

comparable to controls as evidenced by the number of lamellar bodies. These data indicated that functional impairment may result from abnormal development of the alveolar region. Work supported by U.S. Department of Energy under Contract DE-AC06-76RLO 1830.

P40

Toraason, M., and Breitenstein, M.J. (Introduced by B.D. Hardin) CDC, NIOSH, DBBS, 4676 Columbia Parkway, Cincinnati, OH 45226. Electrocardiographic changes in neonatal rats exposed prenatally to ethylene glycol monomethyl ether.

We previously reported electrocardiographic (EKG) changes in fetuses exposed prenatally to ethylene glycol monomethyl ether (EGME) (Teratology 32, 33-39, 1985). The present findings indicate that the same aberrations persist beyond the neonatal period in rats exposed prenatally to EGME. Pregnant dams were treated by gavage on gestation days 7-13 (sperm = day 1) with 50 or 75 mg/kg EGME in 10 ml/kg distilled water. There were no survivors beyond 3 days of age in the 75 mg/kg EGME group. Treatment with 50 mg/kg EGME did not affect maternal body weight gain, but gestation was prolonged. The number of viable litters and litter size were reduced. Growth of offspring and the number of pups surviving through weaning were also reduced by EGME exposure. EKGs were obtained from unanesthetized and unrestrained rats at four and six weeks of age. About ten percent of EGME exposed offspring exhibited EKG abnormalities. The most prevalent abnormality was a QRS aberration that consisted of a double R or S wave, and suggested an intraventricular conduction delay. The delay was of short duration lasting only two-to-four msec in most cases.

P41

MACDONALD*, K.B., D.M. JURILOFF, and M.J. HARRIS, Department of Medical Genetics, The University of British Columbia, Vancouver, B.C., Canada. Genetics and embryopathology of a mouse stock that produces the neural tube defect, exencephaly.

A partially inbred mouse stock, SELH/Bc, produces 16% exencephaly among fetuses or newborns. The genes causing exencephaly have been fixed, and all of 46 SELH/Bc males tested transmitted the defect. The genetic cause of the defect appears to be autosomal recessive mutation(s) at one or two loci, based on analysis of F2, BCL, and BC2 frequencies after an outcross to the normal ICR/Bc strain.

Females are more often affected than males. In the SELH/Bc stock, about 80% of exencephalics and 45% of normals are female. Similar sex ratios were seen in the F2 and BCL generations.

Compared with day 9 embryos from normal strains (SWV/Bc, LM/Bc, ICR/Bc), closure of the anterior neural tube in all SELH/Bc embryos is delayed both chronologically and relative to somite number. In all SELH/Bc embryos, the elevation of the anterior neural folds is delayed, and in some, the folds never elevate and their neural tube therefore remains open. Histological examination of the neural folds is in progress.

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P42

TOCCO, D.R., RENSKERS, K., and E.F. ZIMMERMAN, Children's Hospital Research Foundation, Cincinnati, Ohio. Diazepam-induced cleft palate in the mouse and lack of correlation with the H-2 Locus.

These studies were to determine whether the anxiolytic drug diazepam (DAZ) induces cleft palate through a stress-related mechanism producing glucocorticoid effects or through a phenytoin-like mechanism. Cleft palate frequencies were studied in AJ and SW mice following either one or two day dosing schedules with DAZ. In all cases, mice were food and water deprived for 24 and 48 hr in the one and two day dosing schedules, respectively. High cleft palate frequencies in control mice of both strains resulting from 48 hr food and water deprivation (on day 13.5 and 14.5 of gestation) were reduced in mice deprived for 24 hr, indicating a stress related effect. Two day dosing with DAZ (400mg/kg) produced a net increase in cleft palate frequency in SW (33%) and AJ (18%) mice. Mice treated only on day 13.5 had reduced control and diazepam cleft palate frequencies, neither of which were significant. Clefting was significant but reduced following one day dosing on day 13/20 of gestation (13 days 20 hr) in SW mice (18%), whereas no clefting was seen in the AJ strain. This strain difference was shown not to be related to differences in developmental timing. Production of cleft palate seen in AJ mice after 2 days of dosing may be indicative of an interaction of DAZ with the stresses resulting from food and water deprivation. Genes of the histocompatibility locus, H-2, have been shown to regulate cleft palate formation following glucocorticoid and phenytoin administration to mice. Despite pharmacological similarities between DAZ and phenytoin, comparison of cleft palate frequencies following administration of DAZ to various strains of mice of different H-2 haplotypes indicated that genes associated with the H-2 locus do not regulate DAZ-induced cleft palate in these strains. In summary, these results suggest that diazepam causes cleft palate by a direct action and does not function through a glucocorticoid or phenytoin mechanism.

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P43

TYL, R. W., ^aB. BALLANTYNE*, I. M. PRITTS*, D. R. KLONNE*, L. C. FISHER*, T. A. SAVINE*, D. J. MCNEIL*, and M. F. KUBENA*, Bushy Run Research Center, Export, PA and ^aUnion Carbide Corporation, Danbury, CT. Developmental Toxicity Evaluation of Inhaled Ethylene Glycol Monoethyl Ether (EGHE) in Rats and Rabbits.

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