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A sexual dimorphism in terbufos (S-t-butylthiomethyl-*O,O*-diethyl phosphorodithioate; TBF) toxicity was not reported and remains unclear. Previously, we reported that TBF treatment showed sexual dimorphic effects on acetylcholinesterase (AchE) activity. We further investigated that sexual dimorphism of TBF was affected to age and brain-regional selectivity, and whether ovary plays an important role in the effect. TBF (0.5 mg/kg x 2) was orally administered to 7 and 10 weeks old male and female rats, and ovariectomized rats. Body weights were significantly reduced (10.2%, Pr=0.018) in 7-week-old female rats treated with TBF and not changed in the other groups. TBF-treated ovariectomized group resulted in significant decrease of body weight (5.2%, Pr=0.043). Mortality was 20% for TBF-treated 7-week-old female rats, and 40% for TBF-treated 10-week-old female rats. In all male and ovariectomized groups, however, mortality was not observed. AchE activity was the highest in the frontal cortex than any other brain and non-neural regions used (cerebellum, entorhinal cortex and liver). Main (age, sex, treatment and brain region) and these interaction effects on AchE activity showed statistically significant results. TBF-treated 7-week-old female rats were significantly decreased compared to its corresponding male rats (in the frontal cortex and entorhinal cortex), or the TBF-treated 10-week-old female rats (in the frontal cortex). AchE inhibition in the frontal cortex was more resistant than the other regions as age increased, as well as more resistant in male rats than female. Taken together, the age-related and/or brain-regional selectivity, but not ovary function play important roles on sexual dimorphic effects of TBF.

[PA4-40] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of Gestational Exposure to Di(n-butyl)phthalate, flutamide and diethylstilbestrol on Male Reproductive Development in Rats

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The aims of present study were to compare the effects of in utero exposure to diethylstibestrol (DES), di(n-butyl)phthalate (DBP) and flutamide on the development of reproductive organs and to investigate the specific mechanisms of these abnormalities in the male reproductive system. During gestation days 10-19, pregnant Sparague-Dawley (SD) female rats were administered orally with corn oil (control), DES (25, 50, or 100 ㎍/kg/day), flutamide (1, 12.5, or 25 mg/kg/day) or DBP (250, 500, or 700 mg/kg/day). All animals were killed at 31 days of age. Blood was collected for analysis of serum testosterone levels, and testes and accessory sex organs (epididymides, seminal vesicles, ventral prostate, LABC, Cowper's glands) were weighed and examined histologically. Steroid hormone receptor (AR and ER) and SF-1 expression levels were also examined in the testes. At 31 days of age, effects of DBP and flutamide on the male reproductive tract (hypospadias, cryptorchidism) were dose-dependent. Flutamide (25 mg/kg/day) markedly increased the serum testosterone levels but DBP (700 mg/kg/day) significantly decreased. In the case of DBP and flutamide, the weights of the testes, epididymides, ventral prostate, seminal vesicle, and Cowper's glands were significantly decreased. DBP and flutamide significantly delayed the testes descent in a dose-dependent manner, whereas DES slightly delayed the testes descent only at the high dose group (100 ㎍/kg/day). In addition, flutamide significantly increased the expression of AR and ERα, β, in the testis respectively. DBP also significantly increased the expression of ERα, β in the testis but DES did not change the expression of AR, ERα, β in the testis compared to those of control. These results demonstrate that exposure to antiandrogenic compounds during gestation days 10-19 causes extensive effects on the development of reproductive tract.