

哺乳期雌ラットの子宮及び膣の微細構造に対するビスフェノール A 低用量投与の影響

Low dose effects of bisphenol A on the uterine and vaginal ultrastructure of suckling female rats

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Introduction: We have reported that ultrastructural survey of the reproductive organs by electron microscopy may be useful to detect low dose effects of suspected endocrine disruptors (3rd JSEDR). Tada et al. reported that low dose effects of bisphenol A (BPA) on the uterus and vagina in suckling female rats were not clear by the light microscopic observation (3rd JSEDR). The purpose of this experiment is to examine low dose effects of BPA on the uterus and vagina of suckling female rats at ultrastructural level by transmission electron microscopy.

Methods: BPA was dissolved in DMSO and administered to suckling rats by s.c. injection using micro-syringe. Female rats were given doses of 0, 0.8, 4, 20 or 500 µg BPA/kg/day or 100 µg 17 β -estradiol (E2) /kg /day (positive control), 5 days/week from the 1st day to 21st day after birth. Animals were sacrificed at 22nd day after birth. After the removal of uterus and vagina, pieces of tissue were immediately prefixed in a cold solution of 2.5% glutaraldehyde and postfixed in 1 % osmium tetroxide for 2h. Then they were dehydrated through graded alcohols, and embedded in Polybed 812/Araldite in flat embedding moulds. Approximate 1 µm semithin sections were cut and stained with a toluidine blue before the preparation for ultrathin sections. The ultrathin sections obtained were stained with uranyl acetate and lead citrate and observed using H-7000 operated at 75kv.

Results and Discussion: In the uterus of rats, a slight increase in luminal epithelial height compared to those of control was observed in rats treated with 20 and 500 µg BPA/kg. However, the pseudostratification of the luminal and glandular epithelium of the uterus was scarcely observed. The interdigitation (Fig. 1 . arrows) of plasma membrane was observed in rats treated with 20 and 500 µg BPA/kg and 100 µg E2/kg. The microvilli of the surface of the luminal epithelium in rats treated with 500 µg BPA/kg were longer than those of control rats. In the vagina, thickness of the epithelial cell layers increased slightly in rats treated with 20 µg BPA /kg, but vaginal cornification was not observed. Widening of intercellular spaces, formation of intercellular bridges (Fig.2. arrowheads) and the development of tonofilament (Fig.2. arrow) in prickle cell layers were observed in rats treated with 20 and 500 µg BPA/kg. These results suggest that low dose of BPA may exert estrogenic effects on the uterus and vagina of suckling female rats at ultrastructural level, although these effects could not be detected at light microscopic level. And the ultrastructural observation may be useful to detect low dose effects of suspected endocrine disruptors.

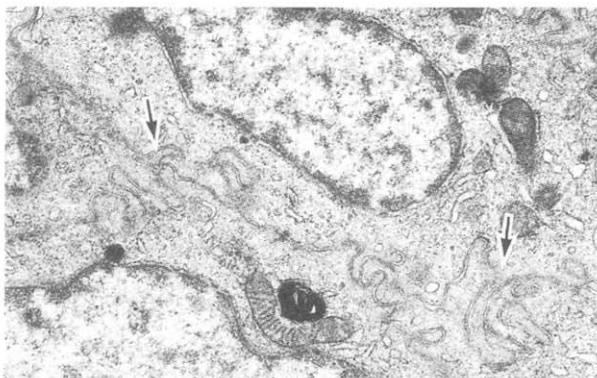


Fig.1. Uterus of 20µg BPA-treated rat

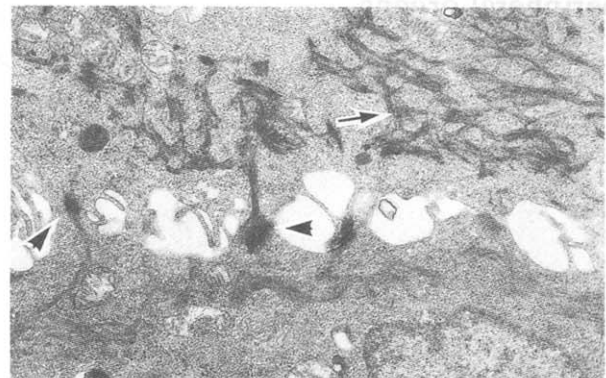


Fig.2. Vagina of 20µg BPA-treated rat