図 7. 幼若雌ラットへの DEHP 吸入曝露によるステロイド合成酵素 mRNA 発現量の変化（＊: P<0.05）

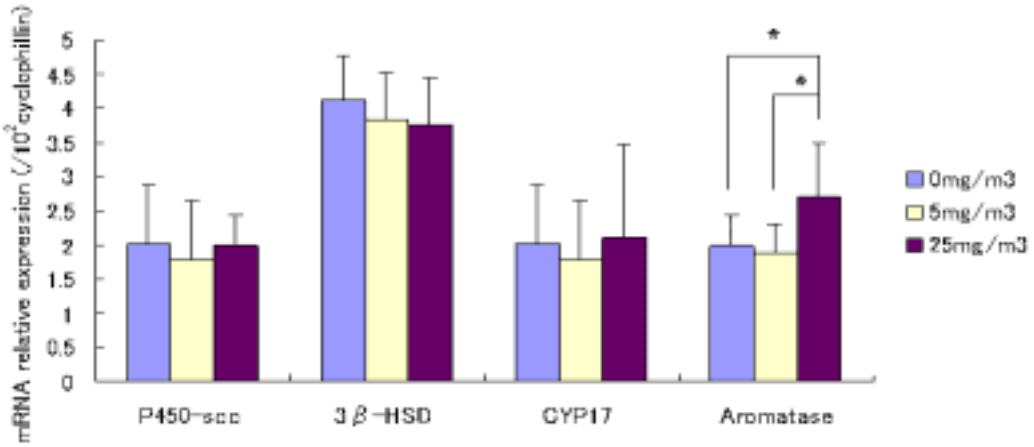


図 8.　幼若雌ラットへの DEHP 吸入曝露による食餌量の変化
（体重による調整を行っていないもの）

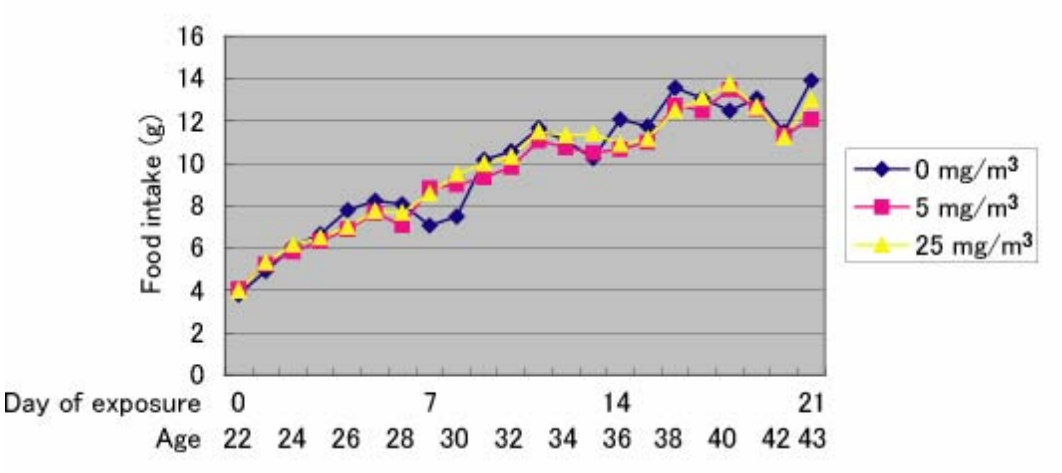


図 9.　幼若雌ラットへの DEHP 吸入曝露による食餌量の変化
（体重による調整を行ったもの）

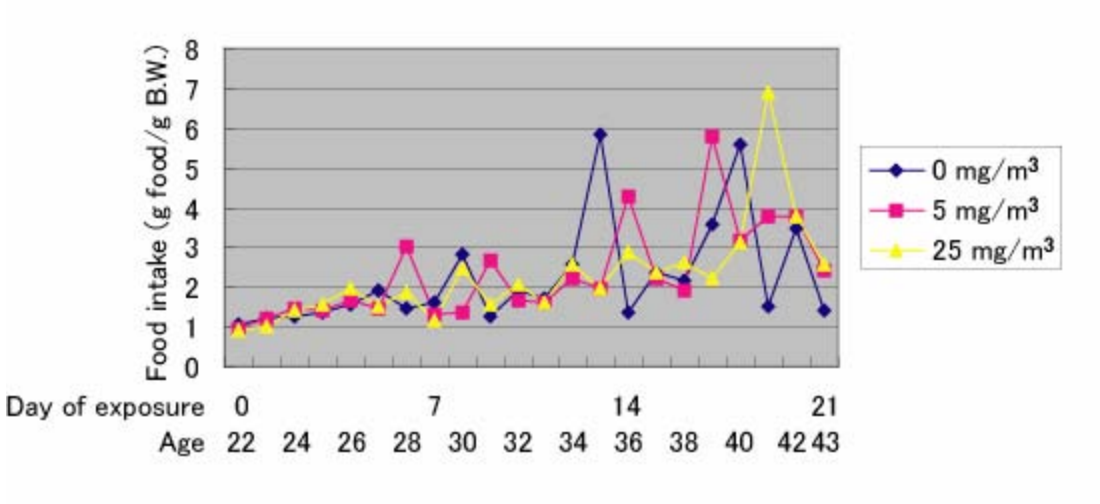


図 10. 幼若雌ラットへの DEHP 吸入曝露による飲水量の変化
（体重による調整を行っていないもの）

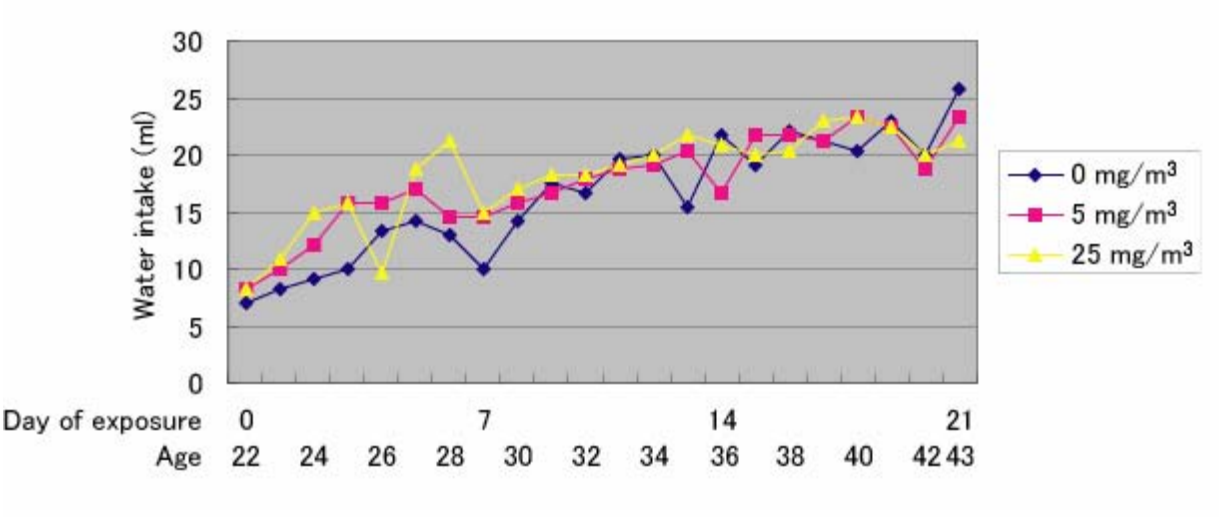
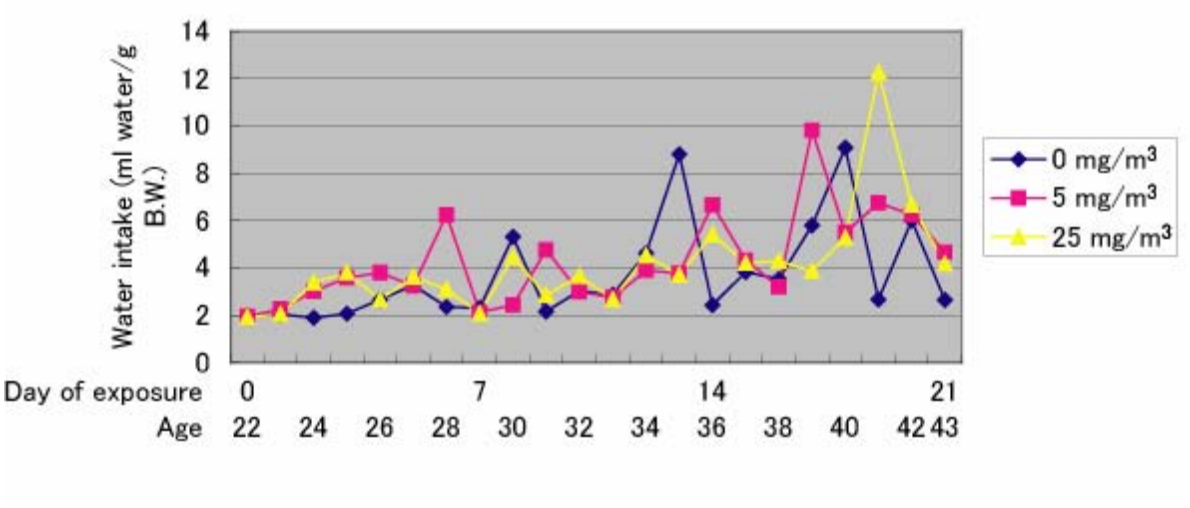


図 11. 幼若雌ラットへの DEHP 吸入曝露による飲水量の変化
（体重による調整を行ったもの）



Clarification and risk evaluation of Di (2-ethylhexyl) phthalate (DEHP) on the organism by inhalation exposure

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Key Word: DEHP, inhalation, developmental toxicity

Abstract

It is well known that phthalate esters could induce the endocrine-disrupting actions, the reproductive and developmental toxicity and the lesions of tissues in animal experiments. Because phthalate esters are widely found in air, water, soil and the other environment, it is concerned whether they may adversely affect the human. However, many studies provided adequate information to identify the effects of phthalate esters on the organism by the oral route. There is limited information about phthalate esters toxicity exposed by inhalation, as a natural route in human exposure, so it is necessary to clarify the risk of phthalate esters on the organism based on inhalation exposure. Utilizing inhalation exposure of Di (2-ethylhexyl) phthalate (DEHP), the purpose of this study was: (1) to clarify the developmental toxicity of DEHP exposure by inhalation; and (2) to examine the effects of reproductive endocrine system in prepubertal female rats to DEHP exposure.

(1) Pregnant rats were treated by inhalation exposure with DEHP from gestation day 1 to 19, and the fetal testes were isolated on gestation day 19. The concentration of testosterone in fetal testes was no significant change, but a decreased tendency was shown. The expressions of steroidogenesis enzyme mRNAs were significantly reduced with DEHP dose-dependent. In terms of maternal toxicity, no changes were seen. In addition, the maturity of reproductive organs in male pups was examined on postnatal week 8 and week 12. Seminal vesicle weights were significantly increased in 5 mg/m^3 DEHP group comparing with the control group at postnatal 8 week. Prostate weights were significantly reduced in 5 mg/m^3 DEHP group

comparing with the 25 mg/m^3 DEHP group at postnatal 12 week.
(2) In the female pubertal onset assay, the age of vaginal opening (VO) was advanced following inhalation exposure to DEHP in prepubertal female rats. Estrous cyclicity was monitored from the day of VO to the day of necropsy. Irregular estrous cycles were significantly more observed in 25 mg/m^3 DEHP group than the control group. Our data demonstrate that DEHP exposure can alter estrous cyclicity in female rats. We determine gene expression of steroidogenic enzyme in the ovary, the expression of mRNA for aromatase, a rate-limiting enzyme to change testosterone into estradiol, was raised by DEHP inhalation. However, estradiol in serum was no change, although a decreased tendency was seen. We will further investigate 17β-HSD Ⅳ, a pathway of metabolism of estradiol, and make clear the mechanism of reproductive effects in prepubertal female rats to DEHP exposure by inhalation.