cells as test model. Testes were obtained from 20 Sprague-Dawley rats and the Leydig isolated. The purity of Leydig cells was determined to be 94.6% and the cells maintained their testosterone capabilities for 48 hours. Fresh medium containing 2-bromopropane (1.00 mM; 0.10 mM, 0.01mM and vehicle control) and human chorionic gonadotropin (hCG) were added in the cell culture. Superoxide dismutase (SOD), Malondialdehyde (MDA), and Glutathione peroxidase (GSH-PX) were examined from the medium of each well and were detected by biochemical methods. The proportion of cells with undamaged DNA was decreased significantly and those with different grades of damaged DNA were increased significantly in the cells exposed to the 2-bromopropane. The level of MDA and GSH-PX activity increased significantly in the cell groups exposed to 0.10 mM and 1.00 mM 2-bromopropane, meanwhile, SOD activity decreased considerably in these two group cells when compared to the control group. It can be concluded that 2-bromopropane exerts its toxicity on testis by inducing DNA damage and impairing functional antioxidant cellular defense as well as enhancing lipid peroxidation process.

350 LACK OF EFFECTS OF PERINATAL EXPOSURE TO LOW DOSES OF BISPHENOL A ON MALE RAT OFFSPRING VENTRAL PROSTATE GLANDS.

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Bisphenol A (BPA) is used in packaging materials for canned foods and beverages. Thus humans may ingest small quantities of BPA which is a weak estrogen suspected of being able to perturb endocrine homeostasis. The experimental design of the present follow-up study was driven by statistical power considerations. In a preceding replicate block design using one or two pups/sex /litter as representative of biological events in same sex littermates, there was an apparent increase in ventral prostate (VP) tissue fresh weights of 6 months old male F1 Sprague–Dawley (SD) offspring whose mothers were exposed to a wide dose range of BPA (Toxicol. Sci. 54, Suppl., 256A, 2000). Those observations raised concerns about sampling design for highly variable end points such as VP weights of SD rats (Elswick *et al.*, Reprod. Toxicol. 14, 359-367, 2000). The current objective was to reach an unequivocal decision as to whether or not BPA-induced effects could be ascertained using a more stringent experimental sampling design. Maternal BPA exposure (n = 20/dose group) occurred *via* drinking water at 0, 0.005, 0.5 or 50 mg BPA/L from gestation day 2 through weaning on postnatal day 21. The estimated daily intakes based on individual water consumption were 0, ~1 µg, ~70-120 µg and ~7-12 mg/kg. After weaning four males, litter sex composition permitting, were randomly assigned to be held (2 per cage) with no further BPA exposure until 6 months old at which time the male reproductive tract organs, including sexual accessory glands, were collected for fresh weight determinations. The prostate was divided into its ventral and dorsolateral lobes and fixed for histological examination. Compared to concurrent controls there were no significant BPA-induced changes in any of the end points examined. No differences in prostate micromorphology were detectable. The data revealed that protracted maternal ingestion of very low to moderate levels of BPA did not affect the VP fresh weights of male rat offspring.

352 DIFFERENTIAL EFFECTS OF 4-*tert*-OCTYLPHENOL (OP), 17β-ESTRADIOL (E2), BISPHENOL A (BIS), OR ENDOSULPHAN (ENDO) ON STEROIDOGENIC COMPETENCE OF CULTURED ADULT RAT LEYDIG CELLS (LC).

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OP (a surfactant additive), Bis (a component of polycarbonate plastics), and Endo (a chlorinated cyclodiene insecticide) exhibit weak estrogenic activity. These studies examined the direct effects of OP (1-2000 nM), E2 (1-1000 nM), Bis (1-1000) or Endo (1-1000 nM) on basal or 10 mIU/ml human chorionic gonadotropin (hCG)-stimulated testosterone (T) formation by cultured LC from adult rats following 4 or 24 h exposures. Exposure to OP alone increased T levels at the highest dose by 100 or 50% above control following 4 or 24 h exposures, respectively. However, hCG-stimulated T declined modestly (10-20%, but not significantly) following 24 h exposure. Exposure to E2, Bis, or Endo had no effect on basal or hCG-stimulated T. To evaluate whether an enzymatic step(s) converting cholesterol to T is affected by OP, cultured LC were exposed to increasing OP + hCG for 24 h. Next, fresh medium containing 1 µM 22(R)hydroxycholesterol (Chol), pregnenolone (Preg), progesterone (Prog) or androstenedione (A-dione) were added to each well, and their conversion to T over 4 h evaluated. Progressive declines in Chol, Preg and Prog conversion to T were observed but not A-dione, suggesting that OP inhibits 17α-hydroxylase/C17,20-lyase activity, and, potentially, P450-cholesterol side-chain cleavage and 3β-hydroxysteroid dehydrogenase activties, but not 17β-hydroxysteroid dehydrogenase. In contrast, exposure to E2, Bis or Endo + hCG for 24 h had no effect on Chol or Prog conversion to T. Furthermore, concomitant exposure to ICI 182,780, a pure estrogen antagonist, or antioxidants did not alter the effects of OP on Chol or Prog conversion to T, suggesting that OP effects are not estrogen receptor mediated or due to generation of free radicals, respectively. In addition, OP, Bis or Endo had no effect on hCG binding to membrane receptors on cultured LC. These results suggest that the effects of OP on steroidogenic competence of adult rat LC differs from that of E2, Bis and Endo.

353 INHIBITION OF CYTOCHROME P450 REDUCTASE EXPRESSION IN TESTES OF NONYLPHENOL (NP)-EXPOSED RATS.

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Nonylphenol, used in the production of nonionic surfactants with a wide use in industrial and residential applications, has been shown to have low affinity for estrogen receptors. Perinatal administration of nonylphenol and related compounds has been reported in some studies to alter sexual development in males. Previous work has indicated a decrease in neonatal serum testosterone (T) and inhibition of 17 α-hydroxylase/C17-20 lyase (P450c17). Our present studies examined the effect of nonylphenol on expression of P450c17and NADPH-cytochrome P450 reductase, key enzymes involved in T synthesis. Male rats (F1 and F2) from a multigeneration study were dietarily exposed to NP (0, 25, 200, and 750 ppm) throughout gestation and until sacrifice at either postnatal day 2 (PND2), PND 50, or PND 140. Total RNA was isolated from testes and examined for relative abundance of P450c17 and P450 reductase mRNA by multiplex reverse transcription-polymerase chain reaction (RT-PCR). The mRNA levels of the enzymes were not affected by NP treatment in either generation. Interestingly, Western blot analysis indicated that protein levels of P450 reducatase in testicular microsomes were significantly reduced in 25, 200 and 750 ppm dose groups at PND 50 and PND 140 in both F1 and F2 generations. These results indicate that NP can decrease levels of cytochrome P450 reductase, an enzyme important to the activity of P450c17, in vivo.

354 MULTIPLE MECHANISMS OF MOLINATE TESTICULAR TOXICITY: TESTOSTERONE *vs* RETINOIC ACID.

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The thiocarbamate herbicide, molinate (MOL), has been previously shown to cause testicular toxicity in rats. In rat testis and liver, MOL is metabolically activated *via* sulfoxidation to form a metabolite that binds to and inhibits the carboxylesterase, hydrolase A. It was proposed that MOL could limit testosterone biosynthesis by inhibiting the esterase-dependent formation of free cholesterol. In support of this hypothesis, the hydrolysis of cholesterol esters has been found to be decreased *in vitro* after *in vivo* MOL exposure. We also examined the effects of MOL and molinate sulfoxide (MSO) on testosterone production in cultured Leydig cells by ELISA and on nonspecific esterase (NSE) activity using paranitrophenyl acetate as substrate. The IC_{50} for NSE inhibition by MOL and MSO (5.42 µM and 1.9 nM, respectively) were more than two orders of magnitude below that required to inhibit testosterone production (750 and 60 µM, respectively) suggesting that the two may not be directly related. However, in addition to hydrolase A, MOL has been reported by others to inhibit aldehyde dehydrogenase in liver. Retinoic acid, required for spermatogenesis, is produced in the testis by the action of an aldehyde dehydrogenase on retinal which in turn can be derived from the hydrolysis of retinyl esters by an esterase. Thus using HPLC and a spectrophotometric assay, we have examined the effects of MOL and MSO on the production of retinoic acid in liver and testis S9 fractions. In both tissues MSO but not MOL inhibited retinal dehydrogenation with an IC_{50} in the testis of approximately 470 nM. The inhibition of dehydrogenation of retinal to form retinoic acid represents a novel mechanism by which MOL exposure could impair testicular function in rats.

355 EFFECT OF DIETARY GENISTEIN ON TESTICULAR ANDROGEN RECEPTORS (AR) IN CD RATS.

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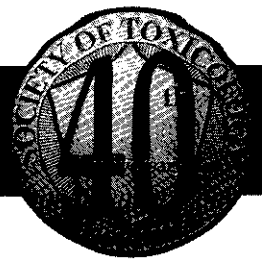
Genistein is an isoflavone and phytoestrogen to which human exposure occurs primarily from soy food products and dietary supplements. Because previous work had indicated possible effects of genistein on spermatogenesis, and because perinatal exposure to estrogens has been reported to alter AR in male reproductive tissues,



Society of Toxicology

40th Annual Meeting

An Official Journal of the
Society of Toxicology
Supplement

TOXICOLOGICAL SCIENCES
Formerly Fundamental and Applied Toxicology

The Toxicologist

Abstracts of the 40th Annual Meeting

Oxford University Press

Volume 60, Number 1, March 2001

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, roundtable, and poster sessions of the 40th Annual Meeting of the Society of Toxicology, held at the Moscone Convention Center, San Francisco, California, March 25–29, 2001.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 451.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 479.

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