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Effects of fetal and neonatal exposure of male mice to diethylstilbestrol as endocrine disrupter on the reproductive and neuroendocrine system

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The purpose of this study is to clarify the effect of exposure in utero and neonate, of diethylstilbestrol (DES) as representative endocrine disrupter on the reproductive function of the male mice. Various doses (0.001-100 μg) of DES or a vehicle (control) were administered on day 3 neonate group (single), on every 2 days from days 3 neonate group (N-long-term) and on every 2 days from 7 dpc fetus group (F-long-term). Endocrinological and morphological changes were evaluated at 25 days of age (just before the onset of puberty), 4, 6, 8, and 12 weeks of age. We established a non-RI solid phase immunoassay method, and made it possible to do multiple microassay (LH, FSH, PRL, testosterone, inhibin) of the same sample with high .sensitivity and specificity. In DES 10, 100 μg of single at 4 weeks, 1.0 μg of N-long-term at 25 days and 10 μg of N-long-term at 6 weeks, and 10 μg of F-long-term at 6 weeks, testis weights were significantly reduced, and no spermatogenesis and immature seminiferous tubules were observed. DES injections caused dose dependent retardation of testicular inhibin, pituitary LH, FSH and plasma inhibin. Using the morphometric immunodetection method of incorporated the thymidine analog, BrdU, the high dose groups (10 & 100 μg) showed a marked disruption of sperm production and significant suppression of cellular proliferation in testes. Immunohistochemical analysis in each group showed that immunoreactive neurons for GnRH were generally fewer in number and had thinner neurites in the high dose groups. Immunoreactivity of ERα and AR in testes was increased, but that of StAR (steroidogenic acute regulatory protein) was decreased. Thus, our findings indicate that 1) single neonatal exposure of male mice to DES under 10 μg can advance the spermatogenesis at 6 weeks of age; 2) long-term exposure mice, especially from fetus could not recover on spermatogenesis even to under 1.0 μg of DES; 3) there is threshold dose of DES, and these delay and damage in the reproduction system due to reduction of pituitary LH production.