

# Library Watch

substance use  
medical aspects

www.projectcork.org

spring 2009

## **Alcohol consumption and heart failure: A systematic review.**

Djouisse L; Gaziano JM. *Current Atherosclerosis Reports* 10(2): 117-120, 2008. (45 refs.)

Heart failure (HF) remains a major public health issue. It is estimated that about 500,000 Americans per year are diagnosed with HF. Despite advanced medical and surgical treatments for HF, mortality after the onset of HF is still high, thereby underscoring the importance of primary prevention. Among modifiable lifestyle factors, alcohol consumption appears to play a role in the development of HF. Although excessive drinking has been known to lead to alcoholic cardiomyopathy and light-to-moderate drinking may confer some cardiovascular benefits, recent studies suggest it is not only the quantity, but also drinking patterns and genetic factors, that may influence the relation between alcohol consumption and cardiovascular disease. This article reviews current evidence on the association between alcohol consumption and HF. Copyright 2008, Current Medicine Group.

## **An overview of genetic influences in alcoholism. (review).**

Schuckit MA. *Journal of Substance Abuse Treatment* 36(1): s5-s14, 2009. (110 refs.)

This review summarizes recent findings from human research regarding genetic influences in alcohol abuse and dependence. Genes explain about 50% of the vulnerabilities leading to heavy drinking and associated problems. Most genetic influences appear to impact at least four prominent intermediate characteristics (phenotypes) that interact with environmental events to produce the alcoholism risk: a flushing response to alcohol; a low level of response to alcohol; personality characteristics that include impulsivity, sensation seeking, and neuronal and behavioral disinhibition; and through psychiatric symptoms. Polymorphisms potentially related to each phenotype have been identified, and studies were conducted to evaluate their characteristics in the context of environmental and psychosocial forces. A search is underway to identify genes that contribute to these phenotypes; the ultimate goals of which are better prediction of how to best prevent heavy drinking and problems, identifying individuals who may

respond best to existing treatments, and development of new therapeutic approaches based on the biological underpinnings of alcoholism. Copyright 2009, Elsevier Science.

## **Attenuation of the stimulant response to ethanol is associated with enhanced ataxia for a GABA(A), but not a GABA(B), receptor agonist.**

Holstein SE; Dobbs L; Phillips TJ. *Alcoholism: Clinical and Experimental Research* 33(1): 108-120, 2009. (80 refs.)

The gamma-aminobutyric acid (GABA) system is implicated in the neurobiological actions of ethanol, and pharmacological agents that increase the activity of this system have been proposed as potential treatments for alcohol use disorders. As ethanol has its own GABA mimetic properties, it is critical to determine the mechanism by which GABAergic drugs may reduce the response to ethanol (i.e., via an inhibition or an accentuation of the neurobiological effects of ethanol). In this study, we examined the ability of 3 different types of GABAergic compounds, the GABA reuptake inhibitor NO-711, the GABA(A) receptor agonist muscimol, and the GABA(B) receptor agonist baclofen, to attenuate the locomotor stimulant response to ethanol in FAST mice, which were selectively bred for extreme sensitivity to ethanol-induced locomotor stimulation. To determine whether these compounds produced a specific reduction in stimulation, their effects on ethanol-induced motor incoordination were also examined. NO-711, muscimol, and baclofen were all found to potently attenuate the locomotor stimulant response to ethanol in FAST mice. However, both NO-711 and muscimol markedly increased ethanol-induced ataxia, whereas baclofen did not accentuate this response. These results suggest that pharmacological agents that increase extracellular concentrations of GABA and GABA(A) receptor activity may attenuate the stimulant effects of ethanol by accentuating its intoxicating and sedative properties. However, selective activation of the GABA(B) receptor appears to produce a specific attenuation of ethanol-induced stimulation, suggesting that GABA(B) receptor agonists may hold greater promise as potential

pharmacotherapies for alcohol use disorders. Copyright 2009, Research Society on Alcoholism.

**Communication networks in the brain neurons, receptors, neurotransmitters, and alcohol. (review).**

Lovinger DM. *Alcohol Research & Health* 31(3): 196-214, 2008. (141 refs.)

Nerve cells (i.e., neurons) communicate via a combination of electrical and chemical signals. Within the neuron, electrical signals driven by charged particles allow rapid conduction from one end of the cell to the other. Communication between neurons occurs at tiny gaps called synapses, where specialized parts of the two cells (i.e., the presynaptic and postsynaptic neurons) come within nanometers of one another to allow for chemical transmission. The presynaptic neuron releases a chemical (i.e., a neurotransmitter) that is received by the postsynaptic neuron's specialized proteins called neurotransmitter receptors. The neurotransmitter molecules bind to the receptor proteins and alter postsynaptic neuronal function. Two types of neurotransmitter receptors exist—ligand-gated ion channels, which permit rapid ion flow directly across the outer cell membrane, and G-protein-coupled receptors, which set into motion chemical signaling events within the cell. Hundreds of molecules are known to act as neurotransmitters in the brain. Neuronal development and function also are affected by peptides known as neurotrophins and by steroid hormones. This article reviews the chemical nature, neuronal actions, receptor subtypes, and therapeutic roles of several transmitters, neurotrophins, and hormones. It focuses on neurotransmitters with important roles in acute and chronic alcohol effects on the brain, such as those that contribute to intoxication, tolerance, dependence, and neurotoxicity, as well as maintained alcohol drinking and addiction. Public Domain.

**Crack-cocaine use accelerates HIV disease progression in a cohort of HIV-positive drug users.**

Baum MK; Rafie C; Lai S; Sales S; Page B; Campa A. *Journal of Acquired Immune Deficiency Syndromes* 50(1): 93-99, 2009. (32 refs.)

Background: HIV infection is prevalent among substance abusers. The effects of specific illicit drugs on HIV disease progression have not been established. We evaluated the relationship between substances of abuse and HIV disease progression in a cohort of HIV-1-positive active drug users. Methods: A prospective, 30-month, longitudinal Study was conducted on 222 HIV-1 seropositive drug users in Miami, FL. History of illicit drug, alcohol, and medication use, CD4(+) cell count, and viral load were performed every 6

months. Results: Crack-cocaine users were 2.14 times [95% confidence interval (CI): 1.08 to 4.25,  $P = 0.029$ ] more likely to present a decline of CD4 to  $\leq 200$  cells/mL, independent of antiretroviral use. Viral load over 30 months was significantly higher in crack users ( $P = 0.315$ ,  $P = 0.037$ ) independent of highly active antiretroviral therapy (HAART) over time. The only multidrug combination that significantly increased the risk of disease progression was crack cocaine with marijuana (hazard ratio = 2.42; 95% CI: 1.042 to 5.617,  $P = 0.04$ ). Of those on HAART, a significantly lower proportion of crack-cocaine users versus nonusers had controlled viral load ( $P < 0.001$ ), suggesting lower medication adherence, whereas crack-cocaine users not on HAART showed a greater risk for HIV disease progression than nonusers (hazard ratio = 3.946; 95% CI: 1.049 to 14.85,  $P = 0.042$ ). Conclusions: Crack-cocaine use facilitates HIV disease progression by reducing adherence in those on HAART and by accelerating HIV disease progression independently of HAART. Copyright 2009, Lippincott, Williams & Wilkins.

**Doctors' knowledge of the appropriate use and route of administration of antidotes in the management of recreational drug toxicity.**

Lidder S; Ovaska H; Archer JRH; Greene SL; Jones AL; Dargan PI; Wood DM. *Emergency Medicine Journal* 25(12): 820-823, 2008. (22 refs.)

Background: Specific antidotes (eg, naloxone, flumazenil, cyproheptadine and benzodiazepines) are available for the management of certain recreational drug-induced toxicities. Some controversies surround the use of some of these antidotes, especially flumazenil in benzodiazepine toxicity. There are no previously published data on doctors' knowledge of the use of these specific antidotes. Methods: A questionnaire survey was designed to determine internal/emergency medicine doctors' knowledge of the appropriate use of antidotes in the management of clinical scenarios of acutely poisoned patients. For nine simulated clinical scenarios of acute toxicity from recreational drugs (benzodiazepines, cocaine, N-methyl-L-(3, 4-methylene-dioxyphenyl)-2-aminopropane (MDMA)-induced serotonin toxicity and opioids), they were asked to indicate whether the suggested antidote and route of administration were correct. Results: 42 physicians of all grades completed the questionnaire. The mean correct score was 5.4 (SD 1.1) (median 6, interquartile range 5-7). The percentages correct for the various clinical scenarios were 68.3% for opioid toxicity, 81% for benzodiazepine toxicity, 28.6% for MDMA-induced serotonin toxicity and 70.2% for cocaine toxicity.

Doctors were more likely to record an answer of "unsure" for the use of cyproheptadine in ST serotonin toxicity (28.6%) compared with the use of the other antidotes (1.4%;  $p < 0.001$ ). Conclusion: Knowledge of the appropriate use of antidotes in recreational drug toxicity is not consistent, with poorer knowledge on the use of newer antidotes such as cyproheptadine in serotonin toxicity. Education is required both to increase overall knowledge on the use of specific antidotes in the management of recreational drug-induced toxicity, as well as focusing on newer antidotes such as cyproheptadine. Copyright 2008, BMJ Publishing Group.

**Influence of energy drinks and alcohol on post-exercise heart rate recovery and heart rate variability.**

Wiklund U; Karlsson M; Ostrom M; Messner T. *Clinical Physiology and Functional Imaging* 29(1): 74-80, 2009. (28 refs.)

Media have anecdotally reported that drinking energy drinks in combination with alcohol and exercise could cause sudden cardiac death. This study investigated changes in the electrocardiogram (ECG) and heart rate variability after intake of an energy drink, taken in combination with alcohol and exercise. Ten healthy volunteers (five men and five women aged 19-30) performed maximal bicycle ergometer exercise for 30 min after: (i) intake of 0.75 l of an energy drink mixed with alcohol; (ii) intake of energy drink; and, (iii) no intake of any drink. ECG was continuously recorded for analysis of heart rate variability and heart rate recovery. No subject developed any clinically significant arrhythmias. Post-exercise recovery in heart rate and heart rate variability was slower after the subjects consumed energy drink and alcohol before exercise, than after exercise alone. The healthy subjects developed blunted cardiac autonomic modulation after exercising when they had consumed energy drinks mixed with alcohol. Although they did not develop any significant arrhythmia, individuals predisposed to arrhythmia by congenital or other rhythm disorders could have an increased risk for malignant cardiac arrhythmia in similar situations. Copyright 2009, Blackwell Publishing.

**Physical pain, common psychiatric and substance use disorders, and the non-medical use of prescription analgesics in the United States.**

Novak SP; Herman-Stahl M; Flannery B; Zimmerman M. *Drug and Alcohol Dependence* 100(1-2): 63-70, 2009. (45 refs.)

This study investigated the link between physical pain and non-medical prescription analgesic use (NMPAU),

as well as the degree to which this association may vary by the presence of psychiatric and substance use disorders. Data were from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative, in-person probability sample of adults ( $n = 43,093$ ) aged 18 or older in the United States (2001-2002). Face-to-face interviews were used to gather information on past-year levels of physical pain (i.e., low, medium, high), in addition to DSM-IV classifications for mood, anxiety, substance use problems (i.e., abuse and/or dependence), and personality disorders. Within the analytic sample of those with valid data ( $n = 42,734$ ), the past-year rate of NMPAU was 1.8%, of which 20% met the DSM-IV criteria for abuse/dependence. Among past-year NMPAUs, 53% was incidental (e.g., less than monthly), but daily use was substantial (13% of NMPAUs). Accounting for our target confounding factors, pain was positively associated ( $p < 0.05$ ) with an increased probability of non-disordered (i.e., no abuse and/or dependence) and disordered (i.e., abuse and/or dependence) NMPAU in the past year. Within each level of pain, the odds of past-year non-disordered and disordered NMPAU were significantly higher ( $p < 0.05$ ) for those with disordered alcohol use compared with non-disordered users. This pattern was similar for illicit drugs, although marginally significant ( $p = 0.060$ ) and specific to disordered NMPAU. In contrast, psychiatric disorders increased the probability of both types of NMPAU, but these associations did not differ by levels of pain. These findings suggest that pain is an independent risk factor for non-disordered and disordered NMPAU, yet its effects are substantially modified by patterns of substance use. Copyright 2009, Elsevier Science.

**Prenatal exposure to methamphetamine presenting as neonatal cholestasis.**

Dahshan A. *Journal of Clinical Gastroenterology* 43(1): 88-90, 2009. (22 refs.)

Introduction: Methamphetamine has been recognized as a common cause of acute toxic hepatitis in adults with clinical and histologic features indistinguishable from acute viral hepatitis. Clinical presentation of methamphetamine hepatotoxicity ranges from mild acute hepatitis with prompt recovery to fulminant hepatic failure. The pathophysiology of this hepatotoxicity is not well elucidated. Prenatal exposure to methamphetamine has been linked to intrauterine growth retardation and variety of withdrawal symptoms. Neonatal cholestasis is rare but serious problem that indicates hepatobiliary dysfunction and has several categories of etiologies. These include infectious, metabolic, endocrine, toxic, structural,

familial, and autoimmune disorders. Cholestatic hepatitis is a recognized complication of exposure to some drugs including carbamazepine and trimethoprim-sulfamethoxazole. Case: A 35-week preterm, appropriate for gestational age, white girl was born to a 39-year-old mother who had no prenatal care. The mother's urine drug screen revealed methamphetamine. The baby passed pale meconium and her subsequent stools were hypopigmented. A detailed work up was done and was unremarkable except for hepatobiliary scintigraphy, with no activity noted in the small bowel on delayed imaging. An operative cholangiogram and liver biopsy were performed. The cholangiogram revealed patent bile ducts. Liver biopsy was consistent with acute viral or toxic hepatitis. Gradual drop of bilirubin was noted. With negative extensive work up for other etiologies, known hepatotoxicity of methamphetamine, early onset of cholestasis that improved without specific therapy it is strongly suspected that prenatal exposure to methamphetamine is the most likely culprit in this patient. Discussion: This is the first recorded case of neonatal cholestasis related to prenatal exposure to methamphetamine. Methamphetamine is considered the fastest-growing illicit drug in United States. Hence, prenatal exposure to methamphetamine is expected to rise. Healthcare providers should become aware of the possibility of methamphetamine effect on the fetal liver. Raising awareness of the expectant mothers through the healthcare profession may reduce the risk of this condition. Copyright 2009, Lippincott, Williams & Wilkins.

#### **Increased stroke risk is related to a binge drinking habit.**

Sundell L; Salomaa V; Vartiainen E; Poikolainen K; Laatikainen T. *Stroke* 39(12): 3179-3184, 2008. (42 refs.)

Background and Purpose-Heavy alcohol consumption increases the risk for all strokes, whereas moderate regular alcohol consumption is associated with a lower risk for ischemic stroke. The purpose of this study was to evaluate the effect of different drinking patterns on stroke risk, independent of average alcohol intake. Methods-A prospective cohort study of 15 965 Finnish men and women age 25 to 64 years who participated in a national risk factor survey and had no history of stroke at baseline were followed up for a 10-year period. The first stroke event during follow-up served as the outcome of interest (N=249 strokes). A binge

drinking pattern was defined as consuming 6 or more drinks of the same alcoholic beverage in men or 4 or more drinks in women in 1 session. Cox proportional-hazards models were adjusted for average alcohol consumption, age, sex, hypertension, smoking, diabetes, body mass index, educational status, study area, study year, and history of myocardial infarction. Results-Binge drinking was an independent risk factor for total and ischemic strokes. Compared with non-binge drinkers, the hazard ratio for total strokes among binge drinkers was 1.85 (95% CI, 1.35 to 2.54) after adjusting for average alcohol consumption, age, and sex; the association was diluted after adjustment for other risk factors. Compared with non-binge drinkers, the risk for ischemic stroke was 1.99 (95% CI, 1.39 to 2.87) among binge drinkers; the association remained statistically significant after adjustment for potential confounders. Conclusions-This study found that a pattern of binge drinking is an independent risk factor for all strokes and ischemic stroke. Copyright 2008, Lippincott, Williams & Wilkins.

#### **Sudden bilateral sensorineural hearing loss following speedballing.**

Fowler CG; King JL. *Journal of the American Academy of Audiology* 19(6): 461-464, 2008. (18 refs.) Background: Hearing loss is an infrequently-reported consequence of recreational drug abuse. Although there are sporadic reports of hearing loss from heroin and cocaine ingested separately, there are no reports of hearing loss resulting from the combination of both drugs ingested simultaneously in the form of speedballing. Purpose: The purpose of this report is to document a case of bilateral sensorineural hearing loss associated with an episode of speedballing. Research Design: Case Report Data Collection and Analysis: The subject of this report was a 40-year-old man with a 20-year history of substance abuse. Data collected included a case history, pure tone audiometry, tympanometry and acoustic reflexes, and transient evoked otoacoustic emissions. Results: The audiologic evaluation indicated a mild to moderate, relatively flat, bilateral sensorineural hearing loss that was worse in the right ear. Conclusions: A bilateral sensorineural hearing loss involving both cochlear and neural pathology may be a rare complication of cocaine, heroin, or the combination of the two drugs. Copyright 2008, American Academy of Audiology.