the Reproductive phase, estrous cycling was followed prior to mating and continued until mating was verified. Mated females were allowed to litter. Their parturition and offspring were assessed. Reproductive phase dams were necropsied 4 or 5 days after parturition. Ovaries from all Interim and Reproductive phase rats were weighed and examined for numbers of corpora lutea. The uteruses of Reproductive phase dams were examined for implantation sites. The day of vaginal opening was not affected by lansoprazole administration except in weanlings dosed at 150 mg/kg/day, where the mean day of opening was significantly increased (Day 34) compared to their controls (Day 31). Individual values were all within the historical range. This delay was attributed to a nonspecific slower growth rate in this group, rather than a specific effect on the reproductive system. Vaginal opening occurred at approximately 110 grams of body weight for the 150 mg/kg/day group and their controls. Lansoprazole had no effects upon ovarian weights, numbers of corpora lutea or reproductive function in this study.

2053 THE INHIBITION OF PROGESTERONE (P) FORMATION OF CULTURED OVARIAN THECA-INTERSTITIAL (TI) CELLS BY THE METHOXYCHLOR (MC) METABOLITE, HPTE, IS NOT MEDIATED THROUGH THE ESTROGEN RECEPTOR (ER) OR ANDROGEN RECEPTOR (AR).

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Sponsor: V. Castranova.

The pesticide MC is used on agricultural crops and livestock. MC exposure in rodents is linked to impaired steroid production, ovarian atrophy and reduced fertility. Following in vivo administration, it is rapidly converted to HPTE, reported active metabolite, by the liver. Both MC and HPTE have weak estrogenic and antiandrogenic activities, and these effects are thought to be mediated through the ER and ARs, respectively. Previous in vivo studies in female animals demonstrated decreased P production but no change in serum estrogen levels following exposure to MC. We showed a decrease in androgen and P production of follicular cells by HPTE in-vitro. The current studies examined the mechanism of actions of HPTE on P production by cultured ovarian TI cells from immature rats. To isolate TI cells, 24-25-day-old female Sprague-Dawley rats were injected (s.c.) with 20 I.U. of pregnant mare serum gonadotropin. Approximately 48 h following treatment, ovarian tissue was digested with collagenase and dispersed. TI cells were cultured in DMEM / F12 medium and exposed to HPTE for 24 h on the day of plating. Exposure to HPTE (0, 10, 50, 100 nM) alone inhibited P formation in a dose-dependent manner with a significant decline to ~12 % of control at 100 nM. In contrast, estrogens (estradiol, bisphenol-A, and 4-tert-octylphenol), pure anti-estrogen ICI 182,780 (ICI), and anti-androgens (4-OH-flutamide or the vinclozolin metabolite M-2) had no effect on P production even at 1000 nM. Co-treatment of HPTE with ICI did not block the effect of HPTE on P formation. These studies revealed that HPTE inhibition of P production by cultured TI cells is unique, and does not appear to be mediated through the ER or AR.
The findings and conclusions in this abstract have not been formally disseminated by NIOSH and should not be construed to represent any agency determination or policy.

2054 *IN VIVO* METHYL-PARATHION EXPOSURE IMPAIRS MALE FERTILIZING ABILITY IN MICE.

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Evidence supports that some environmental agents can interact with sperm DNA causing genetic damage that may affect fertility. Organophosphorous pesticides (OP) are among the most used agrochemicals and have been associated with male reproductive effects. We previously showed that methyl-parathion (Me-Pa), an OP, alters sperm quality and induces genotoxic effects in sperm that were related to oxidative damage. This study was conducted to determine the ability of mice spermatozoa to fertilize oocytes after Me-Pa exposure (20 mg/kg bw/ip), evaluating two stages of spermatogenesis in spermatozoa collected from cauda epididymis-vas deferens at 7 days post-treatment (dpt; cells at epididymal maturation at the time of exposure) and at 28 dpt (cells at meiosis at the time of exposure). Sperm quality, mitochondrial function using JC-1 staining, acrosome reaction induced by GABA (induced-AR), fertilization rate at 8 h after IVF, and lipid peroxidation (LPO) as malondialdehyde (MDA) production, were evaluated. Acute exposure to Me-Pa altered sperm quality (viability and motility) at both times, and a decrease in mitochondrial function was observed that was more pronounced at 7 than at 28 dpt (19% and 77% of the control). The fertilization rate (pronuclear formation) was decreased and was also more severe at 7 dpt than at 28 dpt (21% and 55%) compared with the control group (73%). This suggests that cells at both spermatogenic stages are target of Me-Pa toxicity. An increase (3.2-fold) in MDA production was observed only at 7 dpt and was negatively correlated with mitochondrial activity (r= -0.886) and induced-AR (r= -0.880). These correlations observed between LPO and mitochondrial activity and AR suggests that the induction of oxidative stress by Me-Pa exposure may be involved in the alteration of events preceding fertilization, therefore, compromising the ability of spermatozoa to fertilize. This study was supported by CONACyT-Mexico (Grant #44643 given to BQV).

2055 PROTECTIVE ROLE OF **A**-TOCOPHEROL ON THE OXIDATIVE AND GENETIC DAMAGE CAUSED BY METHYL-PARATHION EXPOSURE IN MICE SPERMATOZOA.

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Organophosphate pesticides (OP) are widely used in Mexico and OP exposure has been associated with fertility problems in agricultural workers. OP induces the generation of reactive oxygen species which alter DNA integrity. We previously showed that methyl parathion (Me-Pa), an OP, alters sperm DNA that was associated with oxidative damage. Since oxidative stress can be reversed by antioxidant treatment, we evaluated the protective effect of α-tocopherol on the oxidative and genetic damage caused in spermatozoa by Me-Pa treatment. Adult ICR male mice were exposed to Me-Pa (3, 6 and 12 mg/kg, bw/i.p/5 days) or co-exposed with the highest dose of Me-Pa (12 mg/kg, bw/i.p/5 days) and α-tocopherol (50 mg/kg/i.g/5 days). Blood and sperm cells from cauda epididymis-vas deferens were extracted 24 h after the last administration, and erythrocyte acetylcholinesterase (AChE), sperm quality, lipid-peroxidation (LPO) by malondialdehyde (MDA) production and the chromatin structure by SCSA (DFI% parameter) were evaluated. Me-Pa exposure caused a dose-response decrease in AChE (52% to 71% inhibition). An increase in MDA at 6 (1.9-fold) and 12 mg/kg (2.5-fold) was observed, as well as an increase in DFI% (fragmented DNA), showing higher values of 6- and 22-fold at doses of 6 and 12 mg/kg, respectively, compared to the controls. Sperm viability and motility also showed dose-response decreases after Me-Pa exposure. On the other hand, animals co-exposed with Me-Pa and the antioxidant α-tocopherol showed values of LPO, DNA damage and sperm quality similar to the controls, compared with the exposed group; while inhibition of AChE was similar to the Me-Pa exposed group. These results strongly suggested that oxidative damage caused by Me-Pa is prevented by the antioxidant treatment, and that oxidative stress is involved in the sperm chromatin structure damage observed after OP exposure, but not in the AChE inhibition. This study was supported by CONACyT-Mexico (Grant #44643 given to BQV).

2056 TIME-DEPENDENT EFFECTS OF DI(N-BUTYL) PHTHALATE ON THE GENE EXPRESSION PATTERNS IN THE TESTIS OF SPRAGUE-DAWLEY RATS.

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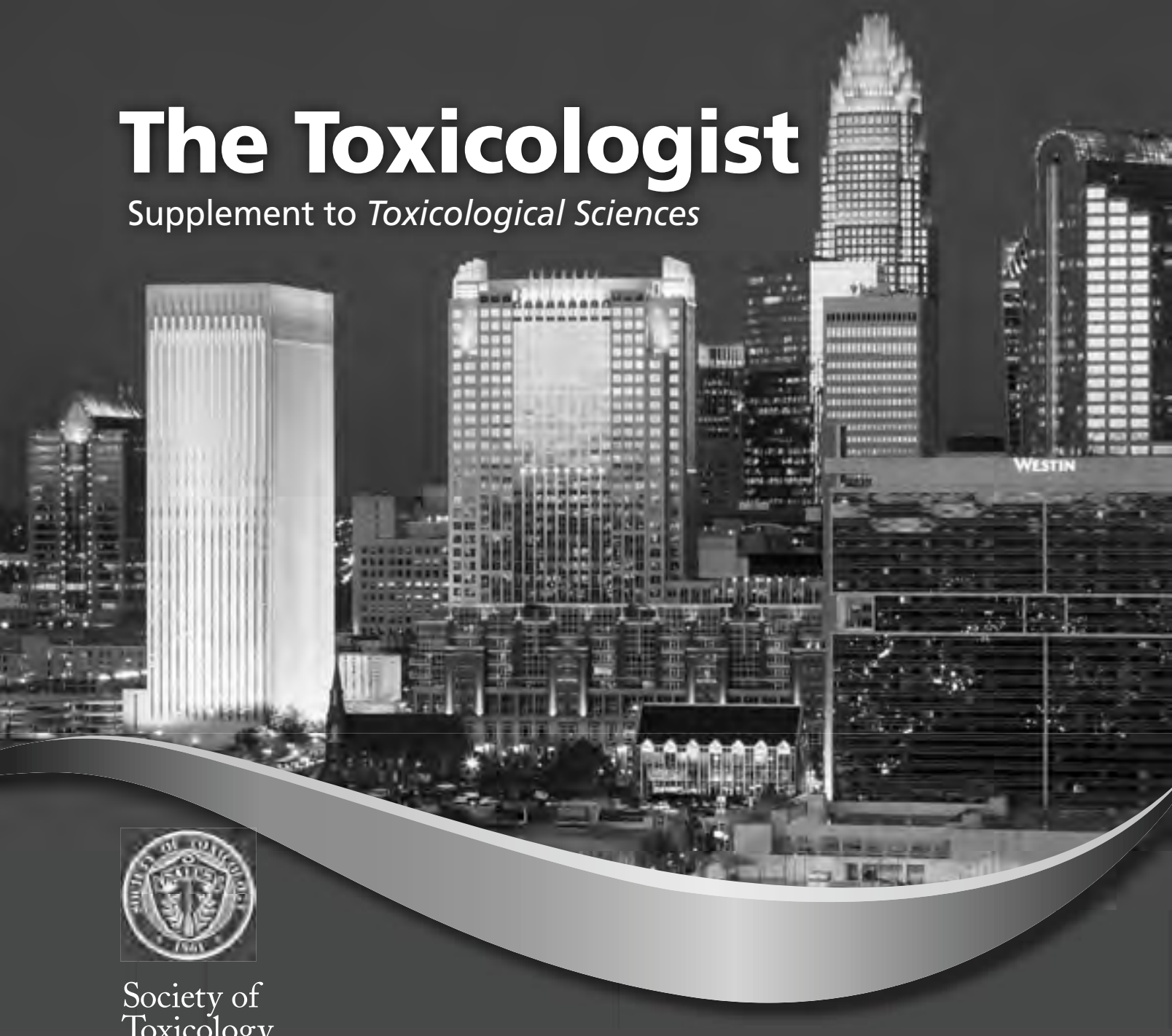
Time-dependent effects of di(n-butyl) phthalate (DBP) on expression patterns of testicular gene were studied in Sprague-Dawley for different periods of exposure (1, 7, 14, and 28 days). A control group receiving corn oil was also monitored for comparative purposes. Gene expression patterns were measured using the reverse transcription-polymerase chain reaction (RT-PCR). Serum concentrations of DBP were increased with the time of exposure and were significantly higher in treated rats when compared to controls. Similar to significant decrease in testes weights, for 14 and 28 days, epididymis weight was also markedly reduced after 14 and 28 days exposure. DBP caused significant induction of steroidogenic acute regulatory (StAR) and SR-B1 mRNA at 14 and 28 days exposure in the group receiving 750 mg/kg/day. P450scc mRNA was decreased in the group treated with 750 mg/kg/day at day 7; thereafter, an apparent increase in P450scc mRNA was observed after 14 and 28 days exposure. High dose of DBP significantly increased the CYP17 mRNA level after 28 days exposure. At 7 days, significant reduction of CYP19 mRNA was observed only in the group exposed to 750 mg/kg/day of DBP. In addition, DBP significantly decreased mRNA levels of Spag4 and LDHA after 7 days exposure. Data indicate that acute and chronic exposure to DBP showed mechanistically distinct effects on steroidogenesis pathway in the testes of Sprague-Dawley rats. These results indicate that the steroidogenesis-related genes investigated in this study may provide insights into the molecular mechanisms underlying DBP induced testicular dysgenesis in humans.

The Toxicologist

Supplement to *Toxicological Sciences*



Society of Toxicology

46th Annual Meeting and ToxExpo™

Charlotte, North Carolina

An Official Journal of the Society of Toxicology

www.toxsci.oxfordjournals.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 96, Number 1, March 2007

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 46th Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

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

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