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ACUTE AND CHRONIC ALCOHOL INTAKE ON CIRCULATING TESTOSTERONE AND LUTEINIZING HORMONE SECRETION IN THE MALE SPRAUGE-DAWLEY RAT. Charles D. Lox* and F. S. Messiha Departments of Pathology, Psychiatry and Obstetrics/Gynecology* Texas Tech University Health Sciences Center School of Medicine Lubbock, Texas 79430

The influence of both acute and chronic low dose (5%) ethanol consumption on serum testosterone (T) and luteinizing hormone (LH) in the male rat has been studied plus intraperitoneal (I.P.) injection of high dose (25%) ethanol, 2.5ug/kg/day, I.P. for 7 consecutive days, on those hormones in the intact and castrate male rat. The gonadal response to exogenous chorionic gonadotrophin (HCG) after chronic exposure to ethanol drinking was also studied. The results indicate that ingestion of 5% ethanol solution from 7 days to 180 days produced no significant effect on the luteinizing hormone-testosterone axis while I.P. injection of ETOH caused a 54% decrease in LH and 27% in T. Subcutaneous injection of HCG caused an increase in circulating testosterone within 6h of administration in animals who had been ingesting 5% ethanol for 60 days, which continued to be significantly elevated for 24 hours. Circulating serum T concentrations measured in water drinking rats and injected same amounts of HCG amounted to 4.49 2.36 ng/ml compared to 6.86 1.99 ng/ml for the ETOH-drinking rats after 24 h of the HCG treatment. Castrated rats injected with I.P. ETOH (25%) had unchanged LH levels. This suggests that the rat testis is not suppressed by 60 days of 5% ETOH injection as related to androgen production and secretion. The increase in serum T levels in water-controls from ETOH treated rats after HCG treatment indicate that there was apparently no graded depression of T biosynthesis by prolonged consumption of diluted ETOH solution. The results suggest that the male rat gonad is not androgen refractory due to the 5% ETOH used for as long as 26 weeks.

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Ethanol Enhances [^{3}H]-Diazepam Binding to Soluble Receptors at the Benzodiazepine-GABA-Receptor-Ionophore Complex. M.K. Ticku, I. Chen and W.C. Davis, Dept. Pharmacology, Univ. Tx. Hlth. Sci. Ctr., San Antonio, TX 78284.

Ethanol has a pharmacological profile very similar to barbiturates and benzodiazepines. All these classes of drugs are known to facilitate the inhibitory transmission mediated by GABA. Ethanol and pentobarbital enhance [^{3}H]-diazepam binding to membrane and soluble receptors. Ethanol-enhanced [^{3}H]-diazepam binding to the soluble receptors in a dose-dependent manner with a maximal enhancement of 85±10% occurring at 110 mM and half-maximal effect occurred at 30 mM. This effect, like pentobarbital, was due to an increase in the affinity of diazepam for its binding sites. 100 mM Ethanol changed the K_D for diazepam from a control value of 9.36± 1.26 mM (n=3) to 4.40±0.33 nM (n=4). The B_{max} in control was 1082±198 fmol/mg protein and in ethanol treated, it was 995±167 fmol/mg protein. Ethanol and pentobarbital enhancement of diazepam binding to soluble receptors was blocked by GABA synaptic antagonists picrotoxinin and (+) bicuculline. The rank order for enhancement of diazepam binding by various alcohols was ethanol>methanol>isopropyl alcohol>n-propyl alcohol=t-butyl alcohol=n-butyl alcohol. This rank order does not correlate with their partition coefficients. These results suggest that small chain alcohols have a specific effect on the benzodiazepine binding component of the benzodiazepine-GABA-receptor-ionophore complex. This interaction will result in facilitation of GABAergic transmission and may be responsible for some of alcohol's central actions, like antianxiety, muscle relaxant and sedative effects.

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WITHDRAWAL SYMPTOMS FROM COMBINED ALCOHOL AND MINOR TRANQUILIZER INTAKE. Robert Franken and F.E. Seale.

In addition to the hazards of simultaneous use, concurrent withdrawal from alcohol and certain tranquilizers presents a dangerous and complex problem to the poorly-informed and unsuspecting clinician. It is recommended that physicians treating alcoholism and related problems have a high index of suspicion toward cross-addiction and to suggest to their patients that a second withdrawal pattern might appear approximately a week after the "hangover" from alcohol is gone. It is further noted that the most severe and dangerous of features of the withdrawal pattern occur when diazepams and related drugs are discontinued abruptly. Gradual withdrawal of the drug or drugs with substitution of decreasing dosages of diazepam has been the most effective method of management in our hands. It has been our experience that complete abstinence from all mind-altering drugs and from alcohol is essential in the long-term cure of the cross-addicted patient.