

# Library Watch

substance use  
medical aspects

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## **Circulating cytokines as biomarkers of alcohol abuse and alcoholism. (review).**

Achur RN; Freeman WM; Vrana KE. *Journal of Neuroimmune Pharmacology* 5(1): 83-91, 2010. (72 refs.)

There are currently no consistent objective biochemical markers of alcohol abuse and alcoholism. Development of reliable diagnostic biomarkers that permit accurate assessment of alcohol intake and patterns of drinking is of prime importance to treatment and research fields. Diagnostic biomarker development in other diseases has demonstrated the utility of both open, systems biology, screening for biomarkers and more rational focused efforts on specific biomolecules or families of biomolecules. Long-term alcohol consumption leads to altered inflammatory cell and adaptive immune responses with associated pathologies and increased incidence of infections. This has led researchers to focus attention on identifying cytokine biomarkers in models of alcohol abuse. Alcohol is known to alter cytokine levels in plasma and a variety of tissues including lung, liver, and very importantly brain. A number of cytokine biomarker candidates have been identified, including: tumor necrosis factor-alpha, interleukin (IL)-1-alpha, IL-1-beta, IL-6, IL-8, IL-12, and monocyte chemoattractant protein-1. This is an emerging and potentially exciting avenue of research in that circulating cytokines may contribute to diagnostic biomarker panels, and a combination of multiple biomarkers may significantly increase the sensitivity and specificity of the biochemical tests aiding reliable and accurate detection of excessive alcohol intake. Copyright 2010, <<\*&find>>

## **Role of ethanol in kava hepatotoxicity. (review).**

Li XZ; Ramzan I. *Phytotherapy Research* 24(4): 475-480, 2010. (44 refs.)

Kava is known for its recreational, ceremonial and medicinal use in the Pacific. The aqueous non-alcoholic drink of kava rhizome produces intoxicating, relaxing and soothing effects. While kava's medicinal effects receive worldwide recognition, kava-containing products came under scrutiny after over 100 reports of spontaneous adverse hepatic effects. Many

mechanisms have been postulated to explain the unexpected toxicity, one being pharmacokinetic interactions between kavalactones and co-administered drugs involving cytochrome P450 enzyme system. Alcohol is often co-injected in kava hepatotoxicity cases. This review evaluates the possible hepatotoxicity mechanisms involving alcohol and kava. Copyright 2010, John Wiley & Sons.

## **ADH1B\*2 allele is protective against alcoholism but not chronic liver disease in the Hungarian population.**

Toth R; Pocsai Z; Fiatal S; Szeles G; Kardos L; Petrovski B et al. *Addiction* 105(5): 891-896, 2010. (32 refs.)

Background: Standardized death rates from chronic liver diseases (CLDs) in Hungary are much higher than the European Union average. Carrying the alcohol dehydrogenase 1B 48His allele (rs1229984 or ADH1B\*2) could decrease the risk of alcoholism, but with persistent drinking may confer a greater risk of CLDs. The aim of this study was to assess the prevalence of this polymorphism in the Hungarian population and its association with alcohol consumption and with CLDs. Methods: and results: A total of 278 cases with diagnosed CLDs and 752 controls without any alterations in liver function, all males aged 45-64, were screened for ADH1B Arg48His polymorphism. ADH1B\*2 allele frequencies in controls and cases were 8.31% and 4.50%, respectively (chi 2 = 9.2; P = 0.01). Carrying the ADH1B\*2 allele was associated with significantly lower odds ratio (OR) for drinking frequency (OR = 0.63; P = 0.003), the number of positive answers on CAGE (Cut-down, Annoyed, Guilt, Eye-opener) assessment (OR = 0.58; P = 0.005) and a positive CAGE status (OR = 0.55; P = 0.007). There was a significant association between ADH1B\*2 and CLDs (OR = 0.50; P = 0.003), but it disappeared after adjusting for CAGE status and scores (OR = 0.67 P = 0.134; OR = 0.67 P = 0.148, respectively) and weakened after adjusting for drinking frequency (OR = 0.61; P = 0.045). Among heavy drinkers the presence of ADH1B\*2 did not increase the risk of cirrhosis but there was a significant interaction between genotype

and CAGE status ( $P = 0.003$ ,  $P = 0.042$ ), with ADH1B\*2 conferring reduced risk of CLDs in CAGE negatives. Conclusion: In Hungarians, the ADH1B 48His allele reduces the risk of alcoholism, but not the risk of chronic liver disease among heavy drinkers. Copyright 2010, Society for the Study of Addiction to Alcohol and Other Drugs.

### **Buprenorphine maintenance therapy hinders acute pain management in trauma.**

Harrington CJ; Zaydfudim V. *American Surgery* 76(4): 397-399, 2010. (8 refs.)

Buprenorphine is a mixed opiate receptor agonist-antagonist growing in popularity as an office-based treatment for opioid-dependent patients. It has high affinity, but only partial agonism at the R-opioid receptor resulting in a ceiling analgesic effect. At higher doses, buprenorphine potentiates antagonism at the kappa-opioid receptor. These properties make buprenorphine an effective maintenance treatment for opioid-dependent patients. These same properties, however, can interfere with the management of acute pain in patients on maintenance buprenorphine therapy. We present a case of a young multisystem trauma patient in whom adequate analgesia could not be achieved due to buprenorphine treatment before and through the early course of admission. Discontinuation of buprenorphine allowed for appropriate pain management and successful analgesia. Further education of acute care clinicians about buprenorphine pharmacology and careful selection of patients for buprenorphine maintenance therapy are needed to avoid delays of pain control in trauma patients. Copyright 2010, Southwestern Surgical Congress.

### **Caffeine intake during pregnancy, late miscarriage and stillbirth.**

Greenwood DC; Alwan N; Boylan S; Cade JE; Charvill J; Chipps KC et al. *European Journal of Epidemiology* 25(4): 275-280, 2010. (29 refs.)

Caffeine is a commonly consumed drug during pregnancy with the potential to affect the developing fetus. Findings from previous studies have shown inconsistent results. We recruited a cohort of 2,643 pregnant women, aged 18-45 years, attending two UK maternity units between 8 and 12 weeks gestation from September 2003 to June 2006. We used a validated tool to assess caffeine intake at different stages of pregnancy and related this to late miscarriage and stillbirth, adjusting for confounders, including salivary cotinine as a biomarker of smoking status. There was a strong association between caffeine intake in the first trimester and subsequent late miscarriage and stillbirth, adjusting for confounders. Women

whose pregnancies resulted in late miscarriage or stillbirth had higher caffeine intakes (geometric mean = 145 mg/day; 95% CI: 85-249) than those with live births (103 mg/day; 95% CI: 98-108). Compared to those consuming < 100 mg/day, odds ratios increased to 2.2 (95% CI: 0.7-7.1) for 100-199 mg/day, 1.7 (0.4-7.1) for 200-299 mg/day, and 5.1 (1.6-16.4) for 300+ mg/day ( $P$  (trend) = 0.004). Greater caffeine intake is associated with increases in late miscarriage and stillbirth. Despite remaining uncertainty in the strength of association, our study strengthens the observational evidence base on which current guidance is founded. Copyright 2010, Springer.

### **Methamphetamine body stuffers: An observational case series.**

West PL; McKeown NJ; Hendrickson RG. *Annals of Emergency Medicine* 55(2): 190-197, 2010. (18 refs.)  
Study objective: We describe the demographics, characteristics, treatment, and clinical course of methamphetamine body stuffers. We also determine the clinical characteristics of methamphetamine body stuffers who have severe outcomes. Methods: A 6.5-year descriptive nonconcurrent observational case series evaluated methamphetamine body stuffers; about whom the Oregon Poison Center was consulted. Poison center charts were supplemented by completed hospital charts (for 95% of patients). Results: Six hundred forty-eight patients with methamphetamine exposure were identified and reviewed, and 55 charts met the criteria for "methamphetamine body stuffer." We found the following characteristics of methamphetamine body stuffers: mean age 29 years (range 16 to 57 years), men in 44 of 55 cases (80%), mean time to arrival 2.7 hours after ingestion, with a median of 1 hour after ingestion. Ninety-seven percent (53/55) stuffed methamphetamine orally (2/55 rectally). Methamphetamine was most frequently swallowed in baggies, but 25% were unpackaged. The median dose ingested was 3.5 g of methamphetamine in 1 package. Outcome-based analysis revealed 29% (16/55) of patients had severe outcomes, as defined by end-organ toxicity, with agitation requiring intubation the most common severe outcome. There was 1 death reported. Toxicity did not appear to be related to the amount of meth or number of packets. Patients with severe outcomes had higher mean initial pulse rates and temperatures. Eighty-eight percent (14/16) of patients with severe outcomes had a presenting pulse rate greater than 120 beats/min or a temperature greater than 38 degrees C versus 18% (7/39) patients with a benign outcome. Twenty-four radiographic studies were obtained; none detected packets. Conclusion: Methamphetamine body stuffers have similar

demographics to those of body stuffers of other stimulants, but tended to ingest fewer baggies with larger masses, and had a higher percentage of severe outcomes (29%) than previously reported with other stimulants. Increases in presenting pulse rate and temperature (pulse rate >120 beats/min or >38.0 degrees C) are common in patients who will develop end-organ damage. Copyright 2010, Elsevier Science.

### **Near-death states reported in a sample of 50 misusers.**

Corazza O; Schifano F. *Substance Use & Misuse* 45(6): 916-924, 2009. (28 refs.)

Increase in recreational ketamine use may be a cause for concern. We aimed here at assessing, in a sample of ketamine misusers, concordance between the typical near-death experience (NDE) features and the on-drug psychoactive effects the subjects experienced. In 2003-2005, a sample of previous ketamine misusers recollecting a ketamine-related NDE were recruited through snowballing and screened with the means of the Greyson NDE Scale; 125 participants made an initial contact with the researcher and 50 reported a minimum score of seven at the "Greyson NDE Scale". Interviewees were in the range 21-66 years old; 27 participants (54%) were educated at BA level, 18 (36%) had an MSc, and 5 (10%) a PhD. Eight (16%) interviewees had a definite religious background. An average lifetime ketamine intake of 140 occasions was reported by the interviewees, who typically presented with a polydrug, including cannabis and MDMA/ecstasy, misuse history. In 45 (90%) cases, the NDE occurred during the first few occasions of intake. Most frequent features of reported NDE states included: altered perception of time (90%), strong sense of detaching from own physical body (88%), and a sense of peace/joy (76% of subjects). Although results here described were elicited from a self-selected, nonrandomized, limited size sample of misusers, we suggest that recreational ketamine intake may be associated with occurrence of near-death related states. Copyright 2009, Taylor & Francis.

### **Seizures induced by recreational abuse of bupropion tablets via nasal insufflation.**

Kim D; Steinhart B. *Canadian Journal of Emergency Medicine* 12(2): 158-161, 2010. (25 refs.)

Bupropion is a newer generation antidepressant that is commonly used for treatment of depression and for smoking cessation. Seizures are a frequently reported adverse effect of bupropion in therapeutic oral doses; however, there are limited data about the consequences of nasal insufflation of bupropion. We report the case of a patient who presented to the

emergency department (ED) with a recent history of generalized tonic-clonic seizures whose etiology was initially a diagnostic mystery. After an initial visit to another ED, the patient presented to our ED later that day with a recurrence of the seizures after crushing and nasally insufflating oral bupropion tablets. We review important implications of this case to emergency medicine, including the potential for abuse of bupropion, the difference between intranasal and oral administration, the changing trends in the etiology of drug-related seizures and the importance of examining the nares in patients with unexplained seizure and delirium. Copyright 2010, Canadian Association of Emergency Physicians.

### **Subjective response to alcohol: A critical review of the literature. (review).**

Morean ME; Corbin WR. *Alcoholism: Clinical and Experimental Research* 34(3): 385-395, 2010. (93 refs.)

Background: Subjective response to alcohol (SR), which reflects individual differences in sensitivity to the pharmacological effects of alcohol, may be an important endophenotype in understanding genetic influences on drinking behavior and alcohol use disorders (AUDs). SR predicts alcohol use and problems and has been found to differ by a range of established risk factors for the development of AUDs (e.g., family history of alcoholism). The exact pattern of SR associated with increased risk for alcohol problems, however, remains unclear. The Low Level of Response Model (LLR) suggests that high-risk individuals experience decreased sensitivity to the full range of alcohol effects, while the Differentiator Model (DM) asserts that high risks status is associated with increased sensitivity to alcohol's positive effects but decreased sensitivity to negative effects. Aims: The current paper (1) reviews two prominent models of subjective response, (2) reviews extant laboratory-based research on subjective response, (3) highlights remaining gaps in our understanding and assessment of subjective response, and (4) encourages collaborative efforts to address these methodological and conceptual concerns. Methods: This paper reviews studies to assess a range of alcohol effects including impairment, stimulation, and sedation. Results: The research literature provides at least partial support for both the LLR and DM models. High-risk individuals have been shown to have a reduced response to alcohol with respect to sedative or impairing effects, particularly on the descending limb of the blood alcohol curve (BAC). There is also evidence that ascending limb stimulant effects are more pronounced or operate differently for high-risk individuals.

Discussion: Despite commendable advances in SR research, important questions remain unanswered. Inconsistent results across studies may be attributable to a combination of an inadequate understanding of the underlying construct and methodological differences across studies (e.g., number and timing of assessments across the BAC, inclusion of a placebo condition). With respect to the underlying construct, existing measures fail to adequately distinguish between cognitive/behavioral impairment and sedation, aspects of which may be perceived positively (e.g., anxiolysis) due to their ability to act as negative reinforcers. Conclusions: Addressing the concerns raised by the current review will be integral to making meaningful scientific progress in the field of subjective response. Copyright 2010, Research Society on Alcoholism.

**Sweet preferences and analgesia during childhood: Effects of family history of alcoholism and depression.**

Mennella JA; Pepino MY; Lehmann-Castor SM; Yourshaw LM. *Addiction* 105(4): 666-675, 2010. (80 refs.)

Aim: To determine whether depression and family history of alcoholism are associated with heightened sweet preferences in children, before they have experienced alcohol or tobacco and at a time during the life-span when sweets are particularly salient. Design: Between- and within-subject experimental study. Participants: Children, 5-12 years old (n = 300), formed four groups based on family history of alcohol dependence up to second-degree relatives [positive (FHP) versus negative (FHN)] and depressive symptoms as determined by the Pictorial Depression Scale [depressed (PDEP) versus non-depressed (NDEP)]. Measurements: Children were tested individually to measure sucrose preferences, sweet food liking and, for a subset of the children, the analgesic properties of sucrose versus water during the cold pressor test. Findings: The co-occurrence of having a family history of alcoholism and self-reports of depressive symptomatology was associated with a preference for more concentrated sucrose, while depressive symptomatology alone was associated with greater liking for sweet-tasting food/candies and increased pain sensitivity. Depression antagonized the analgesic properties of sucrose. Conclusions: While children as a group innately like sweets and feel better after eating them, the present study reveals significant contributions of family history of alcoholism and depression to this effect. Whether the heightened sweet preference and the use of sweets to alleviate depression are markers for developing alcohol-related problems or responses that are protective are important

for future research. Copyright 2010, Society for the Study of Addiction to Alcohol and Other Drugs.

**Verbal and nonverbal memory in adults prenatally exposed to alcohol.**

Coles CD; Lynch ME; Kable JA; Johnson KC; Goldstein FC. *Alcoholism: Clinical and Experimental Research* 34(5): 897-906, 2010. (42 refs.)

Background: Neurocognitive effects of prenatal alcohol exposure in adulthood are not well documented. Questions persist regarding the extent to which there are specific, measurable effects beyond those associated with global ability deficits, whether individuals without the full fetal alcohol syndrome (FAS) demonstrate alcohol-related cognitive impairments, and whether observed memory effects are specific to a particular modality, i.e., verbal vs. visual/spatial domains. Methods: In this study, verbal and nonverbal selective reminding paradigms were used to assess memory function in 234 young adults (M age: 22.78, SD: 1.79). Alcohol exposure was quantified prenatally. Alcohol groups included: Individuals with physical effects of alcohol exposure (Dysmorphic group, n = 47); Exposed individuals without such effects (n = 74). Contrast groups included: Controls (n = 59) matched for ethnicity, socioeconomic status, and hospital of birth; Special Education contrast group (n = 54) included to control for disability status. Memory outcomes entailed total recall, delayed recall, and measures of encoding and retrieval, and learning over trials as indexed by slope. Results: Results: indicated that Dysmorphic individuals were significantly less efficient in memory performance than Controls on all of the outcomes measured, but they did not differ from those in the Special Education contrast group. The nondysmorphic, alcohol-exposed group was intermediate in their performance, suggesting a continuum of effects of prenatal exposure. Evaluation of the encoding and retrieval aspects of memory performance indicated that learning rather than forgetting accounted for the deficits associated with prenatal alcohol exposure. Finally, no interaction was found between modality of presentation (verbal and nonverbal) and effects of alcohol exposure on memory performance. Conclusion: These findings indicate that prenatal alcohol exposure is associated with persistent and specific effects on memory performance, and these problems result from less efficient encoding of information across both verbal and nonverbal modalities. Education and training efforts with this clinical group should take these characteristics into account. Copyright 2010, Research Society on Alcoholism