A7

EFFECTS OF MATERNAL ADMINISTRATION OF ALCOHOL ON FETAL BRAIN DEVELOPMENT. E. Reyes, J.M. Rivera, L.C. Saland and H.M. Murray. Depts. of Pharmacology and Anatomy, The University of New Mexico, School of Medicine, Albq., N.M.

The effects of oral administration of alcohol during pregnancy were determined in the offspring. Female Wistar rats were pair-fed nutritionally adequate liquid diets containing either alcohol (36% total calories) or isocaloric carbohydrates throughout gestation and lactation. Blood samples were obtained from the tail vein of each pregnant animal to monitor blood alcohol levels throughout the experiment. Blood alcohol levels were determined to be approximately 100 mg/dl. The litters were culled to 6 and the weights of the pups monitored daily. Blood alcohol levels of the offspring averaged 80 mg/dl. We examined the brains and livers of 30-day old rat offspring for γGTP activity. An aliquot of the deoxycholic acid liver extract was applied to a concanavalin A column and eluted with buffer containing varying amounts of α-methyl D-glucopyranoside. Routine light microscopic plastic sections revealed large, vacuolated spaces mainly confined to cortical layer V in alcoholic rats, while brains of controls appeared normal. Corresponding light microscopic Golgi studies revealed decreased numbers of dendritic spines on pyramidal cell dendrites in alcohol exposed as compared to control animals. These preliminary data suggest that exposure to alcohol in utero and in the postnatal period has a dramatic effect on neurons and processes in the cerebral cortex, as well as on the membrane bound enzyme, γGTP. Supported, in part, by NIH #2 SO6 RR-081-39-07.

A8

GENDER DIFFERENCES IN ACETALDEHYDE CONCENTRATION AFTER AN ACUTE DOSE OF ETHANOL. Zeiner, A.R., Kegg, P.S., Blackburn, M.R., and Stratton, R. University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma 73190.

Acetaldehyde, the first metabolite of alcohol metabolism, is found in higher concentrations in alcoholics and heavy drinkers after alcohol ingestion than in social drinkers or abstainers. This experiment investigated gender differences related to acetaldehyde. Seventy-nine adult social drinkers (38 females and 41 males) were tested after an overnight fast and at least 4 hours food deprived with 0.52 gm/kg ethanol in water (20% alcohol by volume). Blood alcohol and acetaldehyde concentrations from breath samples were determined every 5 minutes post drink for 70 minutes with a gas chromatograph. The drink was consumed over a 5 minute period. Half of each group ran 30-140 miles per week. The other half were controls. A significant overall gender difference in peak acetaldehyde concentration was obtained ($P<.05$) with males showing higher values than females. Among athletes, these gender differences were greater ($P<.002$). Among controls the gender differences were in the same direction but they were not significant. Groups did not differ reliably on age (M=32.88 yrs., F=31.13 yrs.), drinking history (M=2.07, F=1.92) lean body mass (M=13.02, F=13.02), time to peak blood alcohol concentration (M=30.98 min, F=31.58 min) or ethanol clearance rate (M=0.476 mg%/min, F=0.454 mg%/min). The results have implications for gender differences in alcoholism and biological sensitivity to alcohol. Supported by the Oklahoma Department of Mental Health, Alcohol Division.

A9

THE REVERSIBILITY OF THE MATERNAL STATE RESPONSIBLE FOR THE FETAL ALCOHOL SYNDROME. Dexter, J.D., Tumbleson, M.E. and Middleton, C.C., University of Missouri-Columbia, Medical School and College of Veterinary Medicine, Columbia, Missouri.

In previous reports we have reported the offspring of serial breedings of voluntary alcohol consuming Sinclair (S-1) miniature swine had been evaluated over a three year period. The first and second litters of 12 dams and the third litter of 6 dams were examined. All study animals had been consuming alcohol for at least 18 months prior to the first breeding. The results revealed a progressive decrease in mean litter size from controls of 6.66 in the control litters to 1.8 piglets per litter in the third litter born to alcohol-consuming dams. Perinatal deaths showed a progressive increase from 10% in the controls to 36.4% in the L-3 litter. The birth weight showed a decline from a mean of 719g. in the control group to 467 g. in the L-3 litter. This abstract reports the findings of the breeding 12 of these sows first litter after being withdrawn and kept free from alcohol for 6 months prior to breeding, to the same boars. The results showed 6 sows animals were able to be bred and 6 were unable to be conceived or carry a pregnancy. The 6 bred sows produced a total of 36 piglets for an average of 6.0 piglets/litter. Mean birth weight of 713 gms and percent perinatal deaths was 11%. These findings do not differ from the control animals. These findings indicate the reversibility of the maternal state which produces the fetal alcohol syndrome is reversible.

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A10

ZINC EFFECTS ON HEPATIC FATTY ACIDS IN RATS CONSUMING ETHANOL AND CHOLINE DEFICIENT DIETS. Eskelson, C.D., McDougal, J.N. and Chvapil, M., University of Arizona Health Sciences Center, Medical School, Tucson, Arizona.

One of the major deleterious effects of excessive ethanol (Etoh) consumption is fatty liver which may lead to cirrhosis. The purpose of this study was to investigate hepatic fatty acid changes induced by Etoh and zinc (Zn) in a high fat choline deficient diet. Male Sprague-Dawley rats 29 days old were randomly divided into 5 dietary groups: choline deficient diet; diet plus Etoh; diet plus Zn; diet plus Etoh and Zn; and laboratory chow. Hepatic fatty acid profiles were determined by gas liquid chromatography after 44 and 80 days on the diets. Stearate (C18) levels almost doubled in rats fed the diet. Etoh had no effect; however, Zn diminished the diet effect at 44 days resulting in near normal C18 levels. Palmitate (C16) levels were increased 4 times normal by the diet alone. Both Zn and Etoh decreased the C16 levels at 44 days; however, Zn lost its effect by 80 days. Oleate (C18:1) and linoleate (C18:2) levels were increased fourfold by the diet. Zn and Etoh had no effect on C18:1 or C18:2 at 44 days. At 80 days C18:1 and C18:2 levels more than doubled in rats fed Zn. No changes in hepatic arachidonate (C20:4) levels were induced by the diet, Zn or Etoh. Zn may be acting by either inhibiting the conversion to other fatty acids or inhibiting export of C18:1 and C18:2 from the liver. Zn had different effects when combined with Etoh than when given alone, which suggests Etoh mobilizes C18:1 and C18:2 from the liver or converts them into fatty acids which can be mobilized from the liver.

A11

SUBCELLULAR DISTRIBUTION OF RAT TESTICULAR ALCOHOL DEHYDROGENASE AND THE *IN VITRO* EFFECT OF SELECTED PHARMACOLOGICAL AGENTS. F.S. Messiha and J. Webb, Departments of Pathology and Psychiatry, Texas Tech University Health Sciences Center, School of Medicine, Lubbock, Texas 79430.

Alcohol dehydrogenase (ADH), the probable rate limiting step in the oxidation of ethanol, was found to be distributed between the nuclear (NC) and the cytosolic (CT) fractions of the rat testis. Testicular ADH amounted to 3.8 ± 0.7 nMol/min/mg protein and to 2.7 ± 1.3 units in the NC and CT preparations, respectively. This is compared to 1.3 ± 0.2 units of ADH measured in the 10% (w/v) homogenates of the rat testis. Testicular CT-ADH was inhibited *in vitro* by equimolar concentration (1.0mM) of histamine diphosphate, 38% ($p<0.02$), or 3 methoxytyramine, 33% ($p<0.02$), but not by metanephrine, vanillymandelic acid, homovanillic acid or cimetidine. The inhibition measured was of the noncompetitive type. The compounds studied exerted little changes on testicular CT-ALDH *in vitro*. The results indicate the presence of NAD-dependent ADH activity in NC and CT fraction of the rat testis which may provide a biochemical approach for the evaluation of some of ethyl alcohol-mediated toxicity on the testis.

A12

TESTICULAR ALDEHYDE DEHYDROGENASE: SUBCELLULAR DISTRIBUTION IN THE RAT. F.S. Messiha and J. Webb, Departments of Pathology and Psychiatry, Texas Tech University Health Science Center, School of Medicine, Lubbock, Texas 79430.

The subcellular distribution of aldehyde dehydrogenase (ALDH) in the rat testis shows that the major enzymatic activity was confined to the cytosolic (CT) and to the nuclear (NC) fractions. This is compared to lower specific activity measured in the mitochondrial (MT) and to lesser activity in the microsomal (MC) preparations. Requirement of NAD and sodium pyrophosphate as the respective cofactor and buffer of choice are required for maximal enzymatic activity. The measured activity is of enzymatic source as evidenced by its suppression and deactiviation at 4°C and 50°C, respectively. In addition, testicular ALDH was modified by pharmacological interventions *in vivo* in most subcellular fractions studied. Determinations of K_m show that CT-ALDH possesses the lowest apparent K_m as contrasted with the highest K_m value assayed for MT-ALDH. The results suggest the present of multiple active form of the ALDH, i.e. possibly isoenzymes, and that the testis possesses the metabolic potential in eliminating ethanol-derived acetaldehyde.