1298 PROTECTION AGAINST RADIOSENSITIZER-INDUCED APOPTOSIS BY FREE RADICAL SCAVENGERS.

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CI-1010 is a radiosensitizing nitroimidazole analog which possesses a reactive alkylating functionality and thus has potential utility as an anticancer agent. In the rat, CI-1010 given as a single intravenous dose at ≥225 mg/kg induces a progressive retinal degeneration with an extensive apoptotic response in the outer nuclear layer of the retina. To investigate whether this apoptotic response may be related to free radical generation, the effect of free radical scavengers on CI-1010-induced apoptosis was evaluated in cultured SH-SY5Y human neuroblastoma cells. Assessed quantitatively by MTT cell proliferation assay, CI-1010 caused cell death with an LC_{50} of approximately 750 μM. Apoptotic cell death was confirmed by terminal nucleotidyl transferase labelling. Vitamins A, C, and E, butylated hydroxytoluene, butylated hydroxyanisole, cysteine, mannitol, and catalase afforded some protection against CI-1010-induced apoptosis, but superoxide dismutase (SOD) appeared to be most effective against CI-1010-induced apoptosis in this model. For example, survival of cells exposed to 1000 μM CI-1010 was 15.8% of controls, but 81.7% when coadministered 50 μg/mL SOD. These results indicate that generation of free radicals, particularly superoxide radicals, play a central role in CI-1010-induced apoptosis, although the proximate apogen remains to be determined. Supported by NIH ES06103 to MAP.

1299 PATERNAL EXPOSURE OF RABBITS TO LEAD: BEHAVIORAL DEFICITS IN OFFSPRING.

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Paternal exposures to exogenous agents have produced various developmental defects in the offspring, including decreased litter size and weight, increased stillbirth and neonatal death, birth defects, tumors, and functional/behavioral abnormalities—some of these effects being transmitted to the second and third generations. Most studies assessing function of offspring following paternal exposure have utilized rats, but the NTP is validating the rabbit as an animal model for human reproductive toxicity. An important part of reproductive toxicology is assessment of the reproductive ability of males following exposure, as well as developmental and functional assessment of their offspring. We report here a pilot study and a main study to investigate the feasibility of using rabbits to assess the functional effects of paternal exposure to lead. The pilot study included 7 males/group exposed for 15 weeks to lead acetate to produce 0, 50, or 110 μg/dL blood lead. The main study included 15 males/group exposed for 15 weeks to lead acetate to produce 0, 20, 40, and 80 μg/dL blood lead. The exposed males were mated with unexposed females. The females delivered and reared their own offspring. The offspring were weighed at 5, 10, 15, 20, 25, 30, and some at 35 days of age. They were tested for exploratory activity in a standard figure-8 "maze" for 30 min/day on days 15, 20, 25, and 30. Of the 21 male rabbits that were mated in the pilot study, 16 produced viable litters, with a mean of 6 livebirths/litter in each treatment group (range 2–8). Of the 60 rabbits mated in the main study, 57 produced litters, and 2 died giving birth. Significant postnatal deaths were observed in all groups, with about half of the offspring dying before day 15. There were no treatment-related effects on offspring weight gain through weaning. The data suggest that paternal lead exposure of rabbits may reduce figure-8 activity on day 25, the time of peak activity in the offspring.

1300 BEHAVIORAL EFFECTS OF GESTATIONAL EXPOSURE TO CHLORPYRIFOS IN RATS.

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The developmental neurotoxicity of chlorpyrifos (*O,O*-diethyl-*O*-3,5,6-trichloro-2-pyridyl-phosphorothioate) was assessed in Long-Evans rats following late gestational exposure (days 14–18) to either 0, 3, or 5 mg/kg/day (p.o.; n≥16/dose). Cholinesterase inhibition and other measurements in these rats are reported elsewhere (see Barone *et al.*, this meeting). Maternal effects were evaluated by observations of the dams after dosing. No overt neurological signs were detected in the dams, but there was a trend towards lower open-field activity in the high-dose group. All offspring were evaluated for development of the righting reflex on postnatal day (PND) 2–7. A subset of these rats (n = 10/dose/sex) were also tested for a range of neurobehavioral endpoints using a functional observational battery (FOB) and motor activity on PND 17, 24, 65, and 92. On PND 2, a trend towards slower righting reaction was evident in offspring of the high-dose dams, but by PND 7 all rat pups were righting normally. Few significant behavioral changes were detected at later time points. Male rats in the high-dose group showed decreased handling reactivity (PND 24 only), and decreased activity and rearing in the open field throughout the course of testing. On the other hand, female rats showed increased reactivity before weaning (high-dose group), and increased open-field activity thereafter (low-dose group only). These data suggest qualitative sex-related differences associated with CPF exposure, but the effects were small. Thus there were few persistent neurobehavioral consequences of chlorpyrifos following late gestational exposure. (TLL supported by NIEHS Training Grant T32ES07126)

1301 DEVELOPMENTAL EFFECTS OF GESTATIONAL EXPOSURE TO CHLORPYRIFOS IN THE RAT.

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This study addressed the issue of developmental outcome following late gestational exposure to chlorpyrifos (CPF; *O,O*-diethyl-*O*-3,5,6-trichloro-2-pyridyl-phosphorothioate). Pregnant Long-Evans rats were gavaged with CPF in corn oil (0, 3, 5 mg/kg; n≥16/dose group) on gestational days (GD) 14–18 observed for cholinergic signs and other clinical signs of toxicity (see Phillips *et al.*, this meeting). Dams were sacrificed on GD 19 (n≥4/dose group) and their brain and blood, and fetal brain cholinesterase (ChE) activity were assayed. Remaining litters were carried to term for examination of developmental outcomes. Animals were sacrificed on postnatal day (PND) 1, 4, 7, 12, 17, 21, and 92, and brains dissected into 7 distinct regions for neurochemical analysis. Neurochemical endpoints included ChE activity; regional DNA and protein content; and serum thyroid hormone levels. Other developmental landmarks examined were eye opening (PND 14–17), vaginal opening (PND 32–45), preputial separation (PND 40–50), estrus cyclicity (PND 50–85) and testes weights (PND 92). No overt developmental toxicity was observed following late gestational exposure to CPF as determined by numerous measures including; maternal weight gain, litter size, sex ratio of litters, postnatal survival, pup brain and body weights. ChE activity was markedly inhibited in both the maternal blood (60–80%) and brain (40–75%) on GD 19; whereas, fetal brain ChE inhibition was ≤10%. This CPF exposure had no effect on the ontogeny of circulating thyroid hormones (serum T3 & T4), regional brain DNA or protein levels. Trends emerged in a dose-related fashion for eye opening, vaginal opening and preputial separation which warrant further investigation. These data indicate that, in general, following late gestational exposure to CPF that the dam appears to protect the fetus from colinesterase inhibition and from long term adverse consequences. (TLL supported by NIEHS Training Grant T32ES07126).

1302 RETINAL TOXICITY INDUCED BY PRENATAL COCAINE EXPOSURE IN RAT FETUSES.

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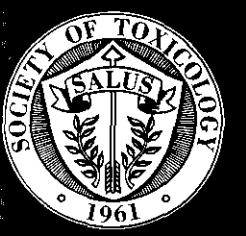
The increased use of cocaine in the United States and World-Wide has created a great concern about its effects on fetuses and neonates of pregnant cocaine abusers. The effects on neonates are varied: fetal growth delay, microcephaly, abnormal neurological functions, microphthalmia and maternal obstetric complicatons. In this study, the effect of cocaine prenatal administration was studied microscopically in the retina of rat fetuses. Twenty-five pregnant Wistar rats were injected IP with an aqueous cocaine solution using a 30mg/kg daily dose during 45 days. Control grup rats (15 pregnant animals) received saline solution for the same period. Day zero of gestation was the day after mating. Dosing begun on this day. The rats were killed on gestation day 21 and fetuses were obtained in order to examine them. The histophatological light and electron microscope studies of the retinas showed interstitial oedema, areas depleted of cells, necrosis and hypercromatic ganglion cells. The number of fetuses of control rat was significantly high compared with exposed fetuses. There also was a significantly lower number of retinal cells as compared to control fetuses. In four cases, teratogenic lesions of the retina were observed while no changes were present in control fetuses. Results indicate that devel-



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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshops, roundtables, and poster sessions of the 36th Annual Meeting of the Society of Toxicology, held at the Cincinnati Convention Center, Cincinnati, Ohio, March 9-13, 1997.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 371.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 395.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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