

A meta-analysis of alcohol consumption and the risk of 15 diseases.

Corrao G; Bagnardi V; Zambon A; La Vecchia C. *Preventive Medicine* 38(5): 613-619, 2004. (29 refs.)

Background. To compare the strength of evidence provided by the epidemiological literature on the association between alcohol consumption and the risk of 14 major alcohol-related neoplasms and non-neoplastic diseases, plus injuries. **Methods.** A search of the epidemiological literature from 1966 to 1998 was performed by several bibliographic databases. Meta-regression models were fitted considering fixed and random effect models and linear and nonlinear effects of alcohol intake. The effects of some characteristics of the studies, including an index of their quality, were considered. **Results.** Of the 561 initially reviewed studies, 156 were selected for meta-analysis because of their a priori defined higher quality, including a total of 116,702 subjects. Strong trends in risk were observed for cancers of the oral cavity, esophagus and larynx, hypertension, liver cirrhosis, chronic pancreatitis, and injuries and violence. Less strong direct relations were observed for cancers of the colon, rectum, liver, and breast. For all these conditions, significant increased risks were also found for ethanol intake of 25 g per day. Threshold values were observed for ischemic and hemorrhagic strokes. For coronary heart disease, a J-shaped relation was observed with a minimum relative risk of 0.80 at 20 g/day, a significant protective effect up to 72 g/day, and a significant increased risk at 89 g/day. No clear relation was observed for gastroduodenal ulcer. **Conclusions.** This meta-analysis shows no evidence of a threshold effect for both neoplasms and several non-neoplastic diseases. J-shaped relations were observed only for coronary heart disease. Copyright 2004, Institute for Cancer Prevention.

Accuracy of carbohydrate-deficient transferrin in the detection of excessive alcohol consumption: A systematic review. (review).

Koch H; Meerkerk GJ; Zaat JOM; Ham MF; Scholten RJPM; Assendelft WJJ. *Alcohol and Alcoholism* 39(2): 75-85, 2004. (58 refs.)

Aims: Excessive alcohol consumption is a common problem in society and medical practice. There is a need for a diagnostic tool with both high sensitivity and specificity for the detection of excessive alcohol consumption in unselected medical populations. Therefore, we evaluated the diagnostic accuracy of carbohydrate-deficient transferrin (CDT) in the detection of excessive alcohol consumption. **Methods:** Computerised literature searches in Medline, Embase and Current Contents databases (01/1966-06/2003) and reference checking. Articles on the detection of excessive alcohol consumption reporting CDT levels and self-reported alcohol

consumption as a reference test were selected (n = 101). Studies concerning treatment, relapse detection and traffic offenders were excluded. Quality assessment and data-extraction was done by two reviewers independently. Only studies scoring positive on core validity criteria by Lijmer were eligible for quantitative analysis (n = 29). **Results:** Only two CDT-assays (CDTect and CDTriTIA) were evaluated in more than two high validity studies fulfilling the criteria for inclusion in the statistical analysis. Sensitivity of CDTect (14 data points) ranged from 20 to 85%, whereas specificity ranged from 77 to 95%. A summary ROC curve was computed for CDTect. Sensitivity of CDTriTIA (4 data points) ranged from 10 to 67%, and specificity ranged from 90 to 100%. No summary measure could be computed for CDTriTIA. The heterogeneity of results could not be explained clinically. **Conclusions:** The validity of CDT as a diagnostic tool is still questionable. If the higher values for sensitivity that some studies report can be confirmed by others it is a useful diagnostic tool in unselected populations. However, more methodologically sound, comparable studies need to be performed before firm conclusions can be drawn. Copyright 2004, Oxford University Press.

Alcohol consumption and cardiovascular disease mortality in hypertensive men.

Malinski MK; Sesso HD; Lopez-Jimenez F; Buring JE; Gaziano JM. *Archives of Internal Medicine* 164(6): 623-628, 2004. (41 refs.)

Background: Heavy alcohol drinking is associated with a dose-dependent increase in blood pressure, but data on the relation between alcohol consumption and mortality in hypertensive patients are sparse. **Objective:** To assess the relation between light to moderate alcohol consumption and total mortality from cardiovascular disease (CVD) among men with hypertension. **Participants and Design:** From the Physicians' Health Study enrollment cohort of 88 882 men who provided self-reported information on alcohol intake, we identified a group of 14 125 men with a history of current or past treatment for hypertension who were free of myocardial infarction, stroke, cancer, or liver disease at baseline. **Main Outcome Measure:** Comparison of total and CVD mortality among men with hypertension who had reported to be either nondrinkers or rare drinkers, or light to moderate drinkers. **Results:** During 75 710 person-years of follow-up, there were 1018 deaths, including 579 from CVD. Compared with individuals who rarely or never drank alcoholic beverages, those who reported monthly, weekly, and daily alcohol consumption, respectively, had multivariate adjusted relative risks (RRs) for CVD mortality of 0.83 (95% confidence interval [CI], 0.62-1.13), 0.61 (CI, 0.49-0.77), and 0.56 (CI, 0.44-0.71) (P<.001 for linear trend). In the same groups, RRs

for total mortality were respectively 0.86 (CI, 0.67-1.10), 0.72 (CI, 0.60-0.86), and 0.73 (CI, 0.61-0.87) ($P < .001$ for linear trend). Among men with a systolic blood pressure of 140 mm Hg or higher or a diastolic blood pressure of 90 mm Hg or higher, the RRs for CVD mortality were, respectively, 1.00 (referent), 0.82 (CI, 0.56-1.21), 0.64 (CI, 0.48-0.85), and 0.56 (CI, 0.42-0.75) ($P < .001$ for linear trend). On the other hand, we found no significant association between moderate alcohol consumption and cancer mortality ($P = .8$ for linear trend). Conclusion: These results, which require confirmation in other large-scale studies, suggest that light to moderate alcohol consumption is associated with a reduction in risk of total and CVD mortality in hypertensive men. Copyright 2004, American Medical Association.

Alcohol intake and risk of dementia.

Luchsinger JA; Tang MX; Siddiqui M; Shea S; Mayeux R. *Journal of the American Geriatrics Society* 52(4): 540-546, 2004. (38 refs.)

Objectives: To examine the association between intake of alcoholic beverages and risk of Alzheimer's disease (AD) and dementia associated with stroke (DAS) in a cohort of elderly persons from New York City. Design: Cohort study. Setting: The Washington Heights Inwood-Columbia Aging Project. Participants: Nine hundred eighty community-dwelling individuals aged 65 and older without dementia at baseline and with data on alcohol intake recruited between 1991 and 1996 and followed annually. Measurements: Intake of alcohol was measured using a semiquantitative food frequency questionnaire at baseline. Subjects were followed annually, and incident dementia was diagnosed using *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, criteria and classified as AD or DAS. Results: After 4 years of follow-up, 260 individuals developed dementia (199 AD, 61 DAS). After adjusting for age, sex, apolipoprotein E (APOE)-epsilon4 status, education, and other alcoholic beverages, only intake of up to three daily servings of wine was associated with a lower risk of AD (hazard ratio=0.55, 95% confidence interval=0.34-0.89). Intake of liquor, beer, and total alcohol was not associated with a lower risk of AD. Stratified analyses by the APOE-epsilon4 allele revealed that the association between wine consumption and lower risk of AD was confined to individuals without the APOE-epsilon4 allele. Conclusion: Consumption of up to three servings of wine daily is associated with a lower risk of AD in elderly individuals without the APOEepsilon-4 allele. Copyright 2004, Blackwell Publishing Inc.

Alcohol related falls: An interesting pattern of injuries.

Johnston JJE; McGovern SJ. *Emergency Medicine Journal* 21(2): 185-188, 2004. (16 refs.)

Objective: To discover if there is a significant difference in the pattern and severity of injury sustained during falls in patients who have consumed alcohol and those who have not. To determine how pattern and severity of injury correlates with blood alcohol concentration. Method: A prospective quasi-randomised controlled study between November 2001 and July 2002. All healthy adults between 16 and 60 years who

had fallen from standing height were included. A systematic history and examination permitted calculation of injury severity scores as per abbreviated injury scale update 1998. Blood alcohol concentrations were obtained from intoxicated patients with consent. Results: 351 healthy adult patients were included in the study, there were 238 in the no alcohol group, 113 had consumed alcohol and blood alcohol intake were obtained for 47. The alcohol group had a higher incidence of head injuries (46(48%) versus 22 (9%)) with a lower incidence of limb injuries (39 (39%) versus 183 (76%)) than the no alcohol group. There was a significant difference in the pattern of injury between the alcohol and no alcohol groups (χ^2 , $p < 0.001$) and there was a significant difference in the injury severity scores ($p < 0.001$, $Z = -2.5$). In the alcohol group severity and pattern correlated with alcohol concentration at the time of injury. Patients with an alcohol concentration < 2 g/l had mostly soft tissue limb injuries (58%), 2-2.5 mostly significant limb fractures (55%), and > 2.5 mostly significant head injuries (90%). Conclusions: Alcohol related falls are more often associated with severe craniofacial injury. The severity of both limb and head injury is greater and correlates directly with blood alcohol concentration. Copyright 2004, British Medical Journal Publishing Group.

Alcohol withdrawal syndrome.

Bayard M; McIntyre J; Hill KR; Woodside J. *American Family Physician* 69(6): 1443-1450, 2004. (29 refs.)

The spectrum of alcohol withdrawal symptoms ranges from such minor symptoms as insomnia and tremulousness; to severe complications such as withdrawal seizures and delirium tremens. Although the history and physical examination usually are sufficient to diagnose alcohol withdrawal syndrome, other conditions may present with similar symptoms. Most patients undergoing alcohol withdrawal can be treated safely and effectively as outpatients. Pharmacologic treatment involves the use of medications that are cross-tolerant with alcohol. Benzodiazepines, the agents of choice, may be administered on a fixed or symptom-triggered schedule. Carbamazepine is an appropriate alternative to a benzodiazepine in the outpatient treatment of patients with mild to moderate alcohol withdrawal symptoms. Medications such as haloperidol, beta blockers, clonidine, and phenytoin may be used as adjuncts to a benzodiazepine in the treatment of complications of withdrawal. Treatment of alcohol withdrawal should be followed by treatment for alcohol dependence. Copyright 2004, American Academy of Family Physicians. Used with permission.

Cerebral reserve capacity: Implications for alcohol and drug abuse.

Fein G; Di Sclafani V. *Alcohol* 32(1): 63-67, 2004. (39 refs.)

Cerebral reserve capacity (or functional reserve) refers to the brain's ability to maintain function when confronted by degenerative processes. Functional reserve can be estimated by several associated measures, including premorbid brain size, premorbid IQ, and level of education attained. There is accumulating evidence that the magnitude of reserve capacity is important in determining the onset and progression of the

clinical manifestations of neurodegenerative brain diseases. Normal aging also whittles away at this cerebral reserve, and there may be a consequent unmasking of morbid effects that was not clinically evident when this compensatory reserve was sufficient. We review the evidence supporting this model for a number of degenerative brain processes, including Alzheimer's disease, presenile dementia, HIV dementia, aging, and chronic (multiyear) substance abuse. The concept of cerebral functional reserve has important implications for alcohol and drug abuse morbidity. First, given the high genetic contribution to substance abuse, there is an increased likelihood that the parents of substance abusers were substance abusers themselves. Substance abuse during pregnancy can inhibit brain growth, resulting in reduced brain size and reduced reserve capacity (and therefore less ability to compensate for loss of function later in life). Second, substance abuse is often coupled with poverty, and both substance abuse and poverty are associated with some of the same conditions that reduce brain growth. Finally, we comment on the most important public health implication of the cerebral reserve capacity model (*vis-à-vis* addiction). Copyright 2004, Elsevier Science.

Does alcohol affect memory for emotional and non-emotional experiences in different ways?

Knowles SKZ; Duka T. *Behavioural Pharmacology* 15(2): 111-121, 2004. (41 refs.)

Alcohol has been shown to have both impairing and facilitating effects on memory, depending on the sequencing of learning and ingestion of the drug. Its effects on memory for emotional material, however, have not been shown reliably. The current experiment sought to investigate the effects of alcohol on later recall of emotional and neutral events experienced before and after alcohol drinking. Using an incidental-learning paradigm, alcohol (0.65 g/kg) or placebo was administered in a double-blind randomized design to 34 participants, between two learning phases in which they viewed and rated positive, negative and neutral images. The drug's effects on memory were assessed in a surprise test of free recall. In addition, impact of alcohol on ratings of mood states, and of valence and arousal that the pictures evoked, was examined. Alcohol facilitated memory for material seen before, and impaired memory for material seen after, its administration. Furthermore, under alcohol, emotional images in the first set were more recalled over neutral than in the second set, indicating a higher retrograde facilitation for emotional than for neutral material. Alcohol improved positive mood states but had no effect on negative mood states. Evaluation of pictures with regard to valence showed an increase of the ratings for the positive and neutral images after alcohol and a decrease after placebo. No drug effects were found for arousal ratings. Whether a picture was likely to be remembered or not (tested only for set 2) was dependent on the intensity of the arousal but not of the valence that the picture evoked in the participants. Pictures that were rated high in arousal were also remembered better, and this effect was irrespective of alcohol or placebo ingestion. These data have shown that alcohol elicits retrograde facilitation and

anterograde impairment for emotional materials. Furthermore, these data demonstrate that alcohol selectively facilitates memories for emotional events experienced before administration, and suggest a possible explanation for the reinforcing effects of drinking. Copyright 2004, Rapid Communications of Oxford, Ltd.

Does drug abuse beget drug abuse? Behavioral analysis of addiction liability in animal models of prenatal drug exposure. (review).

Malanga CJ; Kosofsky BE. *Developmental Brain Research* 147(1-2): 47-57, 2003. (120 refs.)

Prenatal exposure to drugs of abuse is the single largest preventable cause of developmental compromise of American children today. In the clinical population, it is difficult to determine the independent effects of gestational exposure to a single drug on brain development, in part due to the confounding effects of additional risk factors that are encountered in the substance-abusing population. The enormous clinical and societal problem of gestational toxicity of drugs of abuse, both legal and illegal, has driven the need to develop and investigate animal models of gestational drug exposure in which these variables can be controlled. More specifically, as clinical data are gathered suggesting an increased liability to substance abuse among children of drug-abusing mothers, a mechanistic understanding of the lasting effects of early drug exposure on the developing brain and the behavioral repertoire of the developing animal is crucial. In this review we summarize experimental animal research that investigates the role of drug exposure in utero on the functional development of specific brain circuits that are involved in the reinforcing effects of drugs of abuse, and on the behaviors that are mediated by these brain reward systems. Copyright 2003, Elsevier Science BV.

Does in utero exposure to heavy maternal smoking induce nicotine withdrawal symptoms in neonates?

Godding V; Bonnier C; Fiase L; Michel M; Longueville E; Lebecque P et al. *Pediatric Research* 55(4): 645-651, 2004. (32 refs.)

Maternal drug use during pregnancy is associated with fetal passive addiction and neonatal withdrawal syndrome. Cigarette smoking-highly prevalent during pregnancy-is associated with addiction and withdrawal syndrome in adults. We conducted a prospective, two-group parallel study on 17 consecutive newborns of heavy-smoking mothers and 16 newborns of nonsmoking, unexposed mothers (controls). Neurologic examinations were repeated at days 1, 2, and 5. Finnegan withdrawal score was assessed every 3 It during their first 4 d. Newborns of smoking mothers had significant levels of cotinine in the cord blood (85.8 +/- 3.4 ng/mL), whereas none of the controls had detectable levels. Similar findings were observed with urinary cotinine concentrations in the newborns (483.1 +/- 2.5 mug/g creatinine versus 43.6 +/- 1.5 mug/g creatinine; p = 0.0001). Neurologic scores were significantly lower in newborns of smokers than in control infants at days 1 (22.3 +/- 2.3 versus 26.5 +/- 1.1; p = 0.0001), 2 (22.4 +/- 3.3 versus 26.3 +/- 1.6; p = 0.0002), and 5 (24.3 +/-

2.1 versus 26.5 +/- 1.5; $p = 0.002$). Neurologic scores improved significantly from day 1 to 5 in newborns of smokers ($p = 0.05$), reaching values closer to control infants. Withdrawal scores were higher in newborns of smokers than in control infants at days 1 (4.5 +/- 1.1 versus 3.2 +/- 1.4; $p = 0.05$), 2 (4.7 +/- 1.7 versus 3.1 +/- 1.1; $p = 0.002$), and 4 (4.7 +/- 2.1 versus 2.9 +/- 1.4; $p = 0.007$). Significant correlations were observed between markers of nicotine exposure and neurologic and withdrawal scores. We conclude that withdrawal symptoms occur in newborns exposed to heavy maternal smoking during pregnancy. Copyright 2004, International Pediatric Research Foundation, Inc.

Drug smuggling by body packing: What radiologists should know about it.

Hergan K; Kofler K; Oser W. *European Radiology* 14(4): 736-742, 2004. (23 refs.)

Body packing is a distinct method for smuggling drugs. What radiologists need to know is discussed in this pictorial review. Radiologists are confronted with diagnostic imaging of body packers because of two main reasons: complications of body packing and identifying drug packets within the gastrointestinal tract. The standard examination used is plain X-ray of the abdomen in an upright and a supine position. Computed tomography is occasionally used but nevertheless described as a very accurate diagnostic tool. Ultrasound and MR imaging do not play an important role in that field. Depending on the purity of the drug, three different forms of attenuation have been described: hashish is denser than stool; cocaine appears similar to stool; and heroin has a gaseous transparency. The packets are of a round to oval form, usually of a particular uniformity and rarely confused with scybala if arranged like a pearl chain; therefore, plain X-ray is the method of choice to detect drug-filled packets within the gastrointestinal tract of body packers. Copyright 2004, Springer Verlag.

Effect of cannabinoid ingestion (in the form of bhang) on the immune system of high school and university students.

EL-Gohary M; Eid MA. *Human and Experimental Toxicology* 23(3): 149-156, 2004. (37 refs.)

The discovery of cannabinoid receptors in the immune system and a family of endogenous ligands of these receptors provides a basis for understanding the cellular and molecular mechanisms of cannabis-induced immunotoxicity. The present study was conducted on 90 nonsmoker males of high school and university students living in Tanta city of matched age and socioeconomic lifestyle. They were divided into a control group (30 males) and a bhang user group (60 males), which used bhang by eating its sweet juice after boiling with a little water and drying in an oven, 'fola'. The bhang group was divided equally into two subgroups: subgroup 1 used bhang for 6-24 months (average 199 +/- 1.2) and subgroup 2 used bhang for 24-36 months (average 31 +/- 1.7). The immunotoxic effects of using bhang appeared in the form of a

significant decrease in serum immunoglobulins (IgG and IgM), and C3 and C4 complement protein concentrations ($P < 0.05$). In addition, our results demonstrated a significant decrease in the absolute number of functionally different subsets of peripheral blood mononuclear lymphocytes, T and B lymphocytes and natural killer (NK) cells in bhang users as compared to controls ($P < 0.05$). Moreover, the fatty acid amide hydrolase (FAAH) showed significant decrease in bhang users as compared to controls and in subgroup 2 as compared to subgroup 1 ($P < 0.05$), indicating that the decrease in FAAH protein level is closely related to the duration of bhang use. Positive correlations were found between FAAH level and the absolute number of mononuclear cells (T, B lymphocytes and NK cells) among bhang user subgroups. The present study is the first study to report on the effect of bhang on complement proteins and immunoglobulins in humans. Our study revealed that bhang-induced immunotoxicity could be attributed to decrease in FAAH protein. Copyright 2004, Arnold, Hodder Headline PLC.

Comparison of acute lethal toxicity of commonly abused psychoactive substances. (review).

Gable RS. *Addiction* 99(6): 686-696, 2004. (103 refs.)

Aims: To determine the acute lethal toxicity of a range of psychoactive substances in terms of the dose customarily used as a single substance for non-medical purposes. Design and method A structured English-language literature search was conducted to identify experimental studies and clinical reports that documented human and non-human lethal doses of 20 abused substances that are distributed widely in Europe and North America. Four inclusion criteria were specified for the reports, and approximately 3000 relevant records were retrieved from search engines at Biosis, Science Citation Index, Google and the National Library of Medicine's Gateway. In order to account for different drug potencies, a 'safety ratio' was computed for each substance by comparing its reported acute lethal dose with the dose most commonly used for non-medical purposes. Findings The majority of published reports of acute lethal toxicity indicate that the decedent used a co-intoxicant (most often alcohol). The calculated safety ratios varied between substances by more than a factor of 100. Intravenous heroin appeared to have the greatest direct physiological toxicity; several hallucinogens appeared to have the least direct physiological toxicity. Conclusions Despite residual uncertainties, the substantial difference in safety ratios suggests that abused substances can be rank-ordered on the basis of their potential acute lethality. Copyright 2004, Society for the Study of Addiction to Alcohol and Other Drugs.

..