

Accidental ecstasy poisoning in a toddler.

Melian AM; Burillo-Putze G; Campo CG; Padron AG; Ramos CO. *Pediatric Emergency Care* 20(8): 534-535, 2004. (9 refs.)

A child of 14 months accidentally swallowed a portion of an Ecstasy pill. Forty minutes after ingestion, he started a generalized convulsion. He also presented hyperthermia (38 degrees C), hypertension, tachycardia (130 bpm), ventricular extrasystoles, tachypnea (50 rpm), and mydriasis. At the hospital 5 hours later, the urine levels of amphetamine/methamphetamine were >16 mg/L. He was treated with general support measures and benzodiazepines intravenously and admitted to the pediatric intensive care unit. During the first 12 hours, he continued with hypertension, tachycardia, and long periods of trigeminy, without hemodynamic repercussion. He was discharged fully recovered. Gas chromatography/mass spectrometry analysis (8 hours after ingestion) showed a serum level of 3,4 methylenedioxymethylamphetamine (MDMA) of 0.591 mg/L. The 3 cases described in the literature have shown a good evolution of Ecstasy poisoning in toddlers and infants, despite an initial critical situation. Regarding adults, the toddler intoxication seems to present symptoms sooner (20 to 30 minutes), having as an initial manifestation convulsions. However, great care must be taken on accidental ingestion of these attractive design pills. Copyright 2004, Lippincott, Williams & Wilkins.

Alcohol continues to affect sleepiness related driving impairment, when breath alcohol levels have fallen to near-zero.

Barrett PR; Horne JA; Reyner LA. *Human Psychopharmacology: Clinical and Experimental* 19(6): 421-423, 2004. (6 refs.)

Epidemiological findings point to very low blood alcohol levels heightening the risk of sleep-related fatal road crashes. This was further assessed using a full sized interactive car simulator. Twenty, sleep restricted, healthy young men underwent a 2 h simulated afternoon monotonous drive, having previously consumed nil alcohol or 3 units >90 min previously, and having near-zero breath alcohol (BrACs) at the start of the drive. In a repeated

measures, double-blind, balanced design, driving performance, subjective sleepiness and EEG were monitored throughout. Compared with nil alcohol, the alcohol condition initially increased sleepiness-related driving impairment. However, this was not mirrored by subjective sleepiness or EEG. An unexpected reversal (i.e. improvement) in driving impairment occurred with the alcohol group, in the second hour of the drive. This was supported by a trend for improved subjective alertness. Alcohol continued to interact with sleepiness-related driving impairment after BrACs had reached zero. However, a lack of subjective perception of increased sleepiness, at this time, further points to the dangerous combination of even modest alcohol intake and sleepiness, and confirms the road crash findings. BrACs are a poor guide to driver impairment. Copyright 2004, John Wiley and Sons.

Alcohol drinking may increase risk of breast cancer in men: A European population-based case-control study.

Guenel P; Cyr D; Sabroe S; Lyng E; Merletti F; Ahrens W et al. *Cancer Causes and Control* 15(5): 571-580, 2004. (29 refs)

Objective: It has been estimated that alcohol drinking increases the risk of breast cancer in women by approximately 7% for each increment of 10 g alcohol per day. However, the few studies conducted on breast cancer among men have failed to detect an association with quantitative measures of alcohol drinking, even if the alcohol intake is generally higher in men than in women. On the other hand, increased risks of male breast cancer were inconsistently reported in alcoholics or patients with liver cirrhosis. We have investigated the role of alcohol drinking in male breast cancer using data collected in a population-based case-control study on seven rare cancers, conducted in Denmark, France, Germany, Italy, and Sweden. Methods: The cases were 74 histologically verified male breast cancer patients aged 35-70 years. The controls (n = 1432) selected from population registers, and frequency-matched to the cases by age group and geographic area. To check for consistency, a separate analysis was conducted using as controls the patients with a rare cancer other than the breast recruited simultaneously in the European study (n = 519 men).

Results: Based on population controls, the risk of developing breast cancer in men increased by 16% (95% CI: 7-26%) per 10, g alcohol/day ($p < 0.001$). An odds ratio of 5.89 (95% CI: 2.21-15.69) was observed for alcohol intake greater than 90 g per day, as compared with light consumers (< 15 g per day). Similar associations were observed when other rare cancers patients were used as controls. Conclusion: We found that the relative risk of breast cancer in men is comparable to that in women for alcohol intakes below 60 g per day. It continues to increase at high consumption levels not usually studied in women. Copyright 2004, Kluwer Academic.

Alcohol use and sudden infant death syndrome.

Friend KB; Goodwin MS; Lipsitt LP. *Developmental Review* 24(3): 235-251, 2004. (70 refs.)

Despite general evidence of fetal toxicities associated with sudden infant death syndrome (SIDS), there has been limited research focusing on the effects of parental alcohol use on SIDS occurrence, either directly or in interaction with other risk conditions. The purpose of this paper is to review the literature on parental, especially maternal, alcohol use and SIDS. We present a model illustrating the possible association of alcohol exposure with SIDS and then use this model to organize study findings. Results show that, despite some ambiguities, intrauterine alcohol exposure is associated with SIDS. Parental postnatal use appears to be linked as well. We conclude that alcohol ingestion is a presumptive risk factor weakening an infant's life-saving responses, and should be more rigorously studied in order to develop and implement appropriate public-health-based interventions. Copyright 2004, Elsevier Science.

Assessing methylphenidate preference in ADHD patients using a choice procedure.

Fredericks EM; Kollins SH. *Psychopharmacology* 175(4): 391-398, 2004. (66 refs.)

Rationale: Methylphenidate (MPH) is widely used in the treatment of attention deficit hyperactivity disorder (ADHD) and is associated with positive clinical effects across a wide range of domains. Despite the clinical effectiveness of MPH, concern has arisen with respect to its abuse potential. Objectives: To assess MPH preference in adults diagnosed with ADHD using a choice procedure and to evaluate the relationship among drug preference, therapeutic efficacy, and abuse potential in a clinical sample. Methods: Participants were ten volunteers (ages 18-22 years) with ADHD who were receiving MPH treatment. Preference was assessed using a double-blind choice

procedure with four sampling sessions wherein subjects received either placebo or MPH and eight choice sessions when they chose either capsule or no capsules. Results: Overall, MPH was chosen significantly more often than placebo ($\chi^2=52.5$; $P<0.001$) and participants were equally separated into groups of those who chose MPH reliably (MPH choosers) and those who did not (MPH non-choosers). MPH decreased ADHD symptoms and resulted in lower ratings of stimulant effects among MPH choosers. MPH choosers also reported higher levels of baseline ADHD symptoms. Conclusions: Despite higher preference of MPH than placebo in this clinical sample, other measures of abuse potential were not elevated, and MPH choosers were more symptomatic than non-choosers. As such, MPH preference in ADHD populations likely reflects therapeutic efficacy rather than abuse potential. Future work should examine MPH choice in diagnosed and non-diagnosed populations to further explore the role of clinical efficacy in the preference of this stimulant drug. Copyright 2004, Springer.

Beyond the K-hole: A 3-year longitudinal investigation of the cognitive and subjective effects of ketamine in recreational users who have substantially reduced their use of the drug.

Morgan CJA; Monaghan L; Curran HV. *Addiction* 99(11): 1450-1461, 2004. (47 refs.)

Rationale: Ketamine is a dissociative anaesthetic that is also a drug of abuse. Previous studies have demonstrated persisting episodic and semantic memory impairments in recreational ketamine users 3 days after taking ketamine. However, the degree to which these deficits might be reversible upon reduction or cessation of ketamine use was not known. Objective: To follow-up a population of ketamine users tested 3 years previously and examine whether impairments observed 3 days after drug use are enduring or reversible. Methods: Eighteen ketamine users and 10 polydrug controls from studies conducted between 3 and 4 years earlier were re-tested on the same battery of cognitive tasks and subjective measures. These tapped episodic, semantic and working memory and executive and attentional functioning. Subjective schizotypal, dissociative, mood and bodily symptoms were also examined and a drug use history recorded. Results: The ketamine users had reduced their frequency of use of ketamine by an average of 88.3%. Performance of ketamine users on tasks tapping semantic memory had improved and this improvement was correlated with their reduction in ketamine use. On tasks tapping episodic memory and

attentional functioning, ketamine users still showed deficits compared to polydrug controls. Higher levels of schizotypal symptoms and perceptual distortions were exhibited by the ketamine group, although dissociative symptoms were similar to controls. Conclusions: These findings indicate that semantic memory impairments associated with recreational ketamine are reversible upon marked reduction of use; however, impairments to episodic memory and possibly attentional functioning appear long-lasting. In addition, schizotypal symptoms and perceptual distortions may persist after cessation of ketamine use. Ketamine users, or potential users, should be aware of the enduring effects of this drug on aspects of memory and subjective experience. Copyright 2004, Society for the Study of Addiction to Alcohol and Other Drugs.

A critical review of caffeine withdrawal: Empirical validation of symptoms and signs, incidence, severity, and associated features. (review).

Juliano LM; Griffiths RR. *Psychopharmacology* 176(1): 1-29, 2004. (139 refs.)

Rationale: Although reports of caffeine withdrawal in the medical literature date back more than 170 years, the most rigorous experimental investigations of the phenomenon have been conducted only recently. Objectives: The purpose of this paper is to provide a comprehensive review and analysis of the literature regarding human caffeine withdrawal to empirically validate specific symptoms and signs, and to appraise important features of the syndrome. Methods: A literature search identified 57 experimental and 9 survey studies on caffeine withdrawal that met inclusion criteria. The methodological features of each study were examined to assess the validity of the effects. Results: Of 49 symptom categories identified, the following 10 fulfilled validity criteria: headache, fatigue, decreased energy/activeness, decreased alertness, drowsiness, decreased contentedness, depressed mood, difficulty concentrating, irritability, and foggy/not clearheaded. In addition, flu-like symptoms, nausea/vomiting, and muscle pain/stiffness were judged likely to represent valid symptom categories. In experimental studies, the incidence of headache was 50% and the incidence of clinically significant distress or functional impairment was 13%. Typically, onset of symptoms occurred 12-24 h after abstinence, with peak intensity at 20-51 h, and for a duration of 2-9 days. In general, the incidence or severity of symptoms increased with increases in daily dose; abstinence from doses as low as 100 mg/day produced symptoms. Research is reviewed indicating that expectancies are not a prime determinant of caffeine withdrawal and that avoidance of withdrawal

symptoms plays a central role in habitual caffeine consumption. Conclusions: The caffeine-withdrawal syndrome has been well characterized and there is sufficient empirical evidence to warrant inclusion of caffeine withdrawal as a disorder in the DSM and revision of diagnostic criteria in the ICD. Copyright 2004, Springer.

Effects of alcohol and cigarette consumption on human seminal quality.

Martini AC; Molina RI; Estofan D; Senestrari D; de Cuneo MF; Ruiz RD. *Fertility and Sterility* 82(2): 374-377, 2004. (29 refs.)

Objective: To evaluate the effects of alcohol or cigarette consumption on seminal parameters in a large population of men attending an andrology laboratory. Design: Analysis of ten years of data (1990-1999). Setting: Andrology and Reproduction Laboratory (Cordoba, Argentina). Patient(s): Patients (3,976) were grouped according to nonsmokers; less than or equal to 20 cigarettes/day; >20 cigarettes/day; nonalcohol consumers; less than or equal to 500 mL of wine (similar to 52 g of ethanol) or equivalent/day; and >500 mL of wine or equivalent/day. Patients who drank alcohol and smoked were also considered. Intervention(s): A questionnaire was voluntarily filled out by patients. It provided data on drug consumption and genitourinary diseases. Main Outcome Measure(s): Seminal volume, sperm concentration, motility, viability, and morphology. Results: No statistical differences in seminal parameters were found between the degrees of alcohol or tobacco consumption; so, independently of the degree of consumption patients were considered as smokers or alcohol consumers. Conclusion(s): Alcohol or cigarette consumption did not alter the seminal parameters. Nevertheless, when the patients with these two habits were compared to those without these habits, a significant reduction in seminal volume, sperm concentration, percentage of motile spermatozoa, and a significant increase of the nonmotile viable gametes were detected. The synergic or additive effect of these two toxic habits is discussed. Copyright 2004, American Society for Reproductive Medicine.

Neonatal abstinence syndrome in methadone-exposed infants is altered by level of prenatal tobacco exposure.

Choo RE; Huestis MA; Schroeder JR; Shin AS; Jones HE. *Drug and Alcohol Dependence* 75(3): 253-260, 2004. (40 refs.)

Maternal tobacco consumption during pregnancy has been associated with lower birth weight infants,

preterm births, intrauterine growth retardation, smaller head circumference and increase in morbidity, yet few studies have examined the role tobacco has on the opiate neonatal abstinence syndrome (NAS). This study examined the effect of prenatal tobacco exposure on NAS for infants born to mothers maintained on methadone during gestation. Twenty-nine pregnant women and their newborn infants participated in this study. Tobacco exposure was based on maternal self-report with 16 women reporting cigarette consumption of 10 or less per day and 13 reporting smoking 20 cigarettes or more a day. The onset, peak, and duration of NAS were examined. Results showed that infants born to mothers who reported smoking 20 or more cigarettes per day had significantly higher NAS peak scores of 9.8 versus 4.8, and took longer to peak (113.0 h versus 37.8 h), than light smokers of 10 or fewer cigarettes per day. We concluded that tobacco use in conjunction with methadone plays an important role in the timing and severity of NAS in prenatally exposed infants. Copyright 2004, Elsevier Science.

Residual neuropsychological effects of illicit 3,4-methylenedioxymethamphetamine (MDMA) in individuals with minimal exposure to other drugs.

Halpern JH; Pope HG; Sherwood AR; Barry S; Hudson JI; Yurgelun-Todd D. *Drug and Alcohol Dependence* 75(2): 135-147, 2004. (75 refs.)

Background: A substantial literature suggests that users of illicit 3,4-methylenedioxymethamphetamine (MDMA or "ecstasy") display residual cognitive deficits. Most MDMA users, however, use other illicit drugs as well, so it is difficult to be certain that these deficits are due to MDMA, as opposed to other drug use or additional confounding factors. Methods: We administered a battery of neuropsychological tests to 23 young MDMA users who reported minimal exposure to any other drugs, including alcohol, and to 16 comparison individuals equally involved with the rave subculture, but reporting no MDMA use. We compared the groups by regression analyses adjusting for numerous potentially confounding variables. To test for a possible dose-response effect, we also performed a median split of 12 moderate MDMA users (22-50 lifetime uses) and 11 heavy users (60-450 uses), and compared these subgroups with non-users. Results: MDMA users as a whole performed worse

than non-users on most test measures, but these comparisons rarely reached statistical significance. This picture changed markedly in the subgroup analysis: although moderate users displayed virtually no differences from non-users on any measures, the heavy users displayed significant deficits on many measures, particularly those associated with mental processing speed and impulsivity. These differences did not appear explainable by differences in family-of-origin variables, verbal IQ, levels of depression, or time since last MDMA use. Conclusions: The presence of residual cognitive deficits, even among unusually "pure" frequent users of illicit MDMA, analyzed with adjustment for confounding variables, augments the evidence that MDMA itself, rather than some associated factor, is responsible for the deficits observed. Copyright 2004, Elsevier Science.

Transfer of naltrexone and its metabolite 6,beta-naltrexol into human milk.

Chan CF; Page-Sharp M; Kristensen JH; O'Neil G; Ilett KF. *Journal of Human Lactation* 20(3): 322-326, 2004. (16 refs.)

The excretion of naltrexone and its primary metabolite 6,beta-naltrexol in breast milk from a 30-year-old lactating opiate addict undergoing oral naltrexone pharmacotherapy (5 mg/d) was studied. Concentrations of naltrexone and 6,beta-naltrexol in serial milk and plasma samples taken over a 19.3-hour period of a dose interval at steady state were measured by gas chromatography. The calculated infant dose relative to the maternal weight was 0.03% for naltrexone and 0.83% (as naltrexone equivalents) for 6,beta-naltrexol. Total relative infant dose estimated for the complete 24-hour dose interval was 1.06%. Her 6-week-old breastfed infant was healthy, achieving expected milestones, and showed no adverse effects. Only 6,beta-naltrexol was detected in infant plasma and at a very low concentration of 1.1 mug/L. Use of naltrexone during breastfeeding should be undertaken only after an individual risk-benefit analysis. Copyright 2004, Sage Publications Inc.