the treated groups, malformations were noted following exposure at every GD, although the incidence of specific malformations varied by GD. At GD 16, the highest incidence was noted for permanent nipples (46% pups, 60% litters), epispadias (12% pups, 30% litters), and missing epididymal components (5% pups, 20% litters). The highest incidences for hypospadias (58% pups, 80% litters), vaginal pouch (49% pups, 70% litters), cleft prepuce (29% pups, 60% litters) and missing prostate lobes (12% pups, 60% litters) were noted at GD 17. At GD 18 the highest incidence of malformations noted were epispadias (5% pups, 30% litters), reduced prostate size (32% pups, 90% litters) and abnormal kidneys (3% pups, 30% litters) and bladders (7% pups, 30% litters), while on GD 19 70% of the litters had animals with abnormal seminal vesicles. Thus, a single gestational exposure of flutamide induced numerous reproductive tract malformations consistent with previously reports following multiple exposures, with the timing of the exposure producing marked tissue selectivity in the response noted in adult offspring.

913 EFFECTS OF SULFASALAZINE ON SPERM ACROSOME REACTION AND GENE EXPRESSION IN THE REPRODUCTIVE ORGANS.

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Sulfasalazine (SASP) has been reported to depress the fertility in men. This study was undertaken to investigate the mechanism by which SASP affects fertility. After we confirmed the effect of SASP on the fertility of rats administered the drug at the dose of 600 mg/kg/day for 28 days, we investigated its effects on sperm motion and acrosome reaction using FITC-concanavalin A lectin stain and on gene expression using cDNA microarray and real-time RT-PCR in the reproductive organs. We observed a decrease in sperm velocity and a depression of acrosome reaction in the SASP treated group. In the testes, acrosome membrane related genes (CD59) expression was slightly altered in the SASP treated group. There were, however, no changes in the expression of the genes related to spermatogenesis. In the epididymides, the expression of CD59 and other acrosome membrane related genes, membrane cofactor protein (MCP) and decay accelerating factor (DAF), were decreased in the SASP treated group. It is known that CD59, MCP and DAF have biological functions related to sperm motion and that MCP is involved in the acrosome reaction or binding of the sperm with the egg. From these findings, it was elucidated that the effects of SASP on fertility were mediated by a depression of sperm velocity and acrosome reaction. These findings correlated with the decreased expression of CD59, MCP and DAF gene in the epididymides.

914 METHYL TERTIARY-BUTYL ETHER INDUCES ALTERATIONS IN MOUSE TESTIS WEIGHT, TESTOSTERONE PRODUCTION AND MORPHOLOGY.

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Methyl tertiary-butyl ether (MTBE) is the most common fuel oxygenate used today. Oxygenating fuel serves to induce a more complete combustion reaction, thus reducing CO and hydrocarbon emissions. Because of the high water solubility and widespread use of MTBE, there is a high risk of exposure through groundwater that has been contaminated with MTBE oxygenated fuel from leaking, underground storage tanks and pipelines. In this study, mice were exposed to doses of 80, 800, and 8000 ppb MTBE in drinking water for 28 days. Results demonstrated a significant, dose-dependent increase in mean combined testis weight, mean seminal vesicle weight, mean seminiferous tubule diameter, and incidence of abnormal tubules. Serum testosterone was substantially decreased by exposure to 800 and 8000 ppb of MTBE. These results indicate that MTBE may act *via* a disruption in endocrine-mediated Leydig cell testosterone production. Supported by NIH RR16457 from the BRIN Program of the NCRR and a grant from the Rhode Island College Faculty Research Committee.

915 *IN VIVO* EXPOSURE OF YOUNG ADULT RATS TO METHOXYCHLOR (M) REDUCES SERUM TESTOSTERONE (T) LEVELS, BASAL LEYDIG CELL (LC) T FORMATION, LC CYTOCHROME P450 CHOLESTEROL SIDE-CHAIN CLEAVAGE (P450SCC) ACTIVITY AND SERUM DEHYDROEPIANDROSTERONE (DHEA) LEVELS.

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M is a pesticide developed as a replacement for dichlorodiphenyltrichloroethane (DDT). Although its metabolite, 2, 2-bis(p-hydroxyphenyl)-1, 1, 1-trichloroethane (HPTE), is thought to be the active compound, both M and HPTE have been reported to exhibit weak estrogenic and/or antiandrogenic activities and thereby produce adverse reproductive effects in rodents. In the current studies young adult male rats (at least 11 animals per each treatment group) were gavaged once daily between days 54-60 days of age with 0, 5, 40 or 200 mg M/kg body weight in corn oil. Animals were sacrificed ~24 h after the last exposure to assess the effects of M on LC steroidogenic competence. Serum T levels declined from 4.40 ± 0.52 ng/ml (control) to 1.82 ± 0.27 ng/ml at the 200 mg/kg dose. Similarly, both wet and expressed seminal vesicle weights declined to 44 and 60% of control, respectively, at the highest exposure dose. However, serum LH and FSH levels were unaffected by M. In addition, testicular LC isolated from exposed animals produced less T under basal conditions following a 4 h incubation period (2.20 ± 0.13 ng T/4 h/10^5 cells in LC from 200 mg/kg exposed animals vs 4.50 ± 0.31 ng/4 h/10^5 cells in control cells). Also, P450scc activity of isolated LC declined from 20.44 ± 0.92 ng side-chain/h/10^5 cells (control) to 16.10 ± 1.29 and 10.15 ± 0.98 ng/h/10^5 cells in LC from animals exposed to 40 and 200 mg/kg M, respectively. Although serum corticosterone levels were unaffected by M, serum DHEA levels declined from 0.11 ± 0.01 ng/ml (control) to 0.05 ± 0.01 ng/ml in 200 mg/kg exposed animals. Whether this decline in DHEA represents adrenal or LC androgen remains to be determined. These studies suggest that *in vivo* exposure of M to young adult male rats directly reduces LC T formation and that this decline is due to inhibition of LC P450scc activity.

916 DI(*N*-BUTYL) PHTHALATE RAPIDLY REPRESSES STEROIDOGENESIS IN THE FETAL TESTIS AND INTERFERES WITH ADRENAL STEROIDOGENESIS THROUGH AN ALTERNATIVE MECHANISM.

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The phthalate ester di(*n*-butyl) phthalate (DBP) produces antiandrogenic effects on reproductive development in male rats by interfering with testosterone production. We have shown that several genes involved in steroidogenesis are downregulated in the fetal testis following *in utero* exposure to DBP. Expression of these genes returns to control levels within 48 hours of DBP withdrawal. Our aim was to determine how rapidly testosterone synthesis is affected following exposure to DBP. Also, since several genes repressed by DBP are expressed in other steroidogenic tissues, we evaluated the effects of DBP exposure on steroidogenesis in the fetal adrenal. Pregnant Sprague-Dawley rats were dosed *via* oral gavage with 500 mg/kg/day DBP or corn oil from gestational day (gd) 12 to 19. The start of DBP dosing was shifted from gd 12 one day later in gestation for each treatment group, so that the final group was dosed only on gd 19. On gd 19, testes were removed for testosterone, RNA, and protein isolation. Testosterone production was significantly repressed in all groups exposed to DBP. The mean testosterone concentration in the fetuses dosed only on gd 19 was 44% of control. Mean testosterone concentration of all other dose groups was 13% of control. mRNA and protein levels for StAR, SR-B1, $P450_{SCC}$, and CYP17 were correspondingly repressed at all time points. In the adrenal gland, corticosterone content was decreased 42% in male fetuses and 48% in female fetuses following DBP treatment from gd 12-19, although only the decrease observed in the females was statistically significant. mRNA expression of SR-B1, StAR, and $P450_{SCC}$ were not significantly altered in the adrenal following DBP treatment. Our results show that DBP rapidly leads to transcriptional repression in the fetal testis resulting in diminished testosterone production. Diminution of steroid concentrations in the fetal adrenal occurs through a mechanism distinct from the transcriptional repression caused by DBP in the fetal testis.

917 THE EFFECTS OF NEONATAL EXPOSURE TO DIETHYLSTILBESTROL AND 17β-ESTRADIOL IN MOUSE EPIDIDYMIS.

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Recently, several studies have reported that semen quality has decreased. Endocrine disruptors (EDs) have been thought to be one of the possible causes. Epididymis is an important organ for maturation of spermatozoa. Perinatal exposure to EDs has induced morphological changes in epididymis. However, there is little information about the effects of EDs on epididymal gene expression. In this study, we examined

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Preface

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