

Library Watch

substance use
medical aspects

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Acute myocardial infarction in young adults who abuse amphetamines.

Westover AN; Nakonezny PA; Haley RW. *Drug and Alcohol Dependence* 96(1-2): 49-56, 2008. (44 refs.)
Background: Case reports suggest a link between methamphetamine abuse and acute myocardial infarction (AMI), but no epidemiologic studies have examined this link. Our objective was to test the hypothesis that young adults who abuse amphetamines are at higher risk for AMI. Methods: In this study of 3,148,165 discharges from Texas hospitals in a quality indicators database during 2000-2003, among persons aged 18-44 years we identified 11,011 AMIs, defined according to the Agency for Healthcare Research and Quality's AMI mortality inpatient quality indicator. Results: In a multiple logistic regression analysis-while controlling for cocaine abuse, alcohol abuse, tobacco use, hypertension, diabetes mellitus, lipid disorders, obesity, congenital defects, and coagulation defects - amphetamine abuse was significantly associated with AMI (adjusted odds ratio = 1.61; 95% CI = 1.24-2.04, p = 0.0004). The rate of AMIs among amphetamine abusers increased significantly from 2000 to 2003. The population attributable risk suggests that amphetamine abuse is responsible for 0.2% of AMIs in the state of Texas. The geographical distribution of amphetamine abuse varied by region, with the prevalence being highest in the North Texas and Panhandle regions of Texas. Conclusions: This modest, though statistically robust, association suggests that amphetamine abuse may play a role in AMI. Copyright 2008, Elsevier Science.

Baclofen and gamma-hydroxybutyrate withdrawal.

LeTourneau JL; Hagg DS; Smith SM. *Neurocritical Care* 8(3): 430-433, 2008. (26 refs.)
Introduction: Benzodiazepine treatment of life-threatening gamma-hydroxybutyrate (GHB) withdrawal is frequently unsatisfactory. Animal studies suggest strongly that treatment with GABA(B) agonists, such as baclofen, will be a more effective strategy. Methods A case report from the medical intensive care unit (ICU) of the university tertiary care hospital. Results: A 61-year-old woman was admitted to the medical ICU for severe withdrawal symptoms

from chronic GHB use. This manifested as delirium, tremor, and seizures despite only small decreases in GHB dose and treatment with benzodiazepines. The addition of baclofen allowed the rapid sequential decreases in the GHB dose without seizure or delirium and resulted in long-term improvement of her tremor. Conclusions: Baclofen, a GABA(B) agonist, may be a useful agent in the treatment of severe GHB withdrawal. Copyright 2008, Humana Press.

Cigarette smoking and reproductive function.

Scares SR; Mejo MA. *Current Opinion in Obstetrics & Gynecology* 20(3): 281-291, 2008. (84 refs.)
Purpose of review: To perform a systematic review of the literature on the relationship between cigarette smoking and reproductive function. Whenever possible, this review is focused on the most recently published studies (mainly the past 2 years). Nevertheless, in many instances older literature was too relevant not to be taken into account. Recent findings: Tobacco compounds exert a deleterious effect on the process of ovarian follicle maturation. This effect is expressed by worse in-vitro fertilization parameters in cycles performed on women with smoking habits. Also, uterine receptiveness is significantly altered by the smoking habit. In men, cigarette smoking reduces sperm production, increases oxidative stress, and DNA damage. Spermatozoa from smokers have reduced fertilizing capacity, and embryos display lower implantation rates. Even in-utero exposition to tobacco constituents leads to reduced sperm count in adult life. Summary: A strong body of evidence indicates that the negative effect of cigarette smoking on fertility comprises fairly every system involved in the reproductive process. Couples in reproductive age should be strongly discouraged to smoke. Copyright 2008, Lippincott, Williams & Wilkins.

Effects of parental smoking on interferon gamma production in children.

Tebow G; Sherrill DL; Lohman IC; Stern DA; Wright AL; Martinez FD et al. *Pediatrics* 121(6): e1563-e1569, 2008. (27 refs.)
OBJECTIVES. Environmental tobacco smoke is associated with several negative health outcomes in

children, including an increased susceptibility to infections. One of the postulated mechanisms for these effects is the impairment of the immune system function and/ or development. Yet, it remains unknown whether cumulative exposure to parental smoking is associated with altered immune responses in childhood and whether these effects are independent of in utero exposure to maternal smoking. In a population-based birth cohort, we sought to determine the relation of parental smoking, as assessed prospectively since pregnancy, to the child's interferon gamma and interleukin 4 production at 11 years of age. PATIENTS AND METHODS. We used data on 512 children and their parents from the Tucson Children's Respiratory Study cohort. Information on maternal and paternal smoking was collected prospectively by questionnaire, and pack-years for mother, father, and both parents combined were assessed prospectively between the prenatal period and year 11. At age 11 years, children's interferon gamma and interleukin 4 production from mitogen-stimulated peripheral blood mononuclear cells was measured. RESULTS. Children of parents who smoked between the prenatal period and year 11 were more likely to be in lower quartiles of interferon gamma production than children of nonsmoking parents. In addition, maternal, paternal, and parental pack-years showed significant inverse dose-response relationships with interferon gamma production in the child. These dose-response relationships with interferon gamma remained significant for both paternal and parental pack-years among children of mothers who did not smoke during pregnancy, suggesting the existence of specific postnatal effects of environmental tobacco smoke exposure. In contrast, no significant effects of parental smoking were found on interleukin 4 production. CONCLUSIONS. Interferon gamma responses of school-aged children are impacted by parental smoking. Copyright 2008, American Academy of Pediatrics.

Fentanyl and propofol exposure in the operating room: Sensitization hypotheses and further data.

Merlo LJ; Goldberger BA; Kolodner D; Fitzgerald K; Gold MS. *Journal of Addictive Diseases* 27(3): 67-76, 2008. (50 refs.)

Inflated rates of opioid addiction among anesthesiologists may be caused by chronic exposure to low doses of aerosolized anesthetic/analgesic agents in the operating room. Such secondhand exposure produces neurobiological sensitization to the reinforcing effects of these substances, making later addiction more likely. This article extends findings that fentanyl and propofol are detectable in the air of the operating room and demonstrates that fentanyl is

also detectable on surfaces in the operating room. Secondhand exposure could, therefore, occur by inhalation and skin absorption. Additionally, data show that many physicians with opiate addiction have a family history of addiction, suggesting genetic vulnerability to the effects of secondhand exposure. Other new data demonstrate that the rates of marijuana and tobacco smoking are much higher among opioid-addicted physicians, suggesting that prior exposure to THC (the psychoactive component of cannabis) or nicotine might increase vulnerability to secondhand effects. Suggestions for reducing secondhand exposure in the operating room are discussed. Copyright 2008, Haworth Press.

Methadone, commonly used as maintenance medication for outpatient treatment of opioid dependence, kills leukemia cells and overcomes chemoresistance.

Friesen C; Roscher M; Alt A; Miltner E. *Cancer Research* 68(15): 6059-6064, 2008. (20 refs.)

The therapeutic opioid drug methadone (D,L-methadone hydrochloride) is the most commonly used maintenance medication for outpatient treatment of opioid dependence. In our study, we found that methadone is also a potent inducer of cell death in leukemia cells and we clarified the unknown mechanism of methadone-induced cell killing in leukemia cells. Methadone inhibited proliferation in leukemia cells and induced cell death through apoptosis induction and activated apoptosis pathways through the activation of caspase-9 and caspase-3, down-regulation of Bcl-xL and X chromosome-linked inhibitor of apoptosis, and cleavage of poly(ADP-ribose) polymerase. In addition, methadone induced cell death not only in anticancer drug-sensitive and apoptosis-sensitive leukemia cells but also in doxorubicin-resistant, multidrug-resistant, and apoptosis-resistant leukemia cells, which anticancer drugs commonly used in conventional therapies of leukemias failed to kill. Depending on caspase activation, methadone overcomes doxorubicin resistance, multidrug resistance, and apoptosis resistance in leukemia cells through activation of mitochondria. In contrast to leukemia cells, nonleukemic peripheral blood lymphocytes survived after methadone treatment. These findings show that methadone kills leukemia cells and breaks chemoresistance and apoptosis resistance. Our results suggest that methadone is a promising therapeutic approach not only for patients with opioid dependence but also for patients with leukemias and provide the foundation for new strategies using methadone as an additional anticancer drug in leukemia therapy, especially when

conventional therapies are less effective. Copyright 2008, American Association of Cancer Research.

Neonatal outcome of 58 infants exposed to maternal buprenorphine in utero.

Hytinantti T; Kahila H; Renlund M; Jarvenpaa AL; Halmesmaki E; Kivitie-Kallio S. *Acta Paediatrica* 97(8): 1040-1044, 2008. (14 refs.)

Aim: To study the neonatal outcome of infants exposed to buprenorphine in utero. Methods: We prospectively followed 54 buprenorphine-using pregnant women and their 58 infants. Urinary buprenorphine and norbuprenorphine concentrations in the mothers were measured prior to delivery, and in the infants during the first 3 days of life. The Finnegan score was used to evaluate neonatal abstinence syndrome. Other medical problems as well as social outcomes were recorded. Results: All infants had buprenorphine in their urine. A total of 38 infants required 20 +/- 10 days (range 7-48 days) of morphine treatment for neonatal abstinence syndrome. The length of hospital stay for all infants was 25 +/- 19 days (range 3-125 days). The infants' highest urinary norbuprenorphine concentrations across their first 3 days of life correlated with the length of hospital stay and duration of morphine treatment (both $p < 0.05$). The mean birth weight and mean head circumference ($n = 58$) were below average (mean -0.7 standard deviation [SD] and mean -0.5 SD, respectively). Eleven infants were discharged home, 19 infants were placed in foster care and 28 infants were discharged with their mothers to Mother and Child homes or to other institutions. Conclusion: Maternal buprenorphine use at the time of birth may cause neonatal abstinence syndrome, requiring long-term hospitalization. Multiple social problems require a multidisciplinary team approach. Copyright 2008, Blackwell Publishing.

Pharmacologic mechanisms of crystal meth. (review).

Kish SJ. *Canadian Medical Association Journal* 178(13): 1679-1682, 2008. (38 refs.)

Crystal meth is a form of the stimulant drug methamphetamine that, when smoked, can rapidly achieve high concentrations in the brain. Methamphetamine causes the release of the neurotransmitters dopamine, norepinephrine and serotonin and activates the cardiovascular and central nervous systems. The levels of dopamine are low in the brain of some drug users, but whether this represents neuronal loss is uncertain. The areas of the brain involved in methamphetamine addiction are unknown but probably include the dopamine-rich striatum and regions that interact with the striatum. There is no

medication approved for the treatment of relapses of methamphetamine addiction; however, potential therapeutic agents targeted to dopamine and non-dopamine (e. g., opioid) systems are in clinical testing. Copyright 2008, Canadian Medical Association.

Structure of daidzin, a naturally occurring anti-alcohol-addiction agent, in complex with human mitochondrial aldehyde dehydrogenase.

Lowe ED; Gao GY; Johnson LN; Keung WM. *Journal of Medicinal Chemistry* 51(15): 4482-4487, 2008. (50 refs.)

The ALDH2 *2 gene encoding the inactive variant form of mitochondrial aldehyde dehydrogenase (ALDH2) protects nearly all carriers of this gene from alcoholism. Inhibition of ALDH2 has hence become a possible strategy to treat alcoholism. The natural product 7-O-glucosyl-4'-hydroxyisoflavone (daidzin), isolated from the kudzu vine (*Peruraria lobata*), is a specific inhibitor of ALDH2 and suppresses ethanol consumption. Daidzin is the active principle in a herbal remedy for "alcohol addiction" and provides a lead for the design of improved ALDH2. The structure of daidzin/ALDH2 in complex at 2.4 Å resolution shows the isoflavone moiety of daidzin binding close to the aldehyde substrate-binding site in a hydrophobic cleft and the glucosyl function binding to a hydrophobic patch immediately outside the isoflavone-binding pocket. These observations provide an explanation for both the specificity and affinity of daidzin ($IC_{50} = 80$ nM) and the affinity of analogues with different substituents at the glucosyl position. Copyright 2008, American Chemical Society.

The color of meth: Is it related to adverse health outcomes? An exploratory study in Tijuana, Mexico.

Strathdee SA; Case P; Lozada R; Mantsios AR; Alvelais J; Pu MY et al. *American Journal on Addictions* 17(2): 111-115, 2008. (12 refs.)

In a study of injection drug users (IDUs) in Tijuana, Mexico, logistic regression identified factors associated with injection of colored vs. clear methamphetamine in the prior six months ($N = 613$). Colors injected most often were clear (50%), white (47%), yellow (2%), and pink (1%). IDUs injecting colored meth were more likely to experience recent abscesses (34%) compared to those injecting clear meth (24%; $p = 0.008$), an association that persisted after adjusting for confounders. Market characteristics, possibly relating to purity or adulterants, may be associated with abscesses among methamphetamine injectors. Further study is needed to confirm and determine the mechanism of this association to better

inform prevention messages. Copyright 2008, Taylor & Francis.

The risk of death by age, sex, and smoking status in the United States: Putting health risks in context.

Woloshin S; Schwartz LM; Welch HG. *Journal of the National Cancer Institute* 100(12): 845-853, 2008. (19 refs.)

Background To make sense of the disease risks they face, people need basic facts about the magnitude of a particular risk and how one risk compares with other risks. Unfortunately, this fundamental information is not readily available to patients or physicians. We created simple one-page charts that present the 10-year chance of dying from various causes according to age, sex, and smoking status. **Methods** We used the National Center for Health Statistics Multiple Cause of Death Public Use File for 2004 and data from the 2004 US Census to calculate age- and sex-specific death rates for various causes of death. We then combined data on smoking prevalence (from the National Health Interview Survey) and the relative risks of death from various causes for smokers vs never smokers (from the American Cancer Society's Cancer Prevention Study-II) to determine age-, sex-, and smoking-specific death rates. Finally, we accumulated these risks for various starting ages in a series of 10-year life tables. The charts present the 10-year risks of dying from heart disease; stroke; lung, colon, breast, cervical, ovarian, and prostate cancer; pneumonia; influenza; AIDS; chronic obstructive pulmonary disease; accidents; and all causes. **Results** At all ages, the 10-year risk of death from all causes combined is higher for men than women. The effect of smoking on the chance of dying is similar to the effect of adding 5 to 10 years of age: for example, a 55-year-old man who smokes has about the same 10-year risk of death from all causes as a 65-year-old man who never smoked (ie, 178 vs 176 of 1000 men, respectively). For men who never smoked, heart disease death represents the single largest cause of death from age 50 on and the chance of dying from heart disease exceeds the chances of dying from lung, colon, and prostate cancers combined at every age. For men who currently smoke, the chance of dying from lung cancer is of the same order of magnitude as the chance dying from heart disease and after age 50 it is about 10 times greater than the chance of dying from prostate or colon cancer. For women who have never

smoked, the magnitudes of the 10-year risks of death from breast cancer and heart disease are similar until age 60; from this age on, heart disease represents the single largest cause of death. For women who currently smoke, the chance of dying from heart disease or lung cancer exceeds the chance of dying from breast cancer from age 40 on (and does so by at least a factor of 5 after age 55). **Conclusion** The availability of simple charts with consistent data presentations of important causes of death may facilitate discussion about disease risk between physicians and their patients and help highlight the dangers of smoking. Copyright 2008, Oxford University Press.

Toenail nicotine levels as predictors of coronary heart disease among women.

Al-Delaimy WK; Stampfer MJ; Manson JE; Willett WC. *American Journal of Epidemiology* 167(11): 1342-1348, 2008. (32 refs.)

The authors assess the ability of toenail nicotine levels as a biomarker to predict incident coronary heart disease (CHD). A nested case-control study was carried out among 62,641 women aged 36-61 years in the Nurses' Health Study cohort who provided toenail clippings in 1982. Between 1984 and 1998, 905 incident CHD cases were diagnosed and matched with two controls by age and date of toenail collection. Using multivariate logistic regression analyses, the authors found a statistically significant dose-response association between increasing toenail nicotine levels and risk of CHD ($p(\text{trend}) < 0.0001$); women in the highest quintile had a relative risk of 3.44 (95% confidence interval (CI): 2.56, 4.62) compared with women in the lowest quintile. With each increase in the log-transformed unit of continuous toenail nicotine levels, there was a 42% increase in the risk of CHD (relative risk = 1.42, 95% CI: 1.33, 1.52). The association remained significant when the number of cigarettes smoked and passive smoking were included as covariates (relative risk = 1.12, 95% CI: 1.01, 1.24). In conclusion, toenail nicotine levels are predictive of CHD among women independent of other risk factors and remained significant even after adjustment for history of cigarette smoking. Copyright 2008, Oxford University Press.