the brain's primary inhibitory neurotransmitter, and decreasing glutamate, the brain's primary excitatory neurotransmitter. This is also its presumed mechanism of action for alcohol dependence.

Like naltrexone, topiramate primarily affects heavy drinking. A recent meta-analysis demonstrated that it reduced heavy drinking days by about 23% with small improvements in abstinence (Arbaizar B et al, *Actas Esp Psiquiatr* 2010;38(1):8–12). Although the trials used in the meta-analysis were small and more data are needed, topiramate appears to be at least equivalent to naltrexone in head-to-head trials.

Topiramate has a number of clinically relevant side effects including cognitive slowing ("Dopamax"), anorexia and sensory symptoms (numbness, tingling, and taste alteration). It is renally excreted and can cause acid-base issues and kidney stones in some patients. Despite this, I've found it to be well tolerated with slow titration. I start with 25 mg per day and increase by 25 mg per week to an initial target in the 150 mg to 200 mg per day range. Doses as high as 300 mg are a viable option (Johnson BA et al, *JAMA* 2007;298(14):1641–1651), although I typically reserve this for partial responders who aren't experiencing side effects.

Baclofen

Baclofen (Lioresal) is a very old drug recently made new. Originally approved by the FDA in 1977 for neuromuscular spasticity, it acts as an agonist at a subtype of GABA receptors. Like acamprosate and topiramate, this is felt to modulate GABA-glutamate balance.

Most clinical trials in addiction have narrow inclusion criteria that limit external generalizability. Patients with major mental disorders, multiple substance use disorders, and general medical conditions are usually tossed out. The remaining patients are great for research purposes but don't resemble any of the patients that we typically treat.

It was thus refreshing when a trial was conducted on alcohol dependent patients with a history of cirrhosis (Addolorato G et al, *Lancet* 2007;370(9603);1915–1922). Thirty of the 42 patients (71%) allocated to baclofen achieved abstinence compared to only 12 of the 42 (29%) who received placebo. As would be expected, there were no adverse events related to the liver (baclofen is renally excreted). Dosing was initially 5 mg three times per day, increasing to 10 mg three times per day beginning on the fourth day.

I generally initiate baclofen in this range but often titrate much higher (for example, I presently have a patient on 30 mg three times per day). The autobiographical case report that stimulated interest in baclofen involved a physician with alcohol dependence who titrated as high as 270 mg per day before backing off to a maintenance dose of 120 mg (Ameisen O, *Alcohol Alcoholism* 2005;40(2):147–150).

Baclofen is generally well tolerated. Cognitive slowing, somnolence, and neuromuscular weakness, which are dose-related, are possible side effects.

Mix and Match

Combining medications with complementary mechanisms of action has intuitive appeal, but clinical trials have yielded disappointing results. One of the more famous trials, The COMBINE Study, found that naltrexone plus acamprosate was no better than naltrexone alone (Anton RF et al, *JAMA* 2006;295(17):2003–2017). Despite this, some of us cross our fingers and mix and match. If you go this route, I'd suggest sequential introduction to pinpoint possible benefits and harms.

TCPR'S VERDICT: Addiction pharmacotherapy augments but does not replace standard psychosocial supports (eg, mutual help meetings). In the absence of evidence-based treatment algorithms, I typically start with FDA approved options like acamprosate or naltrexone and either rotate to or augment with other agents. For patients who achieve full remission, I generally recommend taking the medication for at least one year before any decisions about discontinuation are made.

Medications Useful for Treating Alcoholism

Medication	Target Dose Range	Notes
Acamprosate (Campral)	666 mg TID	Only modest efficacy, may be best for patients aiming for total abstinence. Well tolerated, diarrhea most common side effect. Renally excreted, can be used in liver impairment.
Baclofen* (Lioresal)	10 mg TID	FDA approved for neuromuscular spasticity. Side effects: cognitive slowing, somnolence, muscular weakness. Renally excreted.
Disulfiram (Antabuse)	250 mg to 500 mg QD	Causes severe symptoms when mixed with alcohol: flushing, nausea, palpitations, tachycardia, hypotension. Avoid in patients with cardiac disease; check liver function tests. Can causes psychosis (rarely).
Naltrexone oral (ReVia)	50 mg to 100 mg QD	Opioid blocker; common side effects: nausea, anorexia, abdominal discomfort, fatigue.
Naltrexone injectable (Vivitrol)	380 mg, once monthly	Expensive: $1,200/month vs $85/month for oral naltrexone. Reserve for chronic alcoholics with documented poor compliance with orals.
Topiramate* (Topamax)	150 mg to 250 mg QD	FDA approved for epilepsy and migraine. Reduces heavy drinking. Can cause cognitive slowing, anorexia, tingling, numbness, taste alteration. Can cause kidney stones (rarely).

*Not FDA approved for alcoholism

Q&A With the Expert

This Month's Expert

Alcoholism in DSM-IV and DSM-5

Mark Willenbring, MD

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Dr. Willenbring has disclosed that he has no relationships or financial interests in any commercial companies pertaining to this educational activity.

TCPR: Dr. Willenbring, there is a proposal to rename and reorganize substance abuse and substance dependence disorders in DSM-5. Please tell us about this.

Dr. Willenbring: Some people, especially those who deal primarily with opioid addiction, felt that the word "dependence" rather than "addiction" in DSM-IV has led to a lot of confusion. For example, people taking opioids for chronic pain would of course become physiologically dependent, but this is not the same thing as addiction. "Addiction" more accurately implies compulsive, destructive drug use, and so there is a proposal that in DSM-V the whole substance use category should be called "Addiction and Related Disorders."

TCPR: What will happen to the term "alcohol abuse"?

Dr. Willenbring: Substance abuse would be eliminated as a separate category, and the disorder would be renamed "substance use disorder." The reasoning here is that over 20 years ago, at the time of planning for DSM-IV, alcohol abuse was thought to be a milder form of alcohol dependence, or perhaps even something separate involving more episodic, as opposed to daily or near daily, drinking. However, new research has proven this is not so. There is no clear categorical distinction between substance abuse and substance dependence.

TCPR: Which research are you referring to in particular?

Dr. Willenbring: The NIAAA (National Institute on Alcohol Abuse and Alcoholism) Epidemiological Study on Alcohol and Related Conditions (NESARC). This is the largest epidemiologic study of substance abuse and psychiatric disorders ever done, and was a random sample of the U.S. adult population, involving 43,000 people, age 18 and older. The first set of interviews was in 2000/2001, the second set was in 2004/2005, and we are currently in the third round.

TCPR: And what have we learned from this study so far?

Dr. Willenbring: It has shown that a lot of what we thought we knew about alcohol dependence was wrong. For example, most abuse symptoms only occur in severe late stage addiction, and abuse is not a less severe form of alcohol involvement. NESARC has also found that about three-quarters of people who have DSM-IV alcohol dependence in their lifetimes have only a single episode lasting on average three or four years. It is relatively mild, they don't become seriously dysfunctional, and it then goes away and never recurs. This is in great contrast to what we thought we knew about alcoholics—many would have predicted that most of these people would have long, chronic courses and would be extremely dysfunctional.

TCPR: I understand that recent studies have identified three main categories of problematic alcohol users. Can you describe them?

Dr. Willenbring: If you look at the subtyping data from NESARC and from other research, you find that about a third, 30 percent, of people who have an episode of alcohol dependence have what I call age-limited heavy drinking, which takes place between ages 18 and 25. Any problems they have at age 20 are usually gone by 25 or 30. This is a group that very seldom seeks any kind of substance-specific help. The second group, about 40 percent, has what I call variable onset. This is similar to sporadic cases of asthma with no family history. The average age of onset for this group is about 35, although it is highly variable. And again, these people are mild to moderate, three to four mainly internal criteria of substance dependence, and most of it is eventually resolved without any clinical intervention. The final 30 percent have an early age of onset, often in the mid teens. This is basically what I would call familial or early onset alcohol dependence. This is characterized by a strong family history, often multigenerational, early onset, and chronicity or recurrence. The worst of these alcohol users—only about 10% to 12% of those with addiction—are the ones who end up going to rehab.

TCPR: And these are the users that have formed the basis of most treatment studies?

Dr. Willenbring: Yes, which is why our understanding of treatment has become so distorted. Consider that the average age of onset for alcohol dependence in the U.S. is 21, the average age of first treatment is about 30, but the average age of people in just about every U.S. treatment trial for alcoholism is 40. So we have been routinely studying this very severe slice of people who have been ill for a couple of decades or more. For years, we have been studying samples of convenience—people who were either in treatment programs or who sought participation in a treatment study. Focusing on people who are in alcohol rehab programs to study alcoholism is equivalent to studying hospitalized asthmatics in order to understand asthma. If you were to only study hospitalized asthmatics and you thought, "This is what asthma is," you would end up with a very distorted picture.

TCPR: So most past studies looked at people who are already full blown alcoholics while the NESARC study looks at the general population, instead.

Dr. Willenbring: Yes. And as you move more into community samples, you discover that there is a much broader continuum of severity, and the lines of demarcation are not clearly written in nature. So we have learned that most alcohol dependence is mild to moderate. I call it functional alcohol dependence.

TCPR: What are the most common symptoms of such patients—how would I recognize such a patient in my office?

Dr. Willenbring: The most common symptoms are what you might call the internal symptoms of addiction—that is, repeatedly setting limits and exceeding them. For example, saying, "I am only going to have two drinks tonight," and then having eight. There is a persistent desire to quit or cut down without success. Internal symptoms also include things like continuing to use in spite of symptoms like hangover, nausea, and insomnia. And a very common pattern that I see clinically in this group is that the drinking is sequestered. These are people who get up on time in the morning, take care of their families, and go to work. And then after their kids go to bed, for example, they drink a pint of vodka or one or two bottles of wine and fall asleep on the couch. The thing clinical psychiatrists should focus on is impaired control, these things like going over limits and desire to cut down or quit.

TCPR: So this would be a so-called functioning alcoholic, who has an alcohol disorder and who needs treatment but whose problem is less severe than alcoholics who end up in rehab.

Dr. Willenbring: Right, and the big lesson from NESARC is that we need to be thinking about substance use on a continuum, rather than dichotomously. It is actually very similar to bipolar disorder or depression, in that some people have a relatively mild episode and it goes away and never comes back.

TCPR: Does that imply that these people don't really need treatment?

Dr. Willenbring: No, I don't think so. Take the analogy of depression, which often also occurs as a single, self-limiting episode. We still treat that episode in order to reduce its length and severity. The same holds true for alcohol use.

TCPR: So to sum it up, you think that instead of viewing people as "you are an alcoholic or you are not an alcoholic," we should view substance use disorder as a continuum, and we should treat more of these patients in an office-based setting rather than referring them to rehab for treatment.

Dr. Willenbring: That is right. And now we have medications that have similar efficacy as SSRI antidepressants, so treating alcohol disorders in the office is much easier.

TCPR: Can you recommend any published guidelines for implementing this updated understanding of substance use disorders?

Dr. Willenbring: Yes, you can find guidelines for treatment in the NIAAA Clinician Guide at www.NIAAA.NIH.gov/guide, which is completely free and downloadable. Screening based on the recommendations here is very easy—it is a single question to screen for nondependent heavy drinking: how many times in the past year have you had five or more drinks in a day for a man or four or more drinks in a day for a woman? Any positive answer is a positive screen. From there, the guide takes you through a decisional process, and it is extremely practical in use, and includes how to prescribe medications for alcohol dependence.

TCPR: Thank you, Dr. Willenbring.

Treating Anxiety in Alcoholics

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It's not clear why anxiety and alcoholism so commonly co-occur, but there are at least three potential, and not mutually exclusive, explanations for this phenomenon. First, anxiety may lead to alcohol abuse. According to this theory, patients use alcohol as a way to "self-medicate" their anxiety (Morris EP et al, *Clin Psychol Rev* 2005;25:734–760). Second, and conversely, excessive alcohol use may generate an anxiety disorder, via a "kindling" effect of repeated withdrawal cycles or disruptions to the stress-response system. Finally, there may be no clear primary disorder, but rather a common underlying vulnerability to both anxiety and to alcohol abuse (Kushner MG et al, *Current Psych* 2007;6(8):55–64). This may be psychological, like high anxiety sensitivity, or biological, like GABA receptor dysfunction or a gene polymorphism.

In most cases, it's not important to determine which disorder came first. In my experience, in fact, this chicken-and-egg problem is irrelevant, because by the time most patients present for treatment, they're stuck in a mutually reinforcing cycle of anxiety, self-medication with alcohol, and increased distress when they attempt to stop or curtail their alcohol use. As a result, it's best to address *both* disorders in treatment.

Precisely *how* to do this, however, is open to debate. Historically, substance use treatment and psychiatric treatment have remained distinct. One common approach has been—and remains—to treat the conditions *sequentially,* usually with an initial focus on alcohol use, to determine whether anxiety symptoms remit with consistent sobriety. While this makes sense intuitively—particularly when the anxiety may be at least partially substance-induced—these efforts often fail because of the vicious cycle of sobriety leading to more anxiety and subsequent alcohol relapse.

Another strategy is *parallel* treatment, in which the anxiety is managed psychiatrically (with medications or therapy directed specifically at the anxious symptoms) while a specialist in addiction simultaneously treats the alcohol disorder. Many chemical dependency (CD) treatment centers take this approach, and it's also the basis of the oft-used strategy of referring patients to AA or CD treatment while you, the psychiatrist, treat the anxiety disorder as you would with any other patient. However, effective treatment requires close coordination and communication among providers, and patients can be frustrated by the division in treatment strategies, especially when they get contradictory messages. For instance, some exposure-based treatment methods for anxiety require the patient to confront situations which they are simultaneously taught to *avoid* because of their high relapse risk.

A third alternative is an *integrated* approach. While such a strategy is most frequently recommended by experts and has theoretical appeal, there are few stan-

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Research Updates IN PSYCHIATRY

Section Editor, Glen Spielmans, PhD

Glen Spielmans, PhD, has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

DEPRESSION

St. John's Wort or Celexa for Minor Depression?

Minor depression is defined in various ways. DSM-IV lists it as a disorder for further study, and defines it as a depressive episode of at least two weeks' duration that includes two or more criteria of major depressive disorder. Whether minor depression responds to antidepressant medication is up for debate, with few studies yielding mixed results. For this reason, any new study of minor depression is worth reviewing.

In this latest U.S. placebo-controlled double blind study, 81 patients with "minor depression" were randomized to either 810 mg/day of St. John's Wort (29 participants), 20 mg/day of citalopram (Celexa) (27 participants), or placebo (25 participants) for 12 weeks. Minor depression was defined differently from the DSM-IV version, namely, by the presence of two to four symptoms of major depression for at least six months, but no more than two years. Thus, these are patients who fit diagnostically somewhere between DSM-IV "minor depression" and "dysthymia."

After early drop-outs, 73 patients were evaluated. On the primary outcome measure, which was reduction in the score on the Inventory of Depression Symptomology—Clinician rated (IDS-C), there were no significant differences among the treatment groups. Treatment response rates were: St. John's Wort, 38.5%, Celexa, 41.7%, and placebo, 52.2% (not statistically different) (Rapaport MH et al, *J Psychiatric Res* 2011;45:931–941).

TCPR's Take: While the study was too small to detect all but very large treatment differences, the fact that the placebo response was so high in this group is intriguing. It implies that mildly depressed patients with few depressive criteria are unlikely to respond better to medications than to unspecified factors such as the passage of time or the expectation of improvement. More research is needed, since depressed patients who fall between the diagnostic cracks seem to be quite common in clinical practice.

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Treating Anxiety in Alcoholics

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dardized, integrated treatment strategies and the data on outcome is both sparse and unimpressive (see for example, Tiet QQ and Mausbach B, *Alcohol Clin Exp Res* 2007;31(4):513–536). This may speak to the lack of trained professionals who can recognize and treat both addiction and anxiety disorders, but also, in my experience, to wide variability in patients' histories, motivations, and circumstances.

Psychotherapy for Anxiety and Alcoholism

Cognitive behavioral therapy (CBT) is well suited for the combined treatment of alcoholism and anxiety, as it can help patients to recognize environmental triggers and identify maladaptive coping strategies and practice new ones, just as CBT for anxiety teaches patients to challenge their own self-destructive thoughts and behaviors. I have actually found that 12-step and other group work teaches patients to identify distorted thoughts and beliefs, and to learn from others' successes and failures.

The "Relapse Prevention" (RP) model (Marlatt GA and Gordon JR, Eds. *Relapse Prevention: Maintenance Strategies in the Treatment of Addictive Behaviors.* New York: Guilford Press, 1985) is a widely used chemical dependency technique based on CBT. The model identifies three general stimuli that precede relapse: negative emotional states, social pressure, and interpersonal conflict. Each of these can heighten anxiety (eg, social pressure can aggravate social phobia and negative emotions can worsen generalized anxiety disorder). Often, patients with worsening anxiety use avoidant coping strategies, specifically relying on alcohol to relieve the anxiety as a form of "negative reinforcement"—that is, it reinforces the value of drinking by taking away the unpleasant anxiety. The RP model can be adapted for the management of anxiety in the context of substance abuse, but it has not yet been empirically tested for comorbid conditions.

Other psychotherapeutic approaches have been developed for specific anxiety disorders, such as "Seeking Safety" for concurrent PTSD and substance abuse (Najavits LM et al, *J Subst Abuse Treatment* 1996;13(1):13–22). However, in a three-month trial of 107 women with PTSD and substance abuse (not limited to alcohol), Seeking Safety was found to be no more effective than outpatient cognitive therapy alone (Hien DA et al, *Am J Psychiatry* 2004;161(8):1426–1432). On the other hand, a two-week pilot trial of CBT-based integrated treatment for panic disorder and alcohol abuse in 48 patients showed benefit over alcoholism treatment alone (Kushner MG et al, *J Mental Health* 2006;15(6):697–707).

Psychopharmacology for Anxiety and Alcoholism

Despite the approval of medications for anxiety and for alcohol dependence, drug trials typically exclude subjects with concurrent disorders. (See the article by Dr. Frenz in this issue for a review of medications for alcoholism.) There are only a handful of published studies focusing specifically on the treatment of comorbid alcoholism and anxiety (reviewed in Smith JP and Book SW, *Psychiatr Times* 2008;25(10):19–23), and results are rather lackluster.

In one study of paroxetine (Paxil), 42 subjects with alcoholism and social anxiety were treated with paroxetine or placebo for 16 weeks. Patients taking paroxetine reported less anxiety but alcohol

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CME Post-Test

To earn CME or CE credit, you must read the articles and log on to www.TheCarlatReport.com to take the post-test. You must answer at least four questions correctly to earn credit. You will be given two attempts to pass the test. Tests must be taken by August 31, 2012. As a subscriber to *TCPR,* you already have a username and password to log on www.TheCarlatReport.com. To obtain your username and password or if you cannot take the test online, please email info@thecarlatreport.com or call 978-499-0583.

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Below are the questions for this month's CME post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Note: Learning objectives are listed on page 1.

1. Which of the following drugs is the best choice for patients with the goal of complete abstinence who have trouble with impulsive drinking (Learning Objective #1)?
   [ ] a. disulfiram (Antabuse) [ ] b. naltrexone (ReVia) [ ] c. topiramate (Topamax) [ ] d. baclofen (Lioresal)

2. If you have a patient with difficulty complying to a medication regime, which of the following might not be a good choice of medication to treat his or her alcoholism, based on the frequency of dosing (LO #1)?
   [ ] a. topiramate (Topamax) [ ] b. acamprosate (Campral) [ ] c. naltrexone oral (ReVia) [ ] d. naltrexone injectable (Vivitrol)

3. Which of the following medications works by decreasing the euphoriant effects of alcohol? (LO #2)?
   [ ] a. acamprosate (Campral) [ ] b. buspirone (BuSpar) [ ] c. naltrexone (ReVia) [ ] d. disulfiram (Antabuse)

4. What does Dr. Willenbring call the alcohol disorder characterized primarily by impaired control over drinking (LO # 3)?
   [ ] a. age-limited heavy drinking [ ] b. functional alcoholism [ ] c. variable onset alcoholism [ ] d. familial alcohol dependence

5. In the Rapaport MH et al study of mild depression, what was the reduction in the score on the Inventory of Depression Symptomology—Clinician rated (IDS-C) among patients who took the placebo (LO #4)?
   [ ] a. 1% [ ] b. 10.5% [ ] c. 38.5% [ ] d. 52.2%

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Treating Anxiety in Alcoholics

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intake was about the same. However, they relied less on alcohol to engage in social situations (Thomas SE et al, *Alcohol Clin Exp Res* 2008;32(1):77–84). Another study on the use of sertraline (Zoloft) for comorbid alcoholism and PTSD randomized 94 patients to 150 mg sertraline or placebo for 12 weeks. Both groups drank less at the end of the trial, although a subgroup analysis showed that sertraline was more effective in reducing alcohol intake in patients with less severe alcohol dependence at baseline (Brady KT et al, *Alcohol Clin Exp Res* 2005;29(3):395–401). But a similar 12-week trial comparing sertraline with placebo for PTSD and alcoholism found no significant differences at all (Labbate LA et al, *Compr Psychiatr* 2004;45:304–310).

At least three studies have examined buspirone (BuSpar) for management of alcohol dependence and anxiety symptoms. Two RCTs comparing 15 mg/day buspirone with placebo showed trends toward reduced anxiety and alcohol intake (Kranzler H et al, *Arch Gen Psych* 1994;51:720–731; Tollefson G et al, *J Clin Psychopharm* 1992;12:19–26) but these were not statistically significant. A third, using a higher buspirone dose (60 mg/day), showed no effect relative to placebo (Malcolm R et al, *Alcohol Clin Exp Res* 1992;16(6):1007–1013).

Using benzodiazepines to treat anxiety in alcohol-abusing patients is controversial. Most treatment guidelines recommend avoiding benzodiazepines in patients with alcohol dependence. Psychiatrists and internists frequently use benzodiazepines to treat alcohol withdrawal symptoms, but their use is time-limited (usually less than seven days) and usually in a highly supervised setting. Patients with known anxiety disorders sometimes require a longer taper (Edwards G et al, *The Treatment of Drinking Problems,* 4th ed. Cambridge, UK: Cambridge University Press, 2003). Continuous use of benzodiazepines should be undertaken with caution, as they may have a high abuse potential in alcoholics; in fact, alprazolam (Xanax), diazepam (Valium), and lorazepam (Ativan) have a mood-enhancing effect in alcoholics that is not observed in non-alcoholics (Ciraulo AD and Nace EP, *Am J Addict* 2000;9:276–284).

On the other hand, there is evidence to suggest that a history of alcohol dependence may not necessarily result in greater abuse of benzodiazepines, particularly in those with less severe dependence (Lingford-Hughes A et al, *Adv Psychiatr Treat* 2002;8(2):107–116). In my practice, I find benzodiazepines to be effective if used judiciously and with very close follow-up. Two red flags that make me suspect my patient is becoming addicted are: (1) requests for escalating doses and (2) overreliance on medications at the expense of other strategies that have proven effective for that patient—for example, a reluctance to engage in therapy or ongoing 12-step work.

The opiate blocker naltrexone (ReVia) is effective for preventing alcohol relapse, presumably because the euphoric effects of both alcohol and benzodiazepines may be mediated by the endogenous opiate system. While naltrexone is not approved for benzodiazepine addiction, one study found that it prevented the euphoric (but not the

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anxiolytic) effects of benzodiazepines when the two drugs were used together (Richardson DK et al, *Pharmacol Biochem Behav* 2005;81(3);657–663).

Controlled studies of all sorts of comorbid anxiety/alcohol treatments—whether separate or integrated, psychotherapy or medication—have been disappointing, most likely due to the wide variability among patients who present for treatment. Like most experts in the field, I have found that the most effective approach is an individualized one.

Engaging the patient in treatment is more than half the battle, so when possible, I start with the condition that the patient identifies as most problematic (which may or may not be the substance abuse), while using therapies such as motivational interviewing to encourage him or her to address other problems.

TCPR'S VERDICT: Comorbid alcoholism and anxiety is an often debilitating condition. A strategic combination of medications and therapy, determined by the patient's progress and not by a formula or manual, seems to be the best way to tackle this common and difficult problem.