880 REPRODUCTIVE EFFECTS OF DICYCLOPENTADIENE IN S-D RATS ASSESSED BY A CONTINUOUS BREEDING PROTOCOL

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Dicyclopentadiene (DCP), was evaluated for reproductive toxicity in Sprague-Dawley rats using the Reproductive Assessment by Continuous Breeding Protocol (NTP, 1989). DCP is used in pesticides, fuel additives and adhesives and was selected for study because of its presence in the environment and lack of reproductive toxicity data. DCP was administered by gavage in corn oil at dose levels of 10, 30, and 100 mg/kg to animals that were housed individually for one week and then cohabitated for 16 weeks (20 animals/sex/group). Newborn litters were euthanized after evaluation on postnatal day (PND) 1. Litters born after Week 17 were reared until PND 21 and selected weanlings were administered the same dose levels as their respective parents. On PND 81 ± 10, F_1 animals were cohabitated within groups for one week and necropsied following delivery of the litters. Reproductive toxicity was observed in the 100 mg/kg group females: 28% fewer F_1 pups born live, 8% lower adjusted live F_1 pup weights, higher F_1 pup mortality, increased cumulative days to litter, and decreased F_1 pup survival in the final litter. At 30 mg/kg there was a 4% decrease in female pup weight. At the crossover mating, pup weight was reduced (9%), in the DCP-treated females, while no effects were observed in litters from DCP-treated males. At necropsy, DCP caused a 2%, 7%, and 17% increase in liver weights and a 16%, 15%, and 16% increase in kidney weights in males from the 10, 30 and 100 mg/kg groups, respectively. Microscopically, an increase in the incidence of clear cell foci was observed in the livers of 30 and 100 mg/kg rats. In the second generation, DCP at 100 mg/kg caused a 12% reduction in F_2 pup weight in the presence of increased F_1 liver and kidney weights. The reproductive effects of DCP were not greater than those observed in the first generation. Thus, DCP is a reproductive toxicant, but not selectively so, as there were systemic toxicities at and below reproductively toxic dose levels.

881 INHIBITION OF STEROID GLUCOSYLTRANSFERASE ACTIVITY BY PENTACHLOROPHENOL AT CONCENTRATIONS THAT REDUCE SURVIVAL AND FECUNDITY OF DAPHNIA MAGNA

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Alterations in steroid metabolism by environmental endocrine disrupters can significantly affect steroid hormone-dependent processes such as growth and reproduction. Exposure to the fungicide pentachlorophenol (PCP) has been shown to elicit a variety of endocrine-related adverse effects. The present study was undertaken to establish whether concentrations of PCP that adversely affect survival, growth, or reproduction of *Daphnia magna,* during chronic exposure, also elicit changes in steroid hormone metabolism. Survival or reproduction of daphnids was significantly reduced from exposure to 1.0, 0.5 and 0.25 mg/L PCP. Following chronic exposure to PCP, daphnids were incubated with [^{14}C]testosterone and the testosterone metabolic profile was assessed. The rate of phase I hydroxy metabolites formed was not significantly different from controls. However, phase II steroid glucosyltransferase activity decreased in a PCP concentration-dependent manner for three of the metabolites produced. This effect occurred at PCP concentrations that reduced survival or reproduction. These results demonstrate that PCP alters steroid biotransformation activities at concentrations that affect survival and reproduction. Thus, this biochemical parameter may serve as a biomarker of chronic toxicity associated with PCP.

882 COMPARATIVE DEVELOPMENTAL TOXICITY OF 2-METHOXYETHANOL (2ME), METHOXYACETIC ACID (MAA) AND METHOXYACETALDEHYDE (MALD) IN *DROSOPHILA*

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To assess the developmental toxicity of selected glycol ethers and their metabolites, *Drosophila melanogaster* larvae were reared on media containing equimolar concentrations of 2ME or its acid metabolite MAA (both documented mammalian developmental toxicants), or its acetaldehyde metabolite MALD. *Drosophila* were exposed throughout development (egg through third instar larvae) to 0.085 mM, 0.17 mM or 0.34 mM of each chemical in culture vials, with each vial containing 1 g of powdered medium and 5 ml of distilled water or a solution of test chemical in water. The highest concentration corresponded to 26 mg/vial of 2ME, a concentration previously shown in our laboratory to increase the incidence of bent humeral bristles in developing flies. A mated, untreated, Oregon-R wild-type female (Mid-American *Drosophila* Stock Center) was added to each culture vial and allowed to oviposit for 20 hours, then removed. Emerging adults, collected over 10 days, were examined microscopically (25x) for bent humeral bristles or wing blade notches — morphological endpoints shown to occur with an increased incidence in flies exposed to developmental toxicants. All chemical treatments statistically increased the incidence of bent bristles compared to concurrent controls (chi-square). The percentage of flies with bent humeral bristles observed with each chemical and at each concentration were: 2ME, 4.1, 9.0 and 11.1%; MAA, 7.7, 7.0 and 12.5%; MALD, 8.8, 6.9 and 15.3%. No bristle defects were seen in controls (n = 242). These results indicate that exposure to 2ME or its aldehyde or acid metabolites can induce defects in developing flies and support further utilization of this *Drosophila*-based assay as a pre-screen in developmental toxicology studies.

883 EFFECTS OF HYPERVITAMINOSIS A ON GAMETOGENESIS IN THE NEMATODE *CAENORHABDITIS ELEGANS*

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Vitamin A (retinol) is required for normal growth, development and reproduction, thus, it is an essential nutrient in the diet of most organisms. Being fat-soluble, retinol is primarily stored in the liver. Although required for survival, excess amounts of retinol result in the pathological condition of hypervitaminosis A, which is characterized in *somatic* tissues by edema, weight and hair loss, fatigue, skeletal abnormalities, headaches and death. Much less is known about the effects of hypervitaminosis on gametogenesis, primarily during pachytene of meiosis prophase I, when homologous chromosomes are in the process of pairing. Results of the present study identified decreases in viability and fecundity, and changes in ultrastructural morphology of the gonad and nuclei through the F_3 generation. Such changes correlated with increased concentrations of retinol in the growth medium. Synaptonemal complexes were not present in nematodes treated with high retinol concentrations (81, 243 and 729 μg/ml) although had normal ultrastructure at lower concentrations.

884 DEVELOPMENTAL EFFECTS OF LOW-FREQUENCY MAGNETIC FIELDS IN MICE

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The possible adverse effects on pregnancy of low-frequency magnetic fields caused by alternating current have been under concern for some time. In most studies, no or only slight effects on fetal development have been observed in mammals exposed to low frequency magnetic fields. In CBA/S mice increased incidence of resorptions have been observed. The present study attempted to replicate the earlier results in CBA/S mice and study further the effects of magnetic field on pregnancy and embryonic development in mice. The pregnant CBA/S mice were exposed continuously to a 20-kHz sawtooth magnetic field from day 0 to day 18 of pregnancy for 24 h/day until necropsied on day 18. Control animals were under similar conditions without magnetic field. The magnetic field strength was 12 A/m peak to peak (flux density 15 μT). On gestation day 18 the uterine contents, ovaries and very early resorptions were examined. Maternal blood samples were collected for determination of hematological parameters. In other experiments the development of fertilized mouse eggs exposed to 50-Hz sinusoidal magnetic field (field strength 10 A/m r.m.s) were studied. Slight increase of resorptions were observed, otherwise results were negative. Supported by the Swedish Work Environment Fund.

885 EVALUATION OF THE SUBCHRONIC, DEVELOPMENTAL, AND REPRODUCTIVE TOXICITY OF 60 Hz MAGNETIC FIELDS

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A series of four *in vivo* studies was performed to evaluate the possible effects of exposure to power frequency magnetic fields (EMF) on overall health status, fetal development, and reproductive function in rodents. In all studies, animals were exposed continuously for 18.5 hrs/day to pure sinusoidal 60 Hz magnetic fields of 10 G, 2 G, 20 mG, or 0 G (control), or intermittently (1 hr on, 1 hr off) to 10 G fields. In the subchronic toxicity study, F344 rats and B6C3F1 mice (10/sex/group) were exposed to EMF for 8 weeks; survival, body

SOCIETY OF TOXICOLOGY

34th Annual Meeting

THE TOXICOLOGIST

Volume 15, No. 1, March 95

FUNDAMENTAL AND APPLIED TOXICOLOGY