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Alcohol and Health: Current Evidence

MAY - JUNE 2006

Alcohol and Health Outcomes

Can Drinking During Pregnancy Raise the Risk of Childhood Leukemia?

Results from the few studies that have examined the association between alcohol use during pregnancy and childhood leukemia are conflicting. Researchers in France aimed to clarify this association through a case-control study of children hospitalized with either newly diagnosed acute leukemia (n=280) or for a disease other than cancer or a birth defect (n=288). Mothers of the studied children completed interviews that covered alcohol use during pregnancy and a range of other topics (e.g., medical history, family history of cancer).

- Any maternal alcohol use, versus abstinence, during pregnancy was significantly associated with childhood acute lymphoid leukemia (ALL) and acute nonlymphoid leukemia (ANLL) in analyses adjusted for potential confounders (odds ratios 2.0 and 2.6, respectively). Results were similar for each alcoholic beverage type.
- Maternal smoking during pregnancy was not significantly associated with child-

hood leukemia. Drinking 4–8 cups of coffee per day, however, appeared to significantly increase the odds of ALL (odds ratio 2.4), but not ANLL.

Comments: Although these findings need to be confirmed in other studies, they have important treatment and research implications. First, clinicians can now add the potential risk of childhood leukemia to the long list of reasons they tell their pregnant patients not to drink. Second, because alcohol is a carcinogen and was linked with childhood ALL and ANLL in this study, future research should explore how alcohol use may lead to these rare cancers.

Richard Saitz, MD, MPH
Rosanne Guerriero, MPH

Reference: Menegaux F, et al. Maternal coffee and alcohol consumption during pregnancy, parental smoking and risk of childhood acute leukemia. *Cancer Detect and Prev.* 2005;29(6):487–493.

Remission and Relapse in the General Population

Most studies investigating the course of alcohol use disorders involve clinical samples. In this study, researchers from the Netherlands studied the course in the general population. Using data from a cohort study on mental health, researchers analyzed the prevalence, remission, and relapse rates of alcohol use disorders over 3 years in 4214 people. Diagnoses were classified according to the Diagnostic and Statistical Manual IV (DSM-IV), International Classification of Diseases 10 (ICD-10), and the craving withdrawal model (CWM).*

- Rates of remission (full or partial) from baseline to the 3-year follow-up were high: 79%–92% for alcohol abuse/harmful use** and 69%–74% for alcohol depend-

ence.

- Rates of relapse were low: 0%–14% of subjects with remitted alcohol abuse/harmful use or dependence at year 1 relapsed by year 3.
- About 1%–5% of subjects with alcohol abuse/harmful use at baseline developed dependence by year 3.
- Results did not significantly differ across the diagnostic classification systems.

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*An alternative classification that tries to address some potential disadvantages of the DSM-IV

**Harmful use is a classification in the ICD-10; it is similar to a DSM-IV diagnosis of alcohol abuse but does not include having alcohol-related social consequences as a criteria.

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Remission and Relapse in the General Population (continued from page 1)

Comments: In a general population sample, alcohol use disorders have a favorable prognosis and may lack the chronic relapsing nature seen in treatment samples. These findings suggest that a substantial population of patients with alcohol use disorders could respond to brief or minimal interventions in primary care or other non-

specialty settings.

Peter Friedmann, MD, MPH

Reference: de Bruijn C, et al. The three year course of alcohol use disorders in the general population: DSM-IV, ICD-10 and the Craving Withdrawal Model. *Addiction*. 2006;101(3):385–392.

Smoking Increases Alcohol Use

Drinking and smoking commonly co-occur. Little is known, however, about how nicotine use influences alcohol consumption. In this study, researchers assessed the desire for alcohol in 15 male occasional smokers* who smoked 4 nicotine-containing cigarettes over 2 hours on 1 day and 4 cigarettes without nicotine (placebo) over 2 hours on another day. During the smoking sessions, subjects could earn drinks of water and alcoholic beverages of their choice by successfully completing a computerized task.

Subjects were more likely to choose alcohol than water, regardless of the type of cigarette smoked. They drank significantly more alcohol when they smoked the nicotine-containing cigarettes than when they smoked the placebo cigarettes. Water consumption did not significantly differ during the 2 smoking sessions.

Comments: These data suggest that smoking cigarettes during drinking sessions may lead to more drinking, which in turn increases the risk of alcohol-related problems. Although the effects of cigarette smoking in people with alcohol dependence need elucidating, healthcare providers should consider multi-behavioral interventions for all of their patients who smoke.

Joseph Conigliaro, MD, MPH

*Smoked cigarettes an average of 2.7 days per week and drank alcohol on 2.3 days per week; all had smoked at least 4 cigarettes during a drinking session at least once in the past year

Reference: Barrett SP, et al. Nicotine increases alcohol self-administration in non-dependent male smokers. *Drug Alcohol Depend*. 2006;81(2):197–204.

The Impact of Substance Dependence on the Course of Depression

Comorbid depression and substance dependence is very common. The impact of current alcohol and drug dependence on the course of depression, however, has received limited attention. Using data from 8098 non-institutionalized participants (aged 15–54 years) of a national study on psychiatric disorders, researchers assessed how substance dependence (SD) influences the prevalence of major depression.

Of 319 subjects with both lifetime substance dependence and major depression, half had remitted SD. Past-year depression was significantly more common in subjects with current SD than in subjects with remitted SD (odds ratio 2.9) and in subjects with remitted SD than in the total study sample (odds ratio 6.7).

Comments: Some patients use substances to self-medicate their depressive symptoms. But just as depression adversely affects the course of alcoholism and drug dependence, active substance dependence appears to worsen depression outcomes. Such negative consequences strongly suggest that healthcare providers should assess their patients with depression for comorbid substance dependence and help those affected to stop using alcohol and/or drugs.

Jeffrey Samet, MD, MA, MPH

Reference: Agosti V, et al. The effects of alcohol and drug dependence on the course of depression. *Am J Addict*. 2006;15(1):71–75.

Moderate Drinking May Lower the Risk of Ischemic Stroke

While moderate drinking appears to protect against coronary disease, its effects on stroke are less clear. To examine whether alcohol use can reduce the risk of stroke and other vascular events, researchers assessed 3176 subjects from Manhattan with no history of stroke (mean age 69 years, 63% female, 52% Hispanic, and 25% non-Hispanic black). During a median of 6 years of follow-up, 190 subjects had a stroke.

- In analyses adjusted for potential confounders (e.g., diabetes, smoking), moderate drinkers had a lower risk of ischemic stroke (odds ratio [OR] 0.7) and of either ischemic stroke, myocardial infarction, or vascular death (OR 0.7) than did subjects who rarely drank.*
- This reduced risk was significant for the cryptogenic subtype (OR 0.3), borderline significant for the lacunar and cardioembolic subtypes (ORs 0.4 and 0.5, respectively), and not significant for the atherosclerotic subtype (OR 0.8).
- In analyses stratified by age, sex, and race, the reduced risk of ischemic stroke was significant only among subjects aged 70 or older and borderline significant for women, Hispanics,

and nonsmokers.

- Heavier drinking* did not significantly affect risk.

Comments: While not large, this population-based prospective study among whites, blacks, and Hispanics showed an approximately 30% lower risk of ischemic stroke in moderate drinkers. This finding is consistent with results from most other recent studies. Small numbers likely accounted for the varied results across stroke subtypes, the limited findings for subjects with hemorrhagic stroke, and the lack of significance associated with heavier drinking.

R. Curtis Ellison, MD

*Rare: <1 drink per month in the past year; moderate: ≥1 drink in the past month to ≤2 per day; heavier: >2 drinks per day

Reference: Elkind MSV, et al. Moderate alcohol consumption reduces risk of ischemic stroke: the Northern Manhattan Study. *Stroke*. 2006;37(1):13–19.

Assessments and Interventions

Brief Interventions Can Prevent DUI Arrests

Strategies that reduce the high recidivism of driving under the influence (DUI) are critical to preventing injuries from motor vehicle crashes, a leading cause of alcohol-attributable death. To determine whether an alcohol brief intervention can prevent DUI arrests, researchers randomized 126 patients hospitalized for an injury from a motor vehicle crash to receive either a 30-minute motivational counseling session or standard care. Subjects were aged 16–80 years and at admission had a blood alcohol concentration of ≥80 mg/dL or an elevated score on the Alcohol Use Disorders Identification Test (AUDIT). DUI arrests during the 3 years after discharge were measured by matching subject data to state traffic-safety data.

- During follow-up, 7 (11%) of subjects in the brief intervention group and 14 (22%) in the standard care group were arrested for DUI. This difference was not statistically significant.
- However, DUI arrests were significantly less common among intervention subjects (odds ratio 0.3) in analyses adjusted for

age, sex, blood alcohol concentration, AUDIT score, and prior DUI arrests.

Comments: These results indicate that brief intervention for unhealthy alcohol use may be useful for preventing DUI arrests among people injured in a motor vehicle crash. The small number of outcomes prevented the unadjusted analysis from reaching significance, but a strong effect was found in adjusted analyses. The study was limited by the absence of out-of-state DUI arrest data and nonreporting of other alcohol outcomes, such as alcohol consumption and consequences.

Kevin L. Kraemer, MD, MSc

Reference: Schermer CR, et al. Trauma center brief interventions for alcohol disorders decrease subsequent driving under the influence arrests. *J Trauma*. 2006;60(1):29–34.

Screening for Unhealthy Alcohol Use: Questionnaire Is Best

Some clinicians have questioned whether blood tests are better than self-report questionnaires for alcohol screening. To compare these screening methods, researchers in Wales first assessed 1794 men with the Alcohol Use Disorders Identification Test (AUDIT), a 10-item alcohol screening questionnaire that, for this

study, was embedded in a general lifestyle questionnaire. They then conducted blood tests in 112 men who screened positive on the AUDIT (score of ≥8) and 82 who screened negative.

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Screening for Unhealthy Alcohol Use: Questionnaire Is Best (continued from page 3)

- For unhealthy alcohol use, sensitivity and specificity* were highest for the AUDIT.

	Sensitivity	Specificity
AUDIT	69%	98%
Carbohydrate-deficient transferrin (CDT)	47%	71%
Gamma-glutamyltransferase (GGT)	37%	72%
Mean corpuscular volume (MCV)	32%	71%
Aspartate aminotransferase (AST)	20%	80%

- For alcohol dependence, sensitivity and specificity were also highest for the AUDIT (84% and 83%, respectively).

- The cost of identifying a patient with unhealthy alcohol use was lowest for the AUDIT (\$12.48 versus \$72.59 for GGT, \$130.92 for MCV, \$132.74 for AST, and \$291.89 for CDT).**

Comments: The results of this study confirm that a validated questionnaire is more sensitive, more specific, and cheaper than blood tests, and therefore is the best way to screen for unhealthy alcohol use.

Richard Saitz, MD, MPH

*Sensitivity is the proportion of patients with the disorder that test positive; specificity is the proportion of patients without the disorder who test negative.

**Costs were converted from British pounds to US dollars in early March 2006.

Reference: Coulton S, et al. Opportunistic screening for alcohol use disorders in primary care: a comparative study. *BMJ*. 2006;332(7540):511–517.

Gabapentin Versus Phenobarbital for Alcohol Withdrawal

Animal studies and several small, uncontrolled clinical trials show that the anticonvulsant gabapentin may reduce alcohol withdrawal symptoms. In this controlled study, researchers assessed gabapentin's efficacy among inpatients on a detoxification unit who had moderate or more severe alcohol withdrawal. Twenty-seven subjects were randomized to receive either oral gabapentin (2400 mg on day 1 tapered to 600 mg on day 4) or oral phenobarbital (240 mg on day 1 tapered to 60 mg on day 4). The severity of alcohol withdrawal was measured by the Clinical Institute Withdrawal Assessment for Alcohol-revised (CIWA-Ar) and the Alcohol Craving scale.

- Mean CIWA-Ar and Alcohol Craving scores decreased at similar rates in both treatment groups.
- Although higher in the gabapentin group, the proportion of subjects needing "rescue" phenobarbital for breakthrough signs and symptoms of withdrawal did not significantly differ between treatment groups (57% of the gabapentin group; 38% of the phenobarbital group).

- The proportion who failed to complete the trial also did not significantly differ between the groups (29% of the gabapentin group; 38% of the phenobarbital group).
- No subject had an alcohol withdrawal seizure or alcohol withdrawal delirium.

Comments: This small study shows that gabapentin may be as effective as phenobarbital for reducing the signs and symptoms of alcohol withdrawal. Gabapentin, however, has been neither shown to prevent alcohol withdrawal seizures and delirium nor compared directly with benzodiazepines. Until these concerns are researched, benzodiazepines should remain the drug class of choice for alcohol withdrawal.

Kevin L. Kraemer, MD, MSc

Reference: Mariani JJ, et al. A randomized, open-label, controlled trial of gabapentin and phenobarbital in the treatment of alcohol withdrawal. *Am J Addict*. 2006;15(1):76–84.

Baclofen May Ameliorate Alcohol Withdrawal Symptoms

Despite their efficacy for treating alcohol withdrawal, benzodiazepines have disadvantages: central nervous system impairment, abuse potential, and overdose risk. As a result, researchers are seeking alternatives with fewer risks. In a study from Italy, researchers randomized 37 patients with alcohol withdrawal but no major medical or psychiatric comorbidity to receive 10 consecutive days of oral baclofen (10 mg 3 times per day) or oral diazepam (0.5–0.75 mg/kg per day for 6 days and tapered doses from

day 7 to day 10). Alcohol withdrawal symptoms were measured using the Clinical Institute Withdrawal Assessment for Alcohol-revised (CIWA-Ar) scale.

- Both treatments significantly reduced CIWA-Ar scores.
- Daily scores after baseline (the first day) did not significantly differ between the 2 treatment groups.

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Baclofen May Ameliorate Alcohol Withdrawal Symptoms (continued from page 4)

- No side effects were reported by patients in either group.

Comments: Like many other medications, including benzodiazepines, baclofen can reduce some alcohol withdrawal symptoms. However, whether baclofen can decrease seizures and delirium tremens—severe consequences of withdrawal that can be prevented by benzodiazepines—remains unknown after this small study. Further, the disadvantages of benzodiazepines may

be less relevant for the short-term management of withdrawal in adults with alcohol dependence. Benzodiazepines remain the gold standard for managing alcohol withdrawal.

Richard Saitz, MD, MPH

Reference: Addolorato G, et al. Baclofen in the treatment of alcohol withdrawal syndrome: a comparative study vs. diazepam. *Am J Med.* 2006;119(3): 276.e13-276.e18.

Natural Remission and Relapse

Much is known about the rate of relapse after formal alcohol treatment but not after “spontaneous” or “natural” remission. Researchers studied remission and relapse in 461 individuals with an alcohol use disorder who had not received help before study entry. Subjects were interviewed at baseline and then 1, 3, 8, and 16 years later. At each follow-up, they were asked about their alcohol use and whether they had obtained professional treatment or participated in Alcoholics Anonymous at any time since the last follow-up.

- At the 3-year follow-up, remission occurred in 62% of subjects who had received help and in 43% of subjects who had not received help ($P < 0.01$).
- Among these remitted subjects, relapse by year 16 occurred in 43% of those who had received help and in 61%

of those who had not received help ($P < 0.05$).

Comments: Like previous studies, this study found that receiving help improves the chances of short-term remission and decreases the risk of relapse. Therefore, clinicians should emphasize the importance of early help seeking to their patients with alcohol use disorders and should offer ongoing support to help their patients in remission remain remitted.

Peter Friedmann, MD, MPH

Reference: Moos RH, et al. Rates and predictors of relapse after natural and treated remission from alcohol use disorders. *Addiction.* 2006;101(2):212–222.

Special Populations

Heavy Drinking and the Risk of Macular Degeneration in Latinos

Data on the relationship between alcohol and age-related macular degeneration (AMD) are conflicting. Further, few studies have assessed this relationship among Latinos. In a population-based, cross-sectional study, researchers explored whether alcohol intake and other behaviors affected the risk of developing early or advanced AMD among Latinos in California. Of 5875 subjects, 551 had early AMD and 25 had advanced AMD. Analyses were adjusted for age.

- Subjects who drank >5 drinks on any day in the past year were significantly more likely than abstainers to have any advanced AMD (odds ratio [OR] 8.7) or retinal pigment epithelium depigmentation (OR 1.8), a marker for early AMD. These associations remained significant in analyses adjusted for sex and smoking.
- Beer drinkers were significantly more likely than non-beer drinkers to have any advanced AMD (OR 2.9). This finding became nonsignificant in analyses adjusted for sex and smoking.

- Wine drinkers, however, were significantly less likely than non-wine drinkers to have increased retinal pigment (OR 0.7), a marker for early AMD.

Comments: This rather large study of Latinos with age-related macular degeneration suffers from very few cases of advanced AMD and inadequate adjustment for confounding. The weak positive association between advanced AMD and beer consumption and the weak inverse association between early AMD and wine consumption have been reported in some, but not all, previous studies. Further research is required to clarify whether alcohol use affects age-related macular degeneration.

R. Curtis Ellison, MD

Reference: Fraser-Bell S, et al. Smoking, alcohol intake, estrogen use, and age-related macular degeneration in Latinos: the Los Angeles Latino Eye Study. *Am J Ophthalmol.* 2006;141(1):79–87.

Are Alcohol Diagnoses Stable From Late Adolescence to Early Adulthood?

The appropriateness of diagnosing alcohol abuse or dependence among adolescents and young adults has been debated because such diagnoses are potentially unstable in these age groups. This study examined both the stability of alcohol diagnoses from ages 18 to 25 and risk factors associated with these diagnoses in a birth cohort of 1265 New Zealanders. Subjects had been assessed annually from birth until age 16 and then at ages 18, 21, and 25 (n=1003 at the last follow-up).

- The prevalence of alcohol abuse was 14% at age 18, 18% at 21, and 10% at 25. The prevalence of alcohol dependence was 6%, 4%, and 4%, respectively.
- Remission was very common: 57%–75% of subjects with alcohol abuse and 50%–54% with alcohol dependence at age 18 had no diagnosis at ages 21 and/or 25.
- An initial alcohol diagnosis was a significant and strong predictor of a later alcohol diagnosis (ORs 3.4–27.6). This remained true in analyses

adjusted for a variety of risk factors (e.g., cannabis use, mental illness, family history of alcohol problems).

Comments: This study illustrates that as adolescents with alcohol diagnoses transition into adulthood, most (particularly those with alcohol abuse) will experience remission. A substantial number, however, will continue to meet diagnostic criteria. Because alcohol diagnoses can be unstable, health-care providers should closely monitor their adolescent and young adult patients and adjust treatment accordingly as these patients grow older.
Joseph Conigliaro, MD, MPH

Reference: Wells JE, et al. Stability and instability in alcohol diagnosis from ages 18 to 21 and ages 21 to 25 years. *Drug Alcohol Depend.* 2006;81(2):157–165.

Journal Alert

National Institute Reports on Teen and Young-Adult Drinking

A recent issue of *Alcohol Research and Health*—a journal published by the National Institute on Alcohol Abuse and Alcoholism—explored the problem of alcohol use by adolescents and young adults. In this issue, experts reviewed the following:

- Prevalence of teen and young-adult drinking
- Patterns of alcohol use as teens transition to adulthood
- International differences in drinking behaviors
- Reasons teens and young adults drink
- Negative consequences associated with drinking, including impaired

brain development and function, and violence

- Prevention and intervention efforts in communities, colleges, and the military

Comments: These expert reviews underscore the gravity of teen and young-adult drinking and remind us that alcohol use by our young patients deserves our immediate attention.

Richard Saitz, MD, MPH
Rosanne Guerriero, MPH

Reference: *Alcohol Research and Health. Focus on Young Adult Drinking.* 2004/2005;28(4).

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Many others periodically reviewed (see www.alcoholandhealth.org)

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