

A9

EFFECT OF PHYSOSTIGMINE ON RAT LIVER ALCOHOL (LADH) AND ALDEHYDE DEHYDROGENASE (L-ALDH). F. S. Messiha and M. M. Sabonghy, Departments of Pathology, Psychiatry and Anesthesiology, Texas Tech University Health Sciences Center, School of Medicine, Lubbock, Texas 79430.

Several findings indicate the implication of cholinergic mechanisms in the action of ethanol (ET) and indirect evidence suggests possible interrelationship between physostigmine (PT) and alcoholism. This is shown by the reversal of the toxicity of various drugs, including anesthetics and ET by PT. Accordingly, the *in vitro* effect of cholinergics and an anticholinergic agent on ET metabolizing enzymes was studied. Inhibition of mitochondrial L-ALDH but not L-ADH occurred in the presence of PT ($3 \times 10^{-4}M$). Choline, neostigmine and scopolamine did not alter the activity of these enzymes *in vitro*. Kinetic studies showed that the PT-produced inhibition on L-ALDH is competitive and is confined to the enzyme with the low km value which is also inhibited by disulfiram. The results are indicative of PT-ET interaction and suggest the contraindication of PT in post-operative recovery of alcoholics and in individuals with alcohol intoxication.

A11

VOLUNTARY ETHANOL CONSUMPTION BY FEMALE OFFSPRING FROM ALCOHOLIC AND CONTROL SINCLAIR(S-1) MINIATURE DAMS. M.E. Tumbleson*, J.D. Dexter and C.C. Middleton, Sinclair Comparative Medicine Research Farm, Veterinary Medicine and Medicine, University of Missouri, Columbia, MO 65201.

Seven gilts were selected from 6 litters farrowed by alcoholic dams and 9 gilts were selected from 6 litters farrowed by control dams to evaluate ad libitum voluntary ethanol consumption beginning at 12 weeks postweaning. Each of the litters was weaned at 5 weeks postpartum. During the lactation period, the offspring from alcoholic dams received ethanol in the milk; however, from 5 to 17 weeks postpartum, neither control nor alcoholic offspring had access to ethanol. During gestation, alcoholic dams consumed 1.7 g ethanol/kg body weight/day; however, they were allowed access to ethanol only for two 1-hour periods per day. At birth, 5 weeks of age (weaning) and 17 weeks of age (initiation of ad libitum voluntary ethanol consumption), mean (\pm SD) body weights were 0.637 ± 0.117 , 3.00 ± 0.73 and 7.43 ± 1.99 kg, respectively, for offspring from alcoholic dams and 0.767 ± 0.139 , 3.88 ± 0.45 and 7.89 ± 2.84 kg, respectively, for offspring from control dams. During 1-5, 6-10, 11-15 and 16-20 weeks on test, gilts from alcoholic dams consumed 6.6, 8.1, 8.5 and 7.1 g ethanol/kg body weight/day, respectively, while gilts from control dams consumed 4.5, 5.7, 6.7 and 7.2 g ethanol/kg body weight/day, respectively. For each of the first 15 weeks on test (17 through 32 weeks postpartum), mean ethanol consumption was greater for alcoholic offspring than for control offspring. Supported in part by a grant from the USBA.

A10

LITHIUM THERAPY, EPISODIC DRINKING AND IMPOTENCE. Richard L. Weddige, Department of Psychiatry, Texas Tech University Health Sciences Center, School of Medicine, Lubbock, Texas 79430.

The clinical efficacy of Li_2CO_3 in manic depressive illness is well established. Recent clinical trials suggest possible beneficial use of Li_2CO_3 in some types of episodic drinking, cyclothymic personality disorders, and episodic substance abuse other than alcohol. Sexual dysfunction has not been reported as a common side effect of lithium therapy. A 62 year old male, diagnosed initially as suffering from bipolar manic depressive illness, was studied longitudinally for approximately 7 years. Maintenance therapy with Li_2CO_3 (0.7 - 0.8mEq/L) failed to modify his drinking behavior. Coadministration of amitriptyline resulted in abolishing his "craving for alcohol intake." Impotence occurred during treatment with Li_2CO_3 alone or with combined drug therapy. Dynamic psychotherapy and testosterone administration did not alter the patient's impotence. Sexual potency reappeared after cessation of lithium therapy on several occasions. In a second case, a 50 year old patient, sexual impotency was evident following lithium therapy. The two case reports suggest that Li_2CO_3 may be associated with sexual dysfunction in man.

A12

ETHANOL AND REPRODUCTIVE FUNCTION IN THE FEMALE RAT. Chas. D. Lox, F. Messiha, M.W. Heine, B. Benson* and Gregory R. Misenhimer, Departments of Ob/Gyn, Pathology & Psychiatry, Texas Tech University Health Sciences Center, Dept. of Anatomy, University of Arizona School of Medicine.

In this study 140 sexually mature female Sprague-Dawley rats were placed on either 5% or 20% ethanol in drinking water or straight water controls for 6 weeks. During this time daily vaginal smears were obtained to evaluate the effects of ethanol on the rat estrus cycle. For the following 14 days the rats were orally given either oil, ethinyl estradiol, Medroxyprogesterone Acetate (*Provera*), or a combination of both steroids in oil. All animals were then sacrificed, with serum being collected for luteinizing hormone and prolactin determinations as well as liver alcohol (ADH) and aldehyde dehydrogenase (ALDH).

Analysis of data showed a disruption of the normal rat estrus cycle due to ethanol alone and almost total ablation from the steroidal compounds. Luteinizing hormone was reduced in the 5% ethanol controls and undetectable in the 20% ethanol and in the contraceptive treated animals. In general prolactin levels were increased due to alcohol and not altered by contraceptives. Levels of ADH decreased in the 5% ethanol treated animals while ALDH levels increased in both the 5% and 20% ethanol ingesting animals.