Perspective

Addressing Alcohol Use in HIV-Infected Persons

Alcohol use is common among persons with HIV infection and is associated with worse HIV treatment outcomes. Patients with hazardous levels of use are less likely to be receiving antiretroviral therapy, to be adherent to therapy, and to achieve virologic suppression. Screening, intervention, and referral to care for alcohol use disorder is an integral part of clinical care for individuals with HIV infection. Brief screening procedures can identify level of risk and determine whether patients require brief alcohol intervention or should be considered for behavioral therapy and pharmacologic treatment. Identification of concurrent mental health disorders is an important aspect of treating alcohol use disorders in HIV infection and other clinical settings. This article summarizes a presentation by Geetanjali Chander, MD, MPH, at the 14th Annual Clinical Conference for the Ryan White HIV/AIDS Program held in Tampa, Florida, in June 2011. The Clinical Conference is sponsored by the IAS–USA under the Health Resources and Services Administration (HRSA) contract number HHSH250200900010C.

Introduction

Alcohol use is common in HIV-infected persons, with data from national samples indicating that 50% report any alcohol use and that the rate of hazardous use is twice that in the general population.[1] Alcohol use worsens common comorbid conditions in HIV-infected persons, including hepatitis C virus (HCV) and hepatitis B virus (HBV) infections, diabetes, and hypertension. It also increases HIV risk behaviors, including having unprotected sex, multiple sex partners, and high-risk injection behaviors.[2,3] Alcohol use is associated with worse HIV treatment outcomes, and mortality.[4,5]

Hazardous alcohol use is defined as more than 7 drinks per week or more than 3 drinks per occasion for women of any age and for men older than 65 years. In men aged 65 years or younger, hazardous use is defined as more than 14 drinks per week or more than 4 per occasion. Data from a study of approximately 1700 patients at the Johns Hopkins HIV Clinic showed that hazardous alcohol use (in the absence of drug use) was associated with reduced likelihood of being on or being adherent to antiretroviral therapy and reduced likelihood of achieving virologic suppression (Table 1).[4]

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See page 135 for information on CME credit for this article.

Screening for Alcohol Use

In HIV clinical settings, all patients presenting for care should be screened for alcohol use. If screening is negative at baseline, it should be repeated at least annually; if positive, it should be repeated at every visit. Screening is relatively easy and straightforward. The National Institute on Alcohol Abuse and Alcoholism recommends asking a single, validated, screening question, "How often in the last year have you had 4 or more drinks?" (for women) or "5 or more drinks?" (for men).[6] If such consumption has occurred on more than 1 occasion, follow-up questions should be used to identify quantity and frequency of drinking, eg, "How many standard drinks do you have on a typical drinking day?" and "How many days per week do you usually drink?" Instruments for follow-up include the AUDIT-C (Alcohol Use Disorders Test–Consumption) and the CAGE (Cut down, Annoyed, Guilty, Eye-opener) questionnaire. Some clues that may prompt screening for alcohol use include changes in medication or appointment adherence, symptoms of depression or anxiety, changes in laboratory measures (eg, an increase in aspartate aminotransferase [AST] on liver function testing [LFT]), changes in blood pressure or diabetes control, or a new sexually transmitted infection.

It is important to note that a "standard" drink is any that contains 14

Table 1. Effects of Alcohol Use or Drug Use on Receipt of Antiretroviral Therapy, Adherence to Antiretroviral Therapy, and Virologic Suppression[a]

Drug Use	Alcohol Use	Antiretroviral Therapy[b]	Adherence[c]	Virologic Suppression[c]
		Adjusted odds ratio (95% confidence interval)		
No	No	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Moderate	1.14 (0.95-1.37)	0.77 (0.62-0.98)	1.00 (0.84-1.20)
	Hazardous	0.57 (0.42-0.77)	0.36 (0.25-0.53)	0.72 (0.52-0.99)
Yes	No	0.54 (0.43-0.68)	0.50 (0.37-0.68)	0.60 (0.46-0.78)
	Moderate	0.68 (0.54-0.88)	0.40 (0.30-0.54)	0.64 (0.50-0.82)
	Hazardous	0.40 (0.29-0.57)	0.32 (0.20-0.51)	0.50 (0.32-0.76)

Adapted from Chander et al.[4]

[a] Adjusted for age, sex, race, CD4+ cell count nadir, and days enrolled in study

[b] Sample includes individuals either receiving antiretroviral therapy or with CD4+ cell count ≤ 350/μL

[c] Adjusted for age, sex, race, CD4+ cell count nadir, and years receiving antiretroviral therapy (days)

grams of alcohol, and that an alcoholic drink includes beer, wine, and liquor. Thus, a standard drink is 12 fluid ounces of regular beer, 8 ounces to 9 ounces of malt liquor, 1 glass of table wine, or 1.5 ounces (1 shot) of 80-proof liquor. Patients may say they have had 2 drinks or "two 40s," referring to two 40-ounce bottles of beer or malt liquor—actually equivalent to approximately 7 standard drinks. They may describe a pint or "a fifth" of vodka as a single drink, actually equivalent to 11 and 17 standard drinks, respectively.

Drinking Definitions

Alcohol use covers a spectrum from "none" or "never exceeds limit" to "at-risk," where there are not yet major consequences to drinking, through "harmful," "severe" (dependent), and "chronic dependent" (Figure 1).[7] At-risk alcohol use includes hazardous alcohol use, defined as more than 7 standard drinks per week in women and more than 14 standard drinks per week in men, and binge drinking, defined as drinking to a blood alcohol content of 0.08% or greater (roughly 5 or more drinks in 2 hours for men, and 4 or more drinks in 2 hours for women).[8] Problem drinking or harmful alcohol use is defined as drinking above these levels with 1 or more additional social, interpersonal, behavioral, or medical consequences, including risk of bodily harm, relationship trouble, role failure (eg, in school or work), and run-ins with the law.[8]

Alcohol dependence or severe alcohol use is defined as the presence of any 3 of the following within the prior 12 months[9]: (1) Tolerance, defined as (a) need for increased amounts of alcohol to achieve intoxication or desired effect, or (b) markedly diminished effect with continued use of same amount. (2) Withdrawal, manifested by (a) tremors, sweating, insomnia, etc, and (b) use of the same (or closely related) substance to avoid or relieve such symptoms. (3) Using the substance in larger amounts or over a longer period than intended. (4) Persistent desire or unsuccessful efforts to cut down or control use. (5) Great expenditure of time in activities necessary to obtain or use the substance or recover from its effects. (6) Withdrawal from or reduced participation in social, occupational, or recreational activities because of substance use. (7) Continued use despite recurrent or persistent physical or psychological problems caused or exacerbated by the substance use. Chronic dependence differs from severe use by the presence of more factors among the criteria for dependence, and is usually exhibited by patients who cycle in and out of treatment programs.[7]

Patients who do not drink or never exceed limits should be screened annually. Those in the at-risk or harmful segment of the spectrum should receive a brief intervention, and those in the harmful to chronic dependent segment are candidates for behavioral therapy and pharmacologic treatment.

Consider a patient who describes her alcohol use as consisting of 4 drinks every Friday night out with friends, with no other alcohol use during the week, no interference with work, no drinking and driving, and no other signs of alcohol abuse or dependence. This patient is actually a hazardous, or "at-risk," drinker, and should receive a brief alcohol intervention.

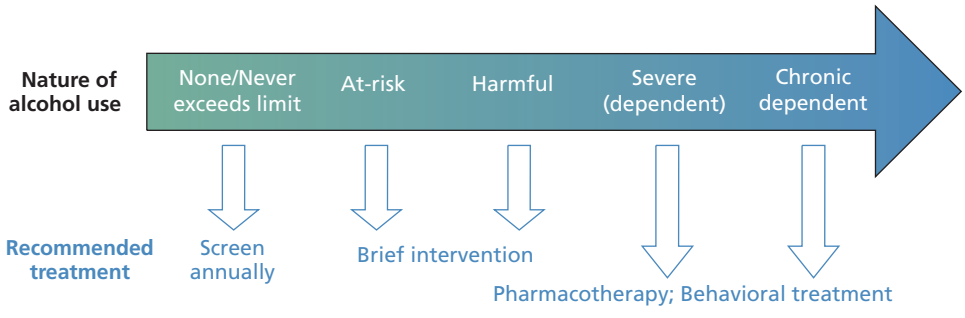

Figure **1**. Spectrum of alcohol use and recommended treatment. Adapted from Willenbring et al[7] and Willenbring.[21]

Brief Alcohol Interventions

A brief alcohol intervention is a short, directed interaction that provides personalized feedback based on alcohol use and related problems (eg, elevated LFTs, depression, increased interpersonal conflicts, poor HIV medication adherence). It offers specific drinking reduction strategies, such as setting goals for safer drinking, alternatives to drinking, and management of risky moods or situations. The brief intervention is a low-cost, cost-effective treatment that promotes reductions in drinking in non–alcohol-dependent persons, as well as facilitates treatment referral in dependent persons.

Components of the brief intervention include the following[8,10]:

- *Ask*: Screen for alcohol use in all patients.
- *Assess*: Assess for risk and consequences, including family history; legal, medical, and social consequences; and alcohol dependence. Assess for readiness to change.
- *Advise*: Provide feedback on drinking and medical, social, and behavioral consequences, and make recommendations for cutting down or quitting alcohol use.
- *Arrange for follow-up*.

Assessing patients' readiness for change can assist in productively advising them on their alcohol use. Readiness to change can be assessed using a question such as: "On a scale of 1 to 10, with 1 being not ready at all and 10 being ready, how ready are you to change your alcohol use?" Patients' confidence in their ability to change can be assessed by asking, "On a scale of 1 to 10, how confident are you that you can change your alcohol use?" If the patient is ambivalent

about changing, a discussion should be initiated about the positive and negative aspects of alcohol use or the "pros" and "cons." A useful technique is to "develop discrepancy"—to have the patient examine alcohol use within the context of their other values and goals and to encourage them to consider how their drinking may conflict with these values and goals. Patients who are ready to change should be helped with goal formulation, guided to resources, and given referrals. Follow-up is imperative for both the ready and the ambivalent.

The basic content of advice for those with drinking problems is as follows:

- *Cut down*: For the hazardous drinker—one with no major consequences from drinking—recommend reducing alcohol use to nonhazardous levels.
- *Cut down or abstain*: For those with harmful alcohol use—eg, no alcohol dependence, but some consequences from drinking—recommend either reduction to nonhazardous levels of alcohol use or abstinence.
- *Abstain*: For those who (a) are alcohol dependent, (b) are pregnant, (c) have HCV infection or other medical conditions in which alcohol use is not recommended, (d) are on medications that interact with alcohol, (e) have blackouts, or (f) are unsuccessful at cutting back on use—recommend abstinence from alcohol.

Treatment for Alcohol-Dependent Patients

Alcohol-dependent patients should be referred to treatment programs. HIV clinicians should be familiar with local resources for substance-abuse treatment and related psychiatric care, including inpatient or residential treatment, outpatient treatment, and support groups such as Alcoholics Anonymous. In addition, clinicians should assess for potential withdrawal symptoms.

Clinicians should also consider the use of pharmacotherapy in dependent individuals. Medications are available that target neurotransmitters involved in the reinforcing effects of alcohol use. Pharmacotherapy for alcohol dependence in combination with behavioral counseling can reduce relapse and help maintain abstinence.

HIV clinics offer a number of advantages as a site for alcohol pharmacotherapy. These clinics are involved in long-term patient care, are generally characterized by integration of a variety of specialty services (eg, psychiatric and ob/gyn services), and have access to funding for prescription medications. Further, many HIV clinics use intensive case management models that promote outreach to and retention of patients who are often challenging to treat. However, currently there are no data on pharmacotherapy for alcohol dependence in patients with HIV infection, although a number of trials are under way. Further, pharmacotherapy for dependence has shown only modest efficacy in clinical trials.

Thus far, US Food and Drug Administration (FDA)-approved treatments for alcohol dependence are naltrexone (oral and injectable forms), acamprosate, and disulfiram.

Naltrexone. Naltrexone blocks opioid receptors and thus lessens the positive reinforcing effects of alcohol consumption. Naltrexone treatment decreases craving, reduces the number of heavy drinking days, and reduces the frequency of relapse to heavy drinking. A Cochrane systematic review of 50 randomized controlled trials of oral naltrexone involving 7793 patients found a 17% reduction in risk of returning to heavy drinking, a 4% reduction in drinking days, and improvement in levels of gamma-glutamyl transferase (GGT, a marker for liver damage).[11]

For oral naltrexone treatment, the patient must be opioid-free for 7 days to 10 days and it is recommended that patients be alcohol-free for at least 5 days to 7 days. The starting dose is 12.5 mg/d to 25 mg/d, increases to 50 mg/d, and treatment is for a minimum of 2 months. Naltrexone is classified by the FDA as pregnancy category C and should not be used during pregnancy. Patients should have LFTs monitored regularly, as naltrexone is associated with hepatitis. Other adverse effects consist mainly of nausea, headache, dizziness, nervousness, insomnia, abdominal pain, and cramping.[12]

Extended-release naltrexone administered via intramuscular (IM) injection is given at a dose of 380 mg monthly, with abstinence required before the start of treatment. Similar to oral naltrexone, individuals should be opioid free before initiating IM naltrexone. Adverse effects include decreased appetite, dizziness, fatigue, vomiting, and injection site reactions including cellulitis, induration, abscess, and necrosis. A randomized, placebo-controlled trial in more than 400 patients showed that monthly IM naltrexone was associated with a 25% reduction in the rate of heavy drinking days.[13]

Acamprosate. Acamprosate affects the glutamate and gamma-aminobutyric acid (GABA) neurostransmitter systems. It has shown moderate efficacy in European trials that has not been replicated in US trials. A Cochrane meta-analysis of 24 randomized, controlled trials involving 6915 patients showed that acamprosate was associated with a statistically significant reduction in risk for any drinking and increased cumulative abstinence duration.[14] A dosage of 666 mg is taken 3 times daily, and alcohol abstinence is required before starting treatment. The drug is categorized as pregnancy category C. Dose adjustment is required with renal insufficency and is contraindicated in individuals with a creatinine clearance of less than 30 mL/min.

Disulfiram. Disulfiram inhibits aldehyde dehydrogenase, increasing levels of acetaldehyde and causing flushing, tachycardia, sweating, nausea, vomiting, and headache if the patient drinks alcohol. Close monitoring of LFTs is necessary, as disulfiram is associated with hepatitis. Neuropathy is also an adverse effect associated with disulfiram. The drug is metabolized by cytochrome P450 3A isoenzymes,

Brief Mental Health Screening Tools for Patients With Alcohol Use

Two-Question Screen for Depression[18]

Over the last 2 weeks, how often have you been bothered by the following problems?

- Have you experienced little interest or pleasure in doing things?
- Have you felt down, depressed, or hopeless?

Generalized Anxiety Disorder 7-Item Scale[19]

How often during the past 2 weeks have you felt bothered by:

- Feeling nervous, anxious, or on edge? _____
- Not being able to stop or control worrying? _____
- Worrying too much about different things? _____
- Trouble relaxing? _____
- Being so restless that it is hard to sit still? _____
- Becoming easily annoyed or irritable _____
- Feeling afraid as if something awful might happen? _____

Total _____

Scoring

0 = not at all 2 = more than half the days

1 = several days 3 = nearly every day

Total score ≥ 10 should prompt further evaluation.

and thus has the potential for interactions with a variety of other drugs that are inhibitors or inducers of these enzymes. Informed consent should be obtained before starting treatment, to ensure that patients are aware of the reactions that occur with alcohol use and that they know to avoid over-the-counter products that contain alcohol. The daily dose is 250 mg. Treatment is best accomplished with monitoring of drug administration, because adherence is low otherwise. Studies of potential pharmacokinetic interactions with antiretroviral agents are under way.

Future pharmacotherapy. Topiramate, ondansetron, and selective serotinin reuptake inhibitors (SSRIs) are currently being investigated for treatment of alcohol dependence, as are combination approaches. Studies with naltrexone, ondansetron, and SSRIs have suggested that treatment response may be correlated with genetic differences at neurotransmitter receptors, raising the possibility of targeted treatment.

Concurrent Substance Use and Mental Health Disorders

Identification and treatment of concurrent mental health disorders is crucial to managing substance use among persons with HIV. Among HIV-infected persons, 13% have been found to have concurrent psychiatric symptoms and either drug dependence or heavy drinking.[15] A study in HIV-infected veterans showed that hazardous drinkers were 2.53 times more likely to meet criteria for depression and binge drinkers were 2.14 times more likely to meet the criteria.[16] Mental health disorders may worsen the negative health and social consequences of drug and alcohol misuse and interfere with treatment of substance use disorders. Substance use among individuals with mental illness can lead to worsening symptoms, increased hospitalizations, and decreased medication or appointment adherence.[17] Concomitant substance-use disorder and mental illness is also associated with a greater financial burden to society. Mental health screening tools that can be used to assess patients with positive screening for alcohol use include a 2-question screen for depression[18] and a 7-item screening instrument for generalized anxiety[19] (see sidebar).

Patients with a triple diagnosis of HIV infection, substance use disorder, and mental health disorder face a number of barriers to care because they must navigate numerous healthcare settings if they are to receive treatment for all disorders. Integrated care in the HIV clinic can greatly facilitate treatment for these individuals. As stated by Soto and colleagues, "Integrated HIV care combines HIV primary care with mental health and substance abuse services into a single coordinated treatment program that simultaneously, rather than in parallel or sequential fashion, addresses the clinical complexities associated with having multiple needs and conditions."[20]

An optimal integrated care system provides such ancillary services as housing and transportation assistance and case management, in addition to providing centralized care for medical, substance use, and mental health issues. Perhaps the most important components of such a system are communication and shared decision making among collaborators involved in patient care.

Lecture presented by Dr Chander in June 2011. First draft prepared from transcripts by Matthew Stenger. Reviewed and edited by Dr Chander in October 2011.

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**Dr Chander's recommended curricula, review articles, and websites.*

Top Antivir Med. 2011;19(4):143-147

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Topics in
Antiviral Medicine™

Continuing Medical Education

The following article in this issue is associated with CME credit:
Chander G. Addressing alcohol use in HIV-infected persons.
Top Antivir Med. 2011;19(4):143-147

Instructions

This journal-based continuing medical education (CME) activity provides a review of alcohol use and HIV infection. To complete the activity, the learner is instructed to:

- Read the article (see pages 143-147)
- Review a selection of the references
- Reflect on how the information might be applied to the clinical practice
- Take the posttest
- Complete the CME claim form and send it to the IAS–USA office.

Learning Objectives

Upon completion of this activity, learners will be able to recognize the impact alcohol misuse has on HIV disease outcomes, screen for hazardous alcohol use, and describe pharmacotherapy and brief interventions for alcohol-dependent patients.

Accreditation Statement

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Intended Audience

This activity is intended for physicians involved in the care of patients infected with HIV or other viruses. It is also relevant to nurse practitioners, physician assistants, nurses, and other health professionals who provide care for people with viral diseases.

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Dr Chander has no relevant financial affiliations to disclose.

Dr Richman has been a consultant to Biota, Bristol-Myers Squibb, CHIMERx, Gen-Probe Inc, Gilead Sciences, Inc, Idenix Pharmaceuticals, Inc, Johnson & Johnson, Merck & Co, Inc, and Monogram Biosciences, Inc; received research grants or contracts from Merck & Co, Inc; and holds stock options in CHIMERx and Idenix Pharmaceuticals, Inc.

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Posttest Questions

Check the box next to the single best answer to each of the questions below. To earn CME credit, you must receive a passing score of 80% or more correct.

1. Which statement about alcohol consumption and HIV-infected patients is **correct?**

- ❑ **A.** Hazardous alcohol use is associated with increased likelihood of being on antiretroviral therapy
- ❑ **B.** The rate of hazardous alcohol use in HIV-infected patients is twice that in the general population
- ❑ **C.** Patients presenting for care who screen positive for alcohol use should be screened annually thereafter

2. Which criterion is included in the definition of "at-risk" alcohol use?

- ❑ **A.** More than 7 standard drinks per week in women of any age or men older than 65 years
- ❑ **B.** More than 7 standard drinks per week in women of any age or men of any age
- ❑ **C.** More than 5 drinks per occasion in women of any age or men older than 65 years

3. A female patient regularly consumes 4 drinks every Friday night, but has no other alcohol use during the week and her drinking has no impact on work or interpersonal relationships. How would you classify her drinking pattern?

- ❑ **A.** A moderate drinking pattern that is safe to maintain
- ❑ **B.** An "at-risk" drinking pattern
- ❑ **C.** Alcohol dependence
- ❑ **D.** Not enough information to diagnose

4. Which statement about oral naltrexone treatment is correct?

- ❑ **A.** The starting dose is 10 mg/d and titrates upward to 50 mg/d, with treatment continued for a maximum of 2 months
- ❑ **B.** Patients must be opioid-free for 7 to 10 days and alcohol-free for 5 to 7 days before treatment initiation
- ❑ **C.** Oral naltrexone is safe to use during pregnancy

5. **Chronic** alcohol dependence is differentiated from alcohol dependence (ie, severe alcohol use) by:

- ❑ **A.** The presence of withdrawal symptoms (tremors, sweating, insomnia, etc) on discontinuation of alcohol use
- ❑ **B.** Unsuccessful efforts to cut down on alcohol use
- ❑ **C.** The presence of more alcohol dependence factors than are found in severe alcohol use
- ❑ **D.** Failure to complete an alcohol treatment program

This CME activity is offered from **December 1, 2011**, to **December 1, 2012**. Participants who receive a passing score on the posttest and submit the registration and evaluation forms are eligible to receive credit. Physicians (MDs, DOs, and international equivalents) may receive CME credit for completing this activity. Nonphysician health care practitioners will receive a certificate of attendance.

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Please complete the following evaluation form for the *Topics in Antiviral Medicine* article for which you are currently claiming CME credit:

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Please list 3 specific measurable changes you will make in your practice based on the information presented in the article:

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