

"Chasing the dragon": Imaging of heroin inhalation leukoencephalopathy.

Hagel J; Andrews G; Vertinsky T; Heran MKS; Keogh C. *Canadian Association of Radiologists Journal* 56(4): 199-203, 2005. (9 refs.)

"Chasing the dragon" refers to the inhalation of heroin pyrolysate vapors produced when the freebase form of heroin is heated. Inhalation of these vapors can result in a rare toxic spongiform leukoencephalopathy. The patients may progress through 3 defined clinical stages, with one-quarter reaching the terminal stage, which invariably leads to death. Imaging and, in particular, magnetic resonance imaging (MRI) demonstrates white matter findings that are felt to be specific for this entity and essential in its early diagnosis. We present the typical imaging findings in a pictorial essay format, using images taken from 9 patients who presented within an 18-month period at UBC-affiliated hospitals. These findings include low computed tomography (CT) attenuation and high T2 MRI signal most commonly in the posterior cerebral and cerebellar white matter, cerebellar peduncles, splenium of the corpus callosum, and posterior limb of the internal capsules. In addition, there is often selective, symmetric involvement of the corticospinal tract, the medial lemniscus, and the tractus solitarius. We also present the variable diffusion-weighted imaging and apparent diffusion coefficient findings from 4 of our patients, which to our knowledge, have not been described in the literature. Copyright 2005, Canadian Society of Clinical Investigation.

Acute medical problems due to Ecstasy use: Case-series of emergency department visits.

Liechti ME; Kunz I; Kupferschmidt H. *Swiss Medical Weekly* 135(43-44): 652-657, 2005. (18 refs.)

Study aim: To describe the clinical characteristics of Ecstasy (3,4-Methylenedioxymethamphetamine, MDMA) toxicity. Methods: Retrospective case-study of 52 self-reported Ecstasy intoxications presenting to our Emergency Department (ED) between January 2001 and December 2003. Results: Most patients ingested Ecstasy together with other substances, including alcohol (51.9%) or other illicit drugs (71.1%). Medical problems leading to ED presentation were collapse or loss of consciousness (36.5%), palpitations (19.2%), dizziness or weakness (15.4%),

and anxiety (13.5%). When other drugs were used in combination with Ecstasy the clinical presentation significantly changed. Panic reactions were observed in 4 of 13 patients with cocaine co-use (30.7%), compared to 3 of 39 patients without cocaine use (7.7%). Deep coma was found in 11 of 16 patients with co-use of gamma-hydroxybutyrate (GHB) or opiates (68.8%) but in none of the 36 patients who took Ecstasy without these drugs. Most patients were monitored in the ED. Six patients (11.5%) were transferred to an intensive care unit. Medical complications were severe in five patients and included cardiac arrest, hyperthermia, rhabdomyolysis, disseminated intravascular coagulation, renal insufficiency and liver failure, seizures, and one fatal outcome. Conclusions. The clinical picture of Ecstasy related problems is complicated by multiple drug ingestion. Co-use of cocaine induces panic reactions. Co-use of GHB or opiates results in depressed levels of consciousness. Copyright 2005, Swiss Medical Publishers.

Areca-nut abuse and neonatal withdrawal syndrome.

Lopez-Vilchez MA; Seidel V; Farre M; Garcia-Algar O; Pichini S; Mur A. *Pediatrics* 117(1): E129-E131, 2006. (12 refs.)

Areca-nut chewing occurs widely in South Asia and the Indian subcontinent. Here we present a case of neonatal withdrawal syndrome in an infant born to a woman who was a chronic areca-nut user. Arecoline, the principal neuroactive alkaloid in areca nuts, was found in the mother's placenta. Copyright 2006, American Academy of Pediatrics.

Caffeine use in sports, pharmacokinetics in man, and cellular mechanisms of action. (review).

Magkos F; Kavouras SA. *Critical Reviews in Food Science and Nutrition* 45(7): 535-562, 2005. (390 refs.)

Caffeine is the most widely consumed psychoactive 'drug' in the world and probably one of the most commonly used stimulants in sports. This is not surprising, since it is one of the few ergogenic aids with documented efficiency and minimal side effects. Caffeine is rapidly and completely absorbed by the gastrointestinal tract and is readily distributed throughout all tissues of the body. Peak plasma

concentrations after normal consumption are usually around 50 µM, and half-lives for elimination range between 2.5-10 h. The parent compound is extensively metabolized in the liver microsomes to more than 25 derivatives, while considerably less than 5% of the ingested dose is excreted unchanged in the urine. There is, however, considerable inter-individual variability in the handling of caffeine by the body, due to both environmental and genetic factors. Evidence from in vitro studies provides a wealth of different cellular actions that could potentially contribute to the observed effects of caffeine in humans in vivo. These include potentiation of muscle contractility via induction of sarcoplasmic reticulum calcium release, inhibition of phosphodiesterase isoenzymes and concomitant cyclic monophosphate accumulation, inhibition of glycogen phosphorylase enzymes in liver and muscle, non-selective adenosine receptor antagonism, stimulation of the cellular membrane sodium/potassium pump, impairment of phosphoinositide metabolism, as well as other, less thoroughly characterized actions. Not all, however, seem to account for the observed effects in vivo, although a variable degree of contribution cannot be readily discounted on the basis of experimental data. The most physiologically relevant mechanism of action is probably the blockade of adenosine receptors, but evidence suggests that, at least under certain conditions, other biochemical mechanisms may also be operational. Copyright 2005, Taylor & Francis.

Consumption of coffee, but not black tea, is associated with decreased risk of premenopausal breast cancer.

Baker JA; Beehler GP; Sawant AC; Jayaprakash V; McCann SE; Moysich KB. *Journal of Nutrition* 136(1): 166-171, 2006. (46 refs.)

Caffeine has been suggested as a possible risk factor for breast cancer, potentially through its effect of facilitating the development of benign breast disease. However, coffee and tea also contain polyphenols, which exhibit anticarcinogenic properties. A hospital-based, case-control study was conducted to evaluate the role of coffee, decaffeinated coffee, and black tea in breast cancer etiology. Study participants included 1932 cases with primary, incident breast cancer and 1895 hospital controls with nonneoplastic conditions. All participants completed a comprehensive epidemiological questionnaire. Among premenopausal women, consumption of regular coffee was associated with linear declines in breast cancer risk (P for trend = 0.03); consumers of ≥ 4 cups/d experienced a 40% risk reduction (odds ratio = 0.62, 95% CI 0.39-0.98). No clear associations between intake of black tea or

decaffeinated coffee and breast cancer risk were noted among premenopausal women, although black tea was associated with a protective effect unique to a subsample of cases with lobular histology. Among postmenopausal women, breast cancer risk was not associated with consumption of coffee, tea, or decaffeinated coffee. Results among postmenopausal women did not differ by histologic subtype. Our findings support a protective effect of coffee intake on premenopausal, but not postmenopausal breast cancer risk. Copyright 2006, American Society of Nutritional Science.

Dextromethorphan psychosis, dependence and physical withdrawal.

Miller SC. *Addiction Biology* 10(4): 325-327, 2005. (13 refs.)

As part of a synthesis of evidence regarding the abuse and addiction liability of dextromethorphan (DM), an over-the-counter cough medicine available in over 140 preparations, all uncommonly published case of dextromethorphan dependence (addiction) is described, with specific, rarely published complications. The individual was interviewed and several medical databases were also reviewed (Medline, 1966 -present; PubMed) for all content relating to the Keywords: dextromethorphan, abuse, dependence, cough medicine, addiction, withdrawal, psychosis. The patient evidenced history suggesting substance dependence, substance-induced psychosis and substance withdrawal in relation to DM. A literature review revealed that DM has specific serotonergic and sigma-1 opioidergic properties. Dextrolphan (DOR), the active metabolite of DM, has similar properties; however, DOR is a weaker sigma opioid receptor agonist, and a stronger NMDA receptor antagonist. DM and DOR display specific biological features of addiction, and are capable of inducing specific psychiatric sequelae. A specific, reproducible toxidrome with significant psychiatric effects occurred, when DM was abused at greater than indicated doses, with more profound and potentially life-threatening effects at even higher doses. DM withdrawal appears evident. DMs active metabolite, DOR, has pharmacodynamic properties and intoxication effects similar to dissociatives, and may be more responsible for the dissociative effect that this DM abuser sought. However, it is this same metabolite that may be fraught with the potentially life-threatening psychoses and dissociative-induced accidents, as well as addiction. While DM has been hypothesized as the most commonly abused dissociative, health-care providers seem largely unaware of its toxidrome and addiction liability. Copyright 2005, Taylor and Francis Ltd.

Cannabis withdrawal among non-treatment-seeking adult cannabis users.

Copersino ML; Boyd SJ; Tashkin DP; Huestis MA; Heishman SJ; Dermand JC et al. *American Journal on Addictions* 15(1): 8-14, 2006. (26 refs.)

This study investigates the clinical significance of a cannabis withdrawal syndrome in 104 adult, nontreatment-seeking, primarily cannabis users who reported at least one serious attempt to stop using cannabis. Retrospective self-report data were obtained on eighteen potential cannabis withdrawal symptoms derived from the literature, including co-occurrence, time course, and any actions taken to relieve the symptom. Study findings provide evidence for the clinical significance of a cannabis withdrawal syndrome, based on the high prevalence and co-occurrence of multiple symptoms that follow a consistent time course and that prompt action by the subjects to obtain relief, including serving as negative reinforcement for cannabis use. Copyright 2006, American Academy of Psychiatrists in Alcoholism and Addictions.

Ethyl sulphate: A direct ethanol metabolite reflecting recent alcohol consumption.

Wurst FM; Dresen S; Allen JP; Wiesbeck G; Graf M; Weinmann W. *Addiction* 101(2): 204-211, 2006. (37 refs.)

Background: Ethyl sulphate (EtS), a direct ethanol metabolite, appears to offer potential as a biomarker for recent alcohol consumption. Although its window of assessment is similar to that of ethyl glucuronide (EtG), there are differences between the two markers in their pathways for formation and degradation. Aims: (a) To assess the excretion of EtS compared to EtG and ethanol in drinking experiments with healthy volunteers, and (b) to elucidate the possibility of using the two metabolites for monitoring abstinence in substance use disorder patients during rehabilitation treatment. Design, setting, participants (a) Nine drinking experiments were performed by six healthy volunteers (two females, four males), with a mean age of 34.1 years (20-62), average oral intake of 0.2 g/kg ethanol (0.1-0.61), and having 74 spot urine samples. (b) Thirty-six substance abuse patients (mean age 41.9 years, 20-59; 22 males, 14 females) in a rehabilitation programme after withdrawal, producing 98 urine samples. Ethyl glucuronide and ethyl sulphate were measured using liquid chromatography tandem mass spectrometry (LC-MS/MS) using d(5)-EtG and d(5)-EtS, respectively, as an internal standard. Findings: (a) Volunteers: EtG and EtS were detectable for up to 36 hours and reached the limits of determination in urine at 20.6 hours and 21.2 hours (median), respectively, after ethanol intake. EtG-100 (standardized to a

creatinine of 100 mg/dl) reached its maximum level at 2.8 hours and EtS-100 at 2.1 hours (median) after the beginning of the experiment. Of the ethanol ingested, 0.022% was excreted as EtS in one volunteer. Eight samples were positive for EtS only and six for EtG only. Spearman's rank correlation coefficients of 0.84 ($P < 0.0001$) between EtG and EtS and 0.87 ($P < 0.0001$) between EtG-100 and EtS-100 were found. (b) Patients: of the 98 urine samples evaluated, 27 were positive for EtS and of these only 20 were also positive for EtG. Spearman's rank correlation coefficients of 0.84 ($P < 0.0001$) between EtG and EtS and 0.82 ($P < 0.0001$) between EtG-100 and EtS-100 were found. Conclusions: The data from patients and volunteers suggest that the direct ethanol metabolite ethyl sulphate has the potential to serve as a biomarker of recent ethanol intake. Because EtG and EtS are formed via different pathways they might be used conjointly, thereby increasing sensitivity. Copyright 2006, Society for Study of Addiction to Alcohol and Other Drugs.

Methadone versus buprenorphine in pregnant addicts: A double-blind, double-dummy comparison study.

Fischer G; Ortner R; Rohrmeister K; Jagsch R; Baewert A; Langer M et al. *Addiction* 101(2): 275-281, 2006. (33 refs.)

Aims: To evaluate the efficacy and safety of methadone versus buprenorphine treatment in pregnant opioid-dependent women. Design: Randomized, double-dummy, double-blind, flexible-dosing comparison study. Setting Addiction Clinic at the Medical University of Vienna, Austria. Participants: Eighteen women were assigned randomly to receive either methadone ($n = 9$) or buprenorphine ($n = 9$) during weeks 24-29 of pregnancy. After dropouts, data were available from 14 cases (six in the methadone and eight in the buprenorphine group). Intervention Sublingual buprenorphine tablets (8-24 mg/day) or oral methadone solution (40-100 mg/day), with matched placebos. Measurements: Mothers: retention in treatment, urine toxicology and nicotine use. Neonates: Routine birth data, neonatal abstinence syndrome (NAS) in severity and duration. Findings There was somewhat greater retention in the buprenorphine group but significantly lowered use of additional opioids in the methadone group ($P = 0.047$). Neonates: There was earlier onset of NAS in neonates born to the methadone (mean 60 hours) than to the buprenorphine groups (mean 72 hours after last medication); 43% did not require NAS-treatment with short treatment duration in both groups (mean 5 days). Conclusion: This preliminary study had limited power to detect differences but the trends observed suggest

this kind of research is practicable and that further studies are warranted. Copyright 2006, Society for the Study of Addiction to Alcohol and Other Drugs.

Multiple cardiac arrests following an overdose of caffeine complicated by penetrating trauma.

Emohare O; Ratnam V. *Anaesthesia* 61(1): 54-56, 2006. (17 refs.)

A 28-year-old man was admitted following a massive caffeine overdose and a self inflicted gunshot wound in an apparent suicide attempt. Although initially stable on admission, he subsequently suffered multiple cardiac arrests and generalised seizures within 23 h of admission; over the next 48 h, he developed rhabdomyolysis. The importance of early management in caffeine overdose is highlighted. Copyright 2006, Association of Anaesthetists of Great Britain and Ireland.

Preliminary evidence that prenatal alcohol damage may be visible in averaged ultrasound images of the neonatal human corpus callosum.

Bookstein FL; Connor PD; Covell KD; Barr HM; Gleason CA; Sze RW et al. *Alcohol* 36(3): 151-160, 2005. (38 refs.)

Brain damage consequent to prenatal alcohol exposure can be detected by measurements of the corpus callosum in the midline magnetic resonance (MR) brain image in adolescents and adults. The present article extends this finding into the neonatal period, when the power of detection to ameliorate the quality of the child's future life is greatest. The midline corpus callosum of the very young infant can be located reliably in multiple frames of clinical transfontanelle ultrasound. We studied a sample of 18 children aged 17 weeks or less, 7 of whom were exposed to high levels of alcohol prenatally and 11 of whom were not exposed or only minimally exposed. The midline callosum of each child was imaged up to 50 times by a standard clinical device, and coplanar subsets of these series were averaged with reference to fiducial image structures. On each average image four semilandmark points were set and their configuration quantified by standard landmark methods. The angle between the terminal bulb of splenium and the long axis of the callosal outline classifies four of the seven exposed infants as different from all 11 of the unexposed infants. This simple angle measurement upon averaged ultrasound images of the human neonatal midline corpus callosum, perhaps a version of the long-sought "biomarker of prenatal alcohol damage," may be able to discriminate baby brains affected by prenatal

alcohol exposure from those that were unaffected. Copyright 2005, Elsevier Science Inc.

Psychopharmacology of the hallucinogenic sage *Salvia divinorum*.

Prisinzano TE. *Life Sciences* 78(5): 527-531, 2005. (32 refs.)

At present, the Mexican mint *Salvia divinorum* is an unregulated hallucinogen. This has resulted in various on-line botanical companies advertising and selling *S. divinorum* as a legal alternative to other regulated plant hallucinogens. It is predictable that its misuse will increase rapidly. The active ingredient in *S. divinorum* is the neoclerodane diterpene, salvinorin A (1a), which has been shown to be a K agonist both in vitro and in vivo. This review will cover the current state of research into the psychopharmacology of *S. divinorum*. Copyright 2005, Elsevier Science.

Study of the efficacy of fluoxetine and clomipramine in the treatment of premature ejaculation after opioid detoxification.

Abdollahian E; Javanbakht A; Javidi K; Samari AA; Shakiba M; Sargolzaee MR. *American Journal on Addictions* 15(1): 100-104, 2006. (8 refs.)

Premature ejaculation is a common symptom that can provoke relapse in formerly opioid-dependent men after detoxification. The purpose of this study was to compare the efficacy of clomipramine and fluoxetine for the treatment of premature ejaculation in formerly opioid-dependent men after detoxification. Sixty opium-detoxified men with A & B DSM-IV diagnostic criteria for premature ejaculation participated in a prospective two-week descriptive inferential clinical trial after a two-week washout period. The subjects did not consume any other medications but naltrexone for maintenance of an opium-free state. The subjects were randomly divided into two groups of thirty subjects, one group received fluoxetine (10 mg/d for the first and 20 mg/d for the second week), and the other received clomipramine (25 mg/d for the first and 50 mg/d for the second week). Twenty five subjects did not continue the treatment and were lost to follow-up. The severity of premature ejaculation did not show any relation to the subjects' age, education level, opioid type, or route of abuse. Fluoxetine and clomipramine both can be equally used in the treatment of premature ejaculation following opioid detoxification, depending on their side effects and other symptoms in the subjects. Copyright 2006, American Academy of Psychiatrists in Alcoholism and Addictions.