

### **Does hepatitis C virus cause severe liver disease only in people who drink alcohol?**

Vento S; Cainelli F. *Lancet Infectious Diseases* 2(5): 303-309, 2002. (125 refs.)

Hepatitis C virus (HCV) infects about 170 million people worldwide, and has been portrayed in the media as a silent killer, incorrectly implying that cirrhosis and hepatocellular carcinoma are the certain final outcomes of infection. Results of numerous population-based surveys indicate that chronic HCV infection is highly prevalent in elderly people who, in most instances, do not develop end-stage liver disease. In individuals who do progress to cirrhosis and hepatocellular carcinoma alcohol plays a fundamental part, via mechanisms that result in increased viral replication, enhanced HCV quasispecies complexity, increased liver-cell death, suppression of immune responses, and iron overload. Although overlaps are present in the histological appearance of the liver in patients with hepatitis C who do and do not drink alcohol, histology could be of some help in revealing the role of alcohol in HCV disease progression even in people who deny drinking. Interventions and high-impact, continuous public-health campaigns are needed to persuade doctors and patients infected with HCV of the importance of abstaining from alcohol if risk of progression towards cirrhosis and hepatocellular carcinoma is to be reduced. 2002, Lancet Ltd.

### **Adolescents prenatally exposed to marijuana: Examination of facets of complex behaviors and comparisons with the influence of in utero cigarettes.**

Fried PA. *Journal of Clinical Pharmacology* 42(11 Supplement): 97S-102S, 2002. (41 refs.)

For the purposes of this review, the impact of prenatal exposure to marijuana in adolescent offspring is discussed in the context that the effects may be apparent only when the multifaceted nature of complex behaviors is examined and that such exposure can be distinguished from those of prenatal exposure to cigarettes. The data are derived from adolescents participating in an ongoing longitudinal study for whom prenatal marijuana and cigarette exposure had been ascertained with the low-risk, predominantly middle-class sample that had been assessed since birth. In this report, cognitive functioning and visual perceptual performance in 9- to 12-year-olds and facets of attention in 13- to 16-year-olds are examined. These three areas of behavior all appear to be affected differentially by

maternal use of marijuana or cigarettes. Prenatal cigarette exposure was associated with lowered IQ, poorer impulse control, and poorer performance on tests requiring fundamental aspects of visuo-perceptual performance. In contrast, prenatal marijuana did not have a negative impact on IQ or on basic visuo-perceptual skills. Rather, in utero exposure to marijuana had an impact on the application of these skills in tasks in problem-solving situations requiring visual integration and analytical skills as well as sustained attention. These differential findings are discussed in terms of cigarette exposure having a "bottom-up" impact and marijuana exposure having a "top-down" impact. The latter is also discussed in terms of prenatal marijuana's negative association with aspects of executive function. Copyright 2002, J.B. Lippincott Co.

### **Alcohol, tobacco and breast cancer: Collaborative reanalysis of individual data from 53 epidemiological studies, including 58515 women with breast cancer and 95067 women without the disease.**

Beral V; Hamajima N; Hirose K; Rohan T; Calle EE; Heath CW Jr et al. *British Journal of Cancer* 87(11): 1234-1245, 2002. (73 refs.)

Alcohol and tobacco consumption are closely correlated and published results on their association with breast cancer have not always allowed adequately for - between these exposures. Over 80% of the relevant information worldwide on alcohol and tobacco consumption and breast cancer were collated, checked and analysed centrally. Analyses included 58515 women with invasive breast cancer and 95067 controls from 53 studies. Relative risks of breast cancer were estimated, after stratifying by study, age, parity and, where appropriate, women's age when their first child was born and consumption of alcohol and tobacco. The average consumption of alcohol reported by controls from developed countries was 6.0 g per day, i.e. about half a unit/drink of alcohol per day, and was greater in ever-smokers than never-smokers, (8.4 g per day and 5.0 g per day, respectively). Compared with women who reported drinking no alcohol, the relative risk of breast cancer was 1.32 (1.19 - 1.45,  $P < 0.00001$ ) for an intake of 35 - 44 g per day alcohol, and 1.46 (1.33 - 1.61,  $P < 0.00001$ ) for greater than or equal to 45 g per day alcohol. The relative risk of breast cancer increased by 7.1% (95% CI 5.5-8.7%;  $P < 0.00001$ ) for each additional 10 g per day intake of alcohol, i.e. for each extra unit or drink of alcohol consumed on a daily basis. This increase was the same in

ever-smokers and never-smokers (7.1 % per 10 g per day,  $P < 0.00001$ , in each group). By contrast, the relationship between smoking and breast cancer was substantially confounded by the effect of alcohol. When analyses were restricted to 22 255 women with breast cancer and 40 832 controls who reported drinking no alcohol, smoking was not associated with breast cancer (compared to never-smokers, relative risk for ever-smokers = 1.03, 95% CI 0.98 - 1.07, and for current smokers = 0.99, 0.92 - 1.05). The results for alcohol and for tobacco did not vary substantially across studies, study designs, or according to 15 personal characteristics of the women; nor were the findings materially confounded by any of these factors. If the observed relationship for alcohol is causal, these results suggest that about 4% of the breast cancers in developed countries are attributable to alcohol. In developing countries, where alcohol consumption among controls averaged only 0.4 g per day, alcohol would have a negligible effect on the incidence of breast cancer. In conclusion, smoking has little or no independent effect on the risk of developing breast cancer; the effect of alcohol on breast cancer needs to be interpreted in the context of its beneficial effects, in moderation, on cardiovascular disease and its harmful effects on cirrhosis and cancers of the mouth, larynx, oesophagus and liver. Copyright 2002, Stockton Press.

#### **Faster absorption of ethanol and higher peak concentration in women after gastric bypass surgery.**

Klockhoff H; Naslund I; Jones AW. *British Journal of Clinical Pharmacology* 54(6): 587-591, 2002. (30 refs.)

**Aims** To investigate the absorption, distribution and elimination of ethanol in women with abnormal gut as a result of gastric bypass surgery. Patients who undergo gastric bypass for morbid obesity complain of increased sensitivity to the effects of alcohol after the operation. **Methods** Twelve healthy women operated for morbid obesity at least 3 years earlier were recruited. Twelve other women closely matched in terms of age and body mass index (BMI) served as the control group. After an overnight fast each subject drank 95% v/v ethanol (0.30 g kg<sup>-1</sup> body weight) as a bolus dose. The ethanol was diluted with orange juice to 20% v/v and finished in 5 min. Specimens of venous blood were taken from an indwelling catheter before drinking started and every 10 min for up to 3.5 h post-dosing. The blood alcohol concentration (BAC) was determined by headspace gas chromatography. **Results** The maximum blood-ethanol concentration (C<sub>max</sub>) was 0.741 ± 0.211 g l<sup>-1</sup> (± s.d.) in the operated group compared with 0.577 ± 0.112 g l<sup>-1</sup> in the controls (mean difference 0.164 g l<sup>-1</sup>), 95% confidence interval (CI) 0.021, 0.307). The median time to peak (t<sub>max</sub>) was 10 min in the bypass patients

compared with 30 min in controls (median difference -15 min (95% CI -10, -20 min). At 10 and 20 min post-dosing the BAC was higher in the bypass patients ( $P < 0.05$ ) but not at 30 min and all later times ( $P > 0.05$ ). Other pharmacokinetic parameters of ethanol were not significantly different between the two groups of women ( $P > 0.05$ ). **Conclusions** The higher sensitivity to ethanol after gastric bypass surgery probably reflects the more rapid absorption of ethanol leading to higher C<sub>max</sub> and earlier t<sub>max</sub>. The marked reduction in body weight after the operation might also be a factor to consider if the same absolute quantity of ethanol is consumed. Copyright 2002, Blackwell Scientific Publications, Ltd.

#### **Fatal versus non-fatal heroin "overdose": Blood morphine concentrations with fatal outcome in comparison to those of intoxicated drivers.**

Meissner C; Recker S; Reiter A; Friedrich HJ; Oehmichen M. *Forensic Science International* 130(1): 49-54, 2002.

(25 refs.)

The study was performed to distinguish fatal from non-fatal blood concentrations of morphine. For this purpose, blood levels of free morphine and total morphine (free morphine plus morphine conjugates) in 207 cases of heroin-related deaths were compared to those in 27 drivers surviving opiate intoxication. The majority of both survivors and non-survivors were found to show a concomitant use of depressants including alcohol or stimulants. Blood morphine levels in both groups varied widely, with a large area of overlap between survivors (free morphine: 0-128 ng/ml, total morphine: 10-2110 ng/ml) and non-survivors (free morphine: 0-2800 ng/ml, total morphine: 33-5000 ng/ml). Five (18.5%) survivors and 87 (42.0%) non-survivors exhibit intoxication only by morphine. In these cases, too, both groups overlapped (survivors-free morphine: 28-93 ng/ml, total morphine: 230-1451 ng/ml; non-survivors-free morphine: 0-2800 ng/ml, total morphine: 119-4660 ng/ml). Although the blood levels of free or total morphine do not allow a reliable prediction of survival versus non-survival, the ratio of free/total morphine may be a criterion to distinguish lethal versus survived intoxication. The mean of the ratio of free to total morphine for all lethal cases (N = 207) was 0.293, for those that survived (N = 27) 0.135, in cases of intoxication only by morphine 0.250 (N = 87) and 0.080 (N = 5), respectively. Applying a cut-off of 0.12 for free/total morphine and performing ROC analyses, fatal outcome can be predicted in 80% of the cases correctly, whereas 16% of the survivors were classified as dead. Nevertheless, in this study, all cases with a blood concentration of 200 ng/ml and more of free morphine displayed a fatal outcome. Copyright 2002, Elsevier Scientific Publishers Ireland, Ltd.

### **Green tea as a potent antioxidant in alcohol intoxication.**

Skrzydłowska E; Ostrowska J; Stankiewicz A; Farbiszewski R. *Addiction Biology* 7(3): 307-314, 2002. (56 refs.)

Ethanol oxidation to acetaldehyde and next to acetate is accompanied by free radical generation. Free radicals can affect cell integrity when antioxidant mechanisms are no longer able to cope with the free radical generation observed in ethanol intoxication. Natural antioxidants are particularly useful in such a situation. The present study was designed to investigate the efficacy of green tea as a source of water-soluble antioxidants (catechins) on the liver and blood serum antioxidative potential of rats chronically (28 days) intoxicated with ethanol. Alcohol caused a decrease in liver superoxide dismutase, glutathione peroxidase, and catalase activities and an increase in activity of glutathione reductase. Moreover, decreases in the level of reduced glutathione, ascorbic acid, vitamins A and E, and beta-carotene were observed. The activity of serum glutathione peroxidase decreased while glutathione reductase activity increased. The level of serum non-enzymatic antioxidants was also decreased in the liver. Alcohol administration caused an increase in the liver and serum lipid peroxidation products, measured as thiobarbituric acid-reactive substances. However, green tea prevents the changes observed after ethanol intoxication. Green tea also protects membrane phospholipids from enhanced peroxidation. These results indicate a beneficial effect of green tea in alcohol intoxication. Copyright 2002, Carfax, Ltd.

### **Kindling of withdrawal: A study of craving and anxiety after multiple detoxifications in alcoholic inpatients.**

Duka T; Townshend JM; Collier K; Stephens DN. *Alcoholism: Clinical and Experimental Research* 26(6): 785-795, 2002. (53 refs.)

This study hypothesizes that patients who had undergone multiple detoxifications would show greater desire for alcohol and might experience more anxiety compared with patients with fewer detoxifications or compared with social drinkers. Forty-two alcoholic inpatients were divided into HI-med (more than two previous detoxifications, n = 6) and LO-med (two or fewer previous detoxifications, n = 36) and compared with 43 matched social drinkers. An additional analysis was performed by dividing participants into HI-total (n = 22) and LO-total (n = 20) previous detoxification groups (three or more and less than three previous detoxifications, respectively) by using all previous detoxifications, which included unsupervised attempts. With medically supervised detoxifications only, alcoholic participants (HI- and LO-med) had higher ratings in trait anxiety and in feelings of

anger, anxiety, depression, and confusion, but also friendliness; had higher craving ratings; and made more errors in the alcohol Stroop test compared with social drinkers. The number of errors in the emotional Stroop for negative words was higher in the group with the higher number of detoxifications. When the total number of detoxifications was analyzed, the emotional Stroop errors were no longer seen. Instead, ratings of anger in the Profile of Mood States were greater in the HI-total compared with the LO-total detoxification group. Effects remained when the correlates alcohol consumption and degree of dependency were introduced as covariates, showing that these effects are probably attributable to the number of withdrawals. For inpatients with short history of alcoholism, the consequences of multiple withdrawals may not relate to anxiety or craving. Copyright 2002, Research Society on Alcoholism. Used with permission.

### **The impact of regular ecstasy use on memory function.**

Simon NG; Mattick RP. *Addiction* 97(12): 1523-1529, 2002. (31 refs.)

**Aim:** To assess memory impairment in a group of regular users of ecstasy compared with a group of regular users of cannabis, after accounting for possible confounding factors such as other drug use, premorbid intelligence and psychopathology. **Method:** Comparative and regression analysis was used to determine the presence or absence of a difference in memory function between 40 regular ecstasy users and 37 regular users of cannabis, who were interviewed at the National Drug and Alcohol Research Centre in Sydney, Australia. Regression analysis was used to find associations between life-time exposure to ecstasy use and memory performance. Memory function was assessed using an age-standardized memory test. Other scales were used to assess premorbid intelligence, physical and psycho-logical health, drug withdrawal and other drug use. **Results** Initial comparative analysis showed a trend towards a significantly poorer performance by the regular ecstasy-using group on the 'auditory immediate memory' and 'auditory delayed memory' indices. When regression analysis was performed an estimate of verbal intelligence was found to be the most predictive of most memory indices including 'auditory immediate memory' and 'auditory delayed memory'. Life-time exposure to ecstasy was not predictive of the memory indices. The current frequency of cannabis use was found to have some predictive effect for immediate and delayed visual memory. **Conclusion:** This study does not show memory impairment in a group of ecstasy users relative to cannabis using controls. The previously reported association of life-time exposure to ecstasy and memory was not found. The findings may indicate a confounding role of cannabis use,

as has been recently reported. Copyright 2002, Society for the Study of Addiction to Alcohol and Other Drugs.

**Chronic drug use and cognitive impairments.**

Block RI; Erwin WJ; Ghoneim MM. *Pharmacology, Biochemistry and Behavior* 73(3): 491-504, 2002. (53 refs.)

Reports regarding the effects of chronic drug use on human cognition and comparisons of different drug user groups have been inconsistent. Methodological flaws may account for some inconsistencies. To determine the effects of chronic drug use on cognition, drug users (n = 192) were tested 17.1 +/- 0.3 days (mean +/-S.E.) and 99.4 +/- 1.7 days on average after their last use of drugs before beginning treatment. Drug users were categorized as stimulant, alcohol, or polydrug users. Their performance on tests of academic achievement, verbal memory, and abstraction was compared to performance of community-dwelling controls (n = 137). The groups were matched on selected demographic and psychiatric characteristics. Historical records of achievement test scores were used to attempt to control for premorbid intellectual ability. Drug users showed impairments on each of the achievement tests (P < .001), as well as poorer total recall (P < .01) and abstraction ability (P < .05). Stimulant users performed worse on several tests relative to the other drug use groups. Only one of six tests demonstrated improvements

following about 3 months of abstinence. Thus, chronic drug use is associated with cognitive impairments that do not improve substantially even after several months of abstinence. Copyright 2002, Elsevier Science Ltd.

**Treatment of neonatal abstinence syndrome.**

Johnson K; Gerada C; Greenough A. *Archives of Disease in Childhood* 88(1): 2-5, 2003. (53 refs.)

Neonatal abstinence syndrome (NAS) is suffered by infants withdrawing from substances on which they have become physically dependent after in utero exposure. They may require prolonged treatment and spend weeks or even months in hospital. A wide range of drugs have been used to treat NAS. The efficacy of few, however, have been adequately investigated. Evidence suggests that opioids are the most appropriate, at least in infants exposed to diamorphine or methadone. In all "head to head" trials, diazepam has been shown to be ineffective. Morphine and methadone are currently the most commonly prescribed opioids to treat NAS, but randomised trials have not been undertaken to determine which is the more beneficial. Many infants with NAS have been exposed to multiple substances in utero. Further research is required into whether a single opiate or a multiple drug regimen is the best option for such patients. Copyright 2003, British Medical Association

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