

Alcohol abuse and acute lung injury: Epidemiology and pathophysiology of a recently recognized association. (review).

Guidot DM; Hart CM. *Journal of Investigative Medicine* 53(5): 235-245, 2005. (61 refs.)

Alcohol is the most commonly used and abused drug in the United States. The deleterious health effects of alcohol can be attributed both to its acute intoxicating effects, which result in temporary impairment of judgment and motor skills, and to its more chronic and toxic effects on the liver, pancreas, heart, and brain, all of which may result in irreversible organ damage. Although recognized for more than a century as a major risk factor for pneumonia, alcohol abuse was until recently perceived to have no significant effects on lung structure and/or function. However, within the past decade, epidemiologic studies have revealed that alcohol abuse independently increases the risk of acute respiratory distress syndrome (ARDS) two- to fourfold in patients with sepsis or trauma and may play a role in ARDS pathogenesis in as many as half of all patients with the syndrome. Although alcohol abuse alone does not cause acute lung injury, it renders the lung susceptible to dysfunction in response to the inflammatory stresses of sepsis, trauma, and other clinical conditions recognized to cause ARDS. Recent investigations in both animal models of chronic ethanol ingestion and in human subjects with a history of alcohol abuse have explored this previously unrecognized connection between alcohol and acute lung injury and have uncovered multiple derangements, which we now characterize as the "alcoholic lung." This review summarizes the epidemiologic association between alcohol abuse and acute lung injury and the recent experimental findings that are unraveling the underlying pathophysiology. Copyright 2005, Slack, Inc.

Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: Effects on the neonatal abstinence syndrome.

Jones HE; Johnson RE; Jasinski DR; O'Grady KE; Chisholm CA; Choo RE et al. *Drug and Alcohol Dependence* 79(1): 1-10, 2005. (47 refs.)

This study was designed to compare the neonatal abstinence syndrome (NAS) in neonates of methadone

and buprenorphine maintained pregnant opioid-dependent women and to provide preliminary safety and efficacy data for a larger multi-center trial. This randomized, double-blind, double-dummy, flexible dosing, parallel-group controlled trial was conducted in a comprehensive drug-treatment facility that included residential and ambulatory care. Participants were opioid-dependent pregnant women and their neonates. Treatment involved daily administration of either sublingual buprenorphine or oral methadone using flexible dosing of 4-24 mg or 20- 100 mg, respectively. Primary a priori outcome measures were: (1) number of neonates treated for NAS; (2) amount of opioid agonist medication used to treat NAS; (3) length of neonatal hospitalization; and (4) peak NAS score. Two of 10 (20%) buprenorphine-exposed and 5 of 11 (45.5%) methadone-exposed neonates were treated for NAS ($p = .23$). Total amount of opioid-agonist medication administered to treat NAS in methadone-exposed neonates was three times greater than for buprenorphine-exposed neonates (93.1 versus 23.6; $p = .13$). Length of hospitalization was shorter for buprenorphine-exposed than for methadone-exposed neonates ($p = .021$). Peak NAS total scores did not significantly differ between groups ($p = .25$). Results suggest that buprenorphine is not inferior to methadone on outcome measures assessing NAS and maternal and neonatal safety when administered starting in the second trimester of pregnancy. Copyright 2005, Elsevier Ireland.

An extract of the Chinese herbal root kudzu reduces alcohol drinking by heavy drinkers in a naturalistic setting.

Lukas SE; Penetar D; Berko J; Vicens L; Palmer C; Mallya G et al. *Alcoholism: Clinical and Experimental Research* 29(5): 756-762, 2005. (39 refs.)

Background: Of the available medications for treating alcohol-related problems, none are universally effective, and all have side effects that may limit their use. Extracts of kudzu containing a variety of isoflavones have been shown to reduce alcohol drinking in rats and hamsters. Methods: The present study was designed to test the efficacy of a kudzu extract in a clinical population. Male and female "heavy" alcohol drinkers were treated with either

placebo or a kudzu ex-tract for 7 days and then given an opportunity to drink their preferred brand of beer while in a naturalistic laboratory setting. Participants served as their own controls, and order of treatment exposure was counterbalanced. Drinking behavior was monitored by a digital scale that was located in the top of an end table. Results: Kudzu treatment resulted in significant reduction in the number of beers consumed that was paralleled by an increase in the number of sips and the time to consume each beer and a decrease in the volume of each sip. These changes occurred in the absence of a significant effect on the urge to drink alcohol. There were no reported side effects of kudzu treatment. Conclusion: These data suggest that an extract of this leguminous plant may be a useful adjunct in reducing alcohol intake in a naturalistic setting. Copyright 2005, Lippincott, Williams & Wilkins.

Effects of biochemically confirmed smoking cessation on white blood cell count.

Abel GA; Hays JT; Decker PA; Croghan GA; Kuter DJ; Rigotti NA. *Mayo Clinic Proceedings* 80(8): 1022-1028, 2005. (33 refs.)

OBJECTIVES: To determine the relationship between white blood cell (WBC) indices and several baseline variables in a large cohort of healthy smokers and to assess whether these changed after biochemically confirmed smoking cessation. **SUBJECTS AND METHODS:** The study consisted of 784 healthy smokers enrolled in a trial of sustained-release bupropion, 300 mg/d, for relapse prevention after smoking cessation from 1995 to 1998. Both WBC counts and absolute neutrophil counts (ANCs) were measured at baseline, week 7, and week 52. Smoking status was assessed at weeks 7 and 52 by self-report and biochemically confirmed with expired air carbon monoxide levels. Multivariate analyses compared changes in WBC count and ANC between smokers who did and did not stop smoking, adjusting for treatment group, age, sex, and body mass index. **RESULTS:** Of 784 smokers enrolled, 461 had biochemically confirmed tobacco abstinence after 7 weeks of bupropion; 429 were randomly assigned to receive continued bupropion therapy or placebo until week 52. Between baseline and week 7, there was a significantly larger decrease in WBC count in continuously abstinent subjects compared with continuing smokers (adjusted $P=.03$). At 52 weeks, continuously abstinent subjects, compared with continuing smokers, had a greater decline from baseline in WBC count ($1.2 \pm 1.9 \times 10^9/L$ vs $0.1 \pm 1.9 \times 10^9/L$; $P < .001$) and ANC ($1.0 \pm 1.6 \times 10^9/L$ vs $0.2 \pm 1.5 \times 10^9/L$; $P < .001$). **CONCLUSION:** Biochemically confirmed tobacco

abstinence leads to a rapid and sustained decrease in WBC and ANC, possibly reflecting a decrease in an underlying state of tobacco-induced inflammation. Copyright 2005, Mayo Foundation for Medical Education and Research.

Caffeine tolerance is incomplete: Persistent blood pressure responses in the ambulatory setting.

Farag NH; Vincent AS; Sung BH; Whitsett TL; Wilson MF; Lovallo WR. *American Journal of Hypertension* 18(5, Part 1): 714-719, 2005. (30 refs.) **Background:** Caffeine in dietary doses is a well-established pressor agent. Tolerance to this pressor effect occurs in only about half of regular consumers in acute laboratory tests. The clinical significance of this incomplete tolerance depends on whether the pressor effect is maintained throughout the day with repeated intake. Therefore, we examined the ability of a standard dose of caffeine (250 mg x 3) to maintain a blood pressure (BP) elevation during 18 hours of ambulatory BP monitoring (ABPM) after 5 days of regular daily intake of varying background doses. **Methods:** Eighty-five men and women completed a four-week double blind, crossover trial. During each week, subjects consumed capsules totaling 0, 300, or 600 mg/day of caffeine in 3 divided doses. On day 6, they consumed capsules with either 0 or 250 mg at 9:00 am and 1:00 pm, in the laboratory, and again at 6:00 pm during ABPM. Tolerance was defined as a reduction in the diastolic BP response to two challenge doses given in the lab in response to increasing daily intake. Data were analyzed using multivariate repeated measures analysis of variance. **Results:** BP responses to caffeine above those found on placebo-placebo (P-P) week were found for both tolerance groups when caffeine was consumed after a week of receiving a placebo. However, only the low tolerance group showed increases, above those found on P-P week, after 300 mg/day in systolic/diastolic BP during the waking hours (mean standard error of the mean = 2.8 plus or minus 1.1, $P = .01$ /2.2 plus/minus 0.9, $P = .02$) and in systolic BP during sleep (2.3 plus/minus 1, $P = .03$). **Conclusions:** Persistent elevations in BP occurring on a daily basis in some habitual caffeine consumers may hold clinical significance. Copyright 2005, Elsevier Science.

Methadone maintenance and male sexual dysfunction.

Brown R; Balousek S; Mundt M; Fleming M. *Journal of Addictive Diseases* 24(2): 91-106, 2005. (58 refs.) **Purpose.** This study reports the prevalence and types of sexual dysfunction in a sample of men on methadone maintenance for opioid dependence, and

describes factors which may contribute to sexual dysfunction. Methods. Ninety-two opioid-dependent men were recruited from a methadone maintenance clinic and completed two questionnaires, a research interview and laboratory measures. Results. Fourteen percent reported some sexual dysfunction. Erectile dysfunction ($r = 0.24$, $p = 0.020$), libido dysfunction ($r = 0.30$, $p = 0.003$), and global dysfunction ($r = 0.26$, $p = 0.013$) increased with increasing age of the patient. Methadone dose showed a significant direct correlation with increased orgasm dysfunction, both before and after adjusting for duration of treatment ($p = 0.012$). None of the sexual dysfunction subscales or global dysfunction were associated with plasma testosterone or plasma prolactin levels. Conclusions. The rate of global sexual dysfunction in methadone-treated men is similar to general population studies and should be evaluated using general population guidelines. Orgasm dysfunction is a special case and may respond to methadone dose reduction. Copyright 2005, Haworth Press Inc.

Smoking during pregnancy and the risk for hyperkinetic disorder in offspring.

Linnet KM; Wisborg K; Obel C; Secher NJ; Thomsen PH; Agerbo E. *Pediatrics* 116(2): 462-467, 2005. (43 refs.)

Objective. Maternal smoking during pregnancy may increase the risk for behavioral disorders. The aim of this study was to investigate the association between smoking during pregnancy and hyperkinetic and attention-deficit/hyper-activity disorder in the offspring in a large population-based study. Methods. This study was designed as a nested case-control study. Data were obtained from Danish longitudinal registers and included 170 children with hyperkinetic disorder and 3765 population-based control subjects, who were matched by age, gender, and date of birth. Potential confounders, including newborn characteristics, socioeconomic status, and family history of psychiatric illnesses, were evaluated by conditional logistic regression analyses. Results. Women who smoked during pregnancy had a 3-fold increased risk for having offspring with hyperkinetic disorder compared with nonsmokers. Socioeconomic factors and history of mental disorder in the parents or siblings seemed to confound the result to some extent (adjusted relative risk: 1.9; 95% confidence interval: 1.3-2.8). Adjustment for parental age or exclusion of children with low birth weight (< 2500 g), preterm delivery (< 37 weeks completed gestation), and Apgar scores < 7 at 5 minutes revealed no changes in the results. Also, excluding children with conduct disorders or comorbid disorders revealed no change in

the results. Conclusions. Our results showed an increased risk for hyperkinetic disorder in children of mothers who smoked during pregnancy. This could not be explained by newborn characteristics, parental socioeconomic status, family history of Psychiatric hospitalizations or contact as outpatients, conduct disorders, or comorbidity. Copyright 2005, American Academy of Pediatrics.

Is coffee a functional food? (review).

Dorea JG; da Costa THM. *British Journal of Nutrition* 93(6): 773-782, 2005. (165 refs.)

Definitions of functional food vary but are essentially based on foods' ability to enhance the quality of life, or physical and mental performance, of regular consumers. The worldwide use of coffee for social engagement, leisure, enhancement of work performance and well-being is widely recognised. Depending on the quantities consumed, it can affect the intake of some minerals (K, Mg, Mn, Cr), niacin and antioxidant substances. Epidemiological and experimental studies have shown positive effects of regular coffee-drinking on various aspects of health, such as psychoactive responses (alertness, mood change), neurological (infant hyperactivity, Alzheimer's and Parkinson's diseases) and metabolic disorders (diabetes, gallstones, liver cirrhosis), and gonad and liver function. Despite this, most reviews do not mention coffee as fulfilling the criteria for a functional food. Unlike other functional foods that act on a defined population with a special effect, the wide use of coffee-drinking impacts a broad demographic (from children to the elderly), with a wide spectrum of health benefits. The present paper discusses coffee-drinking and health benefits that support the concept of coffee as a functional food. Copyright 2005, CABI Publishing.

Smoking during pregnancy and bulimia nervosa in offspring.

Montgomery SM; Ehlin A; Ekblom A. *Journal of Perinatal Medicine* 33(3): 206-211, 2005. (21 refs.)

Because smoking during pregnancy is implicated in influencing appetite and impulse control in offspring, the aim of this study was to establish if it is associated with bulimia nervosa in offspring. Bulimia was identified at age 30 years among 4046 females, born 5-11 April, 1970. After adjustment for potential confounding factors including body mass index (BMI) and maternal psychiatric morbidity, smoking during pregnancy was associated with bulimia in offspring by age 30 years. Compared with nonsmoking mothers, the adjusted odds ratios (95% confidence intervals) for bulimia in offspring were 0.74 (0.25-2.21) for those

who gave up before pregnancy, 3.04 (1.16-7.95) for giving up during pregnancy and 2.64 (1.47-4.74) for smoking throughout pregnancy. Smoking during pregnancy was not associated with anorexia nervosa in offspring. Neither BMI nor variation between childhood and adult BMI explain the association. If the association of smoking during pregnancy with bulimia in offspring is causal, then it may operate through compromised central nervous system development and its influence on impulse or appetite control. The increased risk associated with mothers who gave up smoking during pregnancy emphasizes the importance of smoking cessation prior to conception. Copyright 2005, Walter de Gruyter & Co.

Swift increase in alcohol metabolism (SIAM): Understanding the phenomenon of hypermetabolism in liver.

Bradford BU; Rusyn I. *Alcohol* 35(1): 13-17, 2005. (35 refs.)

The swift increase in alcohol metabolism (SIAM) is a phenomenon defined as a rapid increase in hepatic respiration and alcohol metabolism after administration of a bolus dose of alcohol. Continuous exposure to alcohol is known to produce adaptive changes in liver alcohol and oxygen metabolism. A considerable burst of hepatic respiration can also occur after administration of a single large dose of alcohol and results in a near doubling of alcohol metabolism, a high demand for oxygen, and downstream or pericentral hypoxia. These dramatic changes in rates of alcohol metabolism and tissue concentrations of oxygen are not due to induced enzyme activity in liver. This phenomenon depends on activation of mitochondrial function, an increase in co-factor supply for nicotinamide adenine dinucleotide-dependent alcohol metabolism, depletion of glycogen reserves, liberation of fatty acids through activation of an adrenergic response to alcohol providing substrate for catalase, and activation of Kupffer cells, the hepatic resident macrophages responsible for production of cytokines and prostaglandins. An understanding of the mechanisms of hypermetabolism in liver can have vital ramifications for knowledge of both alcohol-related and alcohol-unrelated liver injury because hypoxia that is a result of hypermetabolism can compound effects of pharmaceuticals and environmental agents on the liver. Swift increase in alcohol metabolism is an excellent example of the

complexity of cell-cell interactions in liver and extrahepatic regulation of biochemical and molecular events in this organ, and this important phenomenon shall be considered in studies of liver disease and biochemistry. Copyright 2005, Elsevier Science.

Histopathological findings in 851 autopsies of drug addicts, with toxicologic and virologic correlations.

Passarino G; Ciccone G; Siragusa R; Tappero P; Mollo F. *American Journal of Forensic Medicine and Pathology* 26(2): 106-116, 2005. (29 refs.)

This investigation was carried out on 851 consecutive judicial autopsies of drug addicts who died mostly of heroin overdose from 1977 to 1996. Research of anti-HIV/HBV/HCV antibodies was performed, and histologic sections were retrospectively reviewed. More than 65% were HBV/HCV-positive and about 17% HIV-positive; females were HIV-positive more often than males. Intracranial microhemorrhages were frequently found; cerebral infectious diseases were rare. Inflammatory heart lesions, myocardial fibrosis, and acute ischemia were common. Interstitial nephritis (found in about 8%) was more frequent in females, in older patients, and in those carrying HIV infection; glomerular sclerosis was detected in about 12%. Acute bronchitis and/or pneumonia was demonstrated in 12%, without significant association with HIV infection; pulmonary hemorrhages, foreign body granulomas, and food aspiration were also commonly seen; hyperplasia of pulmonary perivascular lymphatic tissue was rather characteristic. Liver was carrying steatosis in 66.3% and/or hepatitis in 64.5%; acute hepatitis was more frequent in females, chronic hepatitis in older subjects and in those proven positive for hepatotropic viruses; cirrhosis occurred more often in older patients, in those carrying virus infection, and in consumers of nonnarcotics drugs such as ethanol. No pathologic finding was clearly related to drug abuse; therefore, during autopsy, drug addiction can be suspected, but anamnestic and circumstantial data are needed to lead pathologists to request toxicologic analysis to ascertain the cause of death. The present investigation emphasizes that, in addition to the risk of death by overdose, the high incidence of acute and chronic diseases could seriously undermine the health status of heroin and/or other drug consumers. Copyright 2005, Lippincott, Williams & Wilkins.