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It is well-known that bisphenol A(BPA), an industrial raw material for polycarbonate and epoxy resins, shows estrogenic activity. Recent research from our laboratory has shown that BPA disrupts interaction between thyroid hormone and its receptor in a non-competitive manner, and alters the thyroid-hormone dependent expression of growth hormone(GH) and prolactin(PRL). In this study, we investigated the influence of BPA on the thyroid hormone system in vivo model to establish a screening method for endocrine disruptors. BPA (1mg/kg/day; 2mg/kg/day) were administered to Sprague-Dawley rats in drinking water during the pregnancy and lactation. We determined the maternal plsma levels of total T4 before the day of administration and on days 7, 14, 20 of gestation and day 7 of lactation, and neonatal plasma levels of total T4 on postnatal days of 4, 7, 14, and body weight on postnatal days of 4, 5, 7, 12, 14. In addition that, immunohistochemical study was performed to determine the levels of thyroid hormone receptor protein β1 and β2(TR-β1, β2) in cerebral cortex of neonates on postnatal days of 5, 7, 14. Plasma concentrations of total T4 in dams and those of total T4 in neonates were not altered by maternal treatment with BPA. Strong signals of thyroid receptor were seen in the neonatal brain exposed to BPA or PTU perinatally compared to normal pups', which indicates that TR-β1 and TR-β2 were overexpressed by BPA exposure and hypothyroidism. These results suggest that the perinatal exposure to BPA can disturb the thyroid hormone system resulting in overexpression of thyroid hormone receptor in the cerebral cortex of the neonates.

[PA4-38] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of Polycyclic Aromatic Hydrocarbons on Liver and Lung Cytochrome P450s in Male ICR Mice

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Certain polycyclic aromatic hydrocarbons (PAHs) have been reported to induce cytochrome P450 (P450) 1A1 and 1A2. In the present studies, the effects of six well-known PAHs on the activities of hepatic and pulmonary P450 enzymes were investigated in male ICR mice. When mice were treated intraperitoneally with 3, 10 and 30 mg/kg of individual PAHs for 3 consecutive days, the activities of ethoxyresorufin- and methoxyresorufin-O-dealkylases were significantly and differentially induced in liver and lung. Moreover, other P450 isozyme-associated monooxygenase activities were also induced significantly in liver and lung with characteristic induction profiles. Our present results suggest that individual PAHs might have inductive effects on P450 isozymes, and that the characteristic inductive effects of individual PAHs on certain P450 isozymes would be developed as a marker for determining exposure to certain PAHs. (Supported by the Echotechnopia21 Program, Ministry of Environment).

[PA4-39] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of Age, Brain-regional Selectivity, and Ovariectomy on Sexual Dimorphism of Organophosphate Pesticide Terbufos

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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.