

An overview of medications for the treatment of alcohol withdrawal and alcohol dependence with an emphasis on the use of older and newer anticonvulsants.

Ait-Daoud N; Malcolm RJ; Johnson BA. *Addictive Behaviors* 31(9): 1628-1649, 2006. (87 refs.)

There is a growing interest in the development of new pharmacological tools for treating alcohol withdrawal and dependence. A number of anticonvulsants including valproate and carbamazepine have been shown to be safe and effective alternatives to benzodiazepines for treating alcohol withdrawal. These agents are relatively safe, are free from demonstrated abuse liability, and do not usually potentiate the psychomotor and cognitive effects of alcohol. For the treatment of alcohol dependence, there is a growing literature on the utility of medications that have neurochemical effects at opioid, serotonergic, GABAergic, and glutamate receptors. Furthermore, as a class of medication, there appears to be a growing interest in investigating the utility of novel anticonvulsants such as topiramate for the treatment of alcohol dependence. Copyright 2006, Elsevier Science.

An ethanol protocol to prevent alcohol withdrawal syndrome.

Dissanaike S; Halldorsson A; Frezza EE; Griswold J. *Journal of the American College of Surgeons* 203(2): 186-191, 2006. (18 refs.)

BACKGROUND: Alcohol withdrawal syndrome (AWS) occurs in dependent patients during the initial period of sudden onset abstinence. It is usually manifested by mild symptoms such as disorientation, agitation, and tachycardia, but, if untreated, can lead to severe confusion, seizures, and even cardiovascular collapse. Prevention of AWS has been shown to improve morbidity and mortality and shorten hospital and ICU stays. We examined the efficacy of ethanol as a method of prophylaxis. **STUDY DESIGN:** Our patient population was divided into two groups. Group I consisted of surgical patients receiving alcohol prophylaxis for AWS between January 2001 and July 2004 (n = 124), as identified by retrospective chart review. We then developed a protocol for the initiation, dosage, and weaning of intravenous ethanol in patients at risk for AWS, based on blood alcohol

levels and clinical assessment of withdrawal symptoms and signs. Group 2 consisted of all patients treated prospectively with this protocol during the subsequent year (n = 76). Patients who did not fit inclusion criteria for the protocol were excluded from analysis, resulting in 92 and 68 patients in group I and group 2, respectively. We compared initiation criteria, efficacy, dosage, route, duration, and referral pattern to the substance abuse clinic before and after initiation of the protocol. **RESULTS:** Our initial use of intravenous ethanol was very variable in dosage, duration, and indication. The protocol decreased the duration of treatment between the two groups from 7 days to a mean of 3 days. The failure rate dropped from 20% to 7%. Referral to the substance abuse clinic rose from 7.6% to 20%. The only complication was asymptomatic hyponatremia in one patient. **CONCLUSIONS:** Intravenous ethanol is a viable option for AWS prophylaxis when administered in a systematic protocol. Copyright 2006, Elsevier Science.

Analysis of the impurities in the methamphetamine synthesized by three different methods from ephedrine and pseudoephedrine.

Lee JS; Han EY; Lee SY; Kim EM; Park YH; Lim MA et al. *Forensic Science International* 161(2-3): 209-215, 2006. (24 refs.)

Organic impurities of methamphetamine may show different patterns by synthesis. In the present study, we tried to find the impurities reflecting the conditions of synthesis by comparing impurity patterns of the methamphetamine samples synthesized by different methods. Sixteen methamphetamine samples were synthesized from ephedrine and pseudoephedrine by the three different manufacturing methods of Emde, Nagai and Moscow. The synthesized samples were extracted with ethyl acetate containing four internal standards, and the patterns of the organic impurities were investigated by GC-MS and GC-FID. Through the investigation, we found 10 peaks appearing in the latter part of GC chromatograms are characteristic to synthesis. The areas of the selected peaks were converted to the variables suitable for the statistical calculation, and the synthesized samples could be classified into four groups through the resultant cluster analysis. Copyright 2006, Elsevier Science.

Comparison of the combined marker GGT-CDT and the conventional laboratory markers of alcohol abuse in heavy drinkers, moderate drinkers and abstainers.

Hietala J; Koivisto H; Anttila P; Niemela O. *Alcohol and Alcoholism* 41(5): 528-533, 2006. (29 refs.)

Aims: A combined index based on gamma-glutamyltransferase (GGT) and carbohydrate-deficient transferrin (CDT) measurements (GGT-CDT) has been recently suggested to improve the detection of excessive ethanol consumption. The aim of this work was to compare GGT-CDT with the conventional markers of alcohol abuse in individuals with a wide variety of alcohol consumption. **Methods:** A cross-sectional and follow-up analysis was conducted in a sample of 165 heavy drinkers, consuming 40-540 g of ethanol per day, and 86 reference individuals who were either moderate drinkers (n = 51) or abstainers (n = 35). **Results:** GGT-CDT (5.35 +/- 1.08) in the heavy drinkers was significantly higher than in the reference individuals (3.30 +/- 0.37). The sensitivity of GGT-CDT (90%) in correctly classifying heavy drinkers exceeded that of CDT (63%), GGT (58%), mean corpuscular volume (MCV) (45%), aspartate aminotransferase (AST) (47%), and alanine aminotransferase (ALT) (50%), being also essentially similar for alcoholics with (93%) or without (88%) liver disease. When comparing the data using either moderate drinkers or abstainers as reference population, the sensitivity of GGT-CDT, CDT, and ALT remained unchanged whereas the sensitivity of GGT, MCV, and AST was found to show variation. **Conclusions:** GGT-CDT improves the sensitivity of detecting excessive ethanol consumption as compared with the traditional markers of ethanol consumption. These findings should be considered in the assessment of patients with alcohol use disorders. Copyright 2006, Oxford University Press.

Drug interactions between psychoactive substances and antiretroviral therapy in individuals infected with human immunodeficiency and hepatitis viruses. (review).

Neuman MG; Monteiro M; Rehm J. *Substance Use & Misuse* 41(10-12): 1395-1463, 2006. (412 refs.)

The liver disease characteristic of alcohol dependence encompasses three main related entities: steatosis, alcoholic hepatitis, and cirrhosis. Alcoholic cirrhosis is a leading cause of global morbidity and mortality. Alcohol intake among injecting drug users is a major contributor to transmission of viral infections, such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C viruses (HCV). HIV and HCV coinfecting patients develop liver diseases earlier

and more severely than the mono-infected individuals, including hepatocellular carcinoma. Interactions exist between the therapeutic drugs used to minimize and control the drug and alcohol dependence. Furthermore, drug-drug interactions occur between the highly active antiretroviral therapy (HAART) and alcohol, different HAART components and methadone, or each one of the therapies with the other, thus contributing to a higher toxicity level. With the evolution of effective antiretroviral therapy, survival of persons with HIV, and the syndrome it causes, acquired immunodeficiency syndrome (AIDS) has increased dramatically. Drug-drug interactions may appear between alcohol and anti-HBV or anti-HCV, therapy in the presence or absence of anti-HIV therapy. Several other medical-, social-, and drug-related factors of this population have to be considered when providing HAART. Because many coinfecting patients also have problems with substance use, dealing with their drug dependence is an important first step in an attempt to improve adherence to and tolerance of antiviral therapy. It is necessary to minimize the risk of liver disease acceleration and/or reinfection with hepatitis viruses. Knowledge of potential drug interactions between methadone, antiretroviral therapy, psychoactive drugs, and antipsychotics and the role of coinfection with HBV or HCV and the drugs used in eradicating viral hepatitis permits suitable antiretroviral combinations. Copyright 2006, Taylor & Francis.

Effects of preoperative smoking cessation on the incidence and risk of intraoperative and postoperative complications in adult smokers: A systematic review. (review).

Theadom A; Cropley M. *Tobacco Control* 15(5): 352-358, 2006. (42 refs.)

Objectives: To establish the effect of preoperative smoking cessation on the risk of postoperative complications, and to identify the effect of the timing of preoperative cessation. **Data sources:** The Cochrane Library Database, PsycINFO, EMBASE, Medline, and CINAHL databases were searched, using the terms: "smoking", "smoking-cessation", "tobacco-use", "tobacco-abstinence", "cigarette\$", "complication\$", "postoperative-complication\$", "preoperative", "perioperative" and "surg\$". Further articles were obtained from reference lists. The search was limited to articles on adults, written in English and published up to November 2005. **Study selection:** Prospective cohort designs exploring the effects of preoperative smoking cessation on postoperative complications were included. Two reviewers independently scanned abstracts of relevant articles to determine eligibility.

Lack of agreement was resolved through discussion and consensus. Twelve studies met the inclusion criteria. Data extraction: Methodological quality was assessed by both reviewers, exploring validation of smoking status, clear definition of the period of smoking cessation, control for confounding variables and length of follow-up. Data synthesis: Only four of the studies specified the exact period of smoking cessation, with six studies specifying the length of the follow-up period. Five studies revealed a lower risk or incidence of postoperative complications in past smokers than current smokers or reported that there was no significant difference between past smokers and non-smokers. Conclusions: Longer periods of smoking cessation appear to be more effective in reducing the incidence/risk of postoperative complications; there was no increased risk in postoperative complications from short term cessation. An optimal period of preoperative smoking cessation could not be identified from the available evidence. Copyright 2006, BMJ Publishing Group.

Drug-related overdoses within a medically supervised safer injection facility.

Kerr T; Tyndall MW; Lai C; Montaner JSG; Wood E. *International Journal of Drug Policy* 17(5): 436-441, 2006. (31 refs.)

Background: In September 2003, North America's first supervised injection facility (SIF) opened in Vancouver, Canada. We sought to examine the incidence and characteristics of overdose events at the SIF. Methods: The Vancouver SIF evaluation involves a comprehensive database within the SIF and the Scientific Evaluation of Supervised Injection (SEOSI) cohort consisting of 1046 SIF users. We examined the incidence and features of overdoses at the SIF and the responses made by SIF staff. Cox regression was used to examine factors associated with time to overdose among SEOSI participants. Results: Between 1 March 2004 and 30 August 2005, there were 336 overdose events at the SIF, yielding a rate of 1.33 (95% CI: 0.0-3.6) overdoses per 1000 injections. The most common indicator of overdose was depressed respiration (60%), and the most common intervention involved the administration of oxygen (87%). In total, 90 SEOSI participants had an overdose at the SIF during the study period. Factors independently associated with time to overdose included fewer years injecting (RH=0.98, 95% CI: 0.96-1.00 per year), daily heroin use (RH=1.82, 95% CI: 1.16-2.85), and having a history of overdose (RH = 1.92, 95% CI: 1.21-3.06). Conclusions: There have been a large number of overdoses within the SIF, and it is noteworthy that none of these overdoses resulted in a fatality. These

findings suggest that SIF can play a role in managing overdoses among IDU and indicate the need for further evaluation of the impact of SIF on morbidity and mortality associated with overdose. Copyright 2006, Elsevier Science.

Outcome after heroin overdose and cardiopulmonary resuscitation.

Boyd JJ; Kuisma MJ; Alaspaa AO; Vuori E; Repo JV; Randell TT. *Acta Anaesthesiologica Scandinavica* 50(9): 1120-1124, 2006. (27 refs.)

Background: The survival of heroin overdose patients resuscitated from cardiac arrest is reported to be poor. The aim of our study was to investigate the outcome and characteristics of survivors after cardiac arrest caused by heroin overdose. Methods: This was a retrospective study in a medium-sized city (population, 560,000). Between 1 January 1997 and 31 December 2000, there were 94 combined cardiac arrests caused by acute drug poisonings. The main outcome measure was survival to discharge. Results: Cardiopulmonary resuscitation was attempted in 19 heroin overdose patients (group A) and in 53 patients with cardiac arrest caused by other poisonings (group B). Three (16%) vs. six (11%) patients were discharged alive (group A vs. B, respectively). The survivors in group A had an Emergency Medical Service (EMS)-witnessed cardiac arrest or the Emergency Dispatching Centre was called before the arrest occurred. There was no statistically significant difference between the two groups in terms of survival. Survivors in both groups suffered from acute renal failure (two), hypoglycaemia (four) and hypothermia (three). Conclusion: Survival after cardiac arrest caused by heroin overdose is possible if the arrest is EMS witnessed or the Emergency Dispatching Centre is called before the cardiac arrest occurs. In comparison with cardiac arrests caused by other poisonings, there was no difference in survival. The incidence and mechanism of hypoglycaemia should be examined in further studies. Copyright 2006, Blackwell Publishing.

Prenatal drug exposure effects on subsequent vulnerability to drug abuse. (review).

Glantz MD; Chambers JC. *Development and Psychopathology* 18(3): 893-922, 2006. (253 refs.)

Research has shown that both prenatal alcohol and tobacco exposure are associated with increased risk of significant adverse medical, developmental, and behavioral outcomes including substance abuse. Research on the outcomes of prenatal exposure to illicit drugs (PNDE) has also found increased physical and behavioral problems for gestationally drug-exposed children. However, a clear picture has not

emerged on whether the consequences of PNDE are independent from those associated with having a substance abusing parent and whether PNDE increases vulnerability to drug abuse. Because of its typical co-occurrence with factors inherent in having a drug-abusing parent, PNDE is at least a marker of significant increased risk for a range of negative outcomes including greater vulnerability to substance abuse. Although a review of the relevant research literatures indicates that the direct consequences of PNDE appear to be generally both subtle and nonglobal, PNDE does appear to have negative developmental and behavioral outcomes, and there is evidence that it is a modest direct contributor to increased substance abuse vulnerability. Copyright 2006, Cambridge University Press.

The acute effects of cannabinoids on memory in humans: A review. (review).

Ranganathan M; D'Souza DC. *Psychopharmacology* 188(4): 425-444, 2006. (135 refs.)

Rationale: Cannabis is one of the most frequently used substances. Cannabis and its constituent cannabinoids are known to impair several aspects of cognitive function, with the most robust effects on short-term episodic and working memory in humans. A large body of the work in this area occurred in the 1970s before the discovery of cannabinoid receptors. Recent advances in the knowledge of cannabinoid receptors' function have rekindled interest in examining effects of exogenous cannabinoids on memory and in understanding the mechanism of these effects. Objective The literature about the acute effects of cannabinoids on memory tasks in humans is reviewed. The limitations of the human literature including issues of dose, route of administration, small sample sizes, sample selection, effects of other drug use, tolerance and dependence to cannabinoids, and the timing and sensitivity of psychological tests are discussed. Finally, the human literature is discussed against the backdrop of preclinical findings. Results Acute administration of Delta-9-THC transiently impairs immediate and delayed free recall of information presented after, but not before, drug administration in a dose- and delay-dependent manner.

In particular, cannabinoids increase intrusion errors. These effects are more robust with the inhaled and intravenous route and correspond to peak drug levels. Conclusions This profile of effects suggests that cannabinoids impair all stages of memory including encoding, consolidation, and retrieval. Several mechanisms, including effects on long-term potentiation and long-term depression and the inhibition of neurotransmitter (GABA, glutamate, acetyl choline, dopamine) release, have been implicated in the amnesic effects of cannabinoids. Future research in humans is necessary to characterize the neuroanatomical and neurochemical basis of the memory impairing effects of cannabinoids, to dissect out their effects on the various stages of memory and to bridge the expanding gap between the humans and preclinical literature. Copyright 2006, Springer.

Smoking and cognitive change from age 11 to 66 years: A confirmatory investigation.

Starr JM; Deary IJ; Fox HC; Whalley LJ. *Addictive Behaviors* 32(1): 63-68, 2007. (16 refs.)

Previously we reported that smoking is associated with a small relative decline in cognition from childhood to old age. In this study we perform confirmatory analyses on a further wave of data collected from 298 of the participants, all with age 11 IQ scores, at age 66 years, 2 years after the original observations. Non-smokers scored a mean 4.9 memory test and 2.6 information processing speed test points and ex-smokers 3.5 memory test and 1.9 information processing speed test points higher than current smokers respectively over the two waves of testing, equivalent to 4-8% of mean test scores, adjusted for the effects of childhood IQ. Across tests a 100 l/min higher Peak Expiratory Flow Rate was associated with a 3-4% higher test score at ages 64 and 66 years. These data confirm the adverse effect of smoking on information processing speed, and provide new evidence for a similar adverse effect on memory for people in their mid-sixties. Copyright 2007, Elsevier Science.