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Positive feedback effect of the drug DES in mouse fetuses

We examined the effect of maternal exposure to the estrogenic chemical diethylstilbestrol (DES) on circulating levels of estradiol in mouse fetuses. Whenever an adult mouse is exposed to an estrogenic chemical, estradiol production is reduced through negative feedback that is proportional to the administered dose. Our hypothesis was that the endocrine response of a mouse fetus to DES would be similar to the adult. This prediction was confirmed for both male and female fetuses whose mothers were fed a high 50 mg/kg dose of DES. This high DES dose produced a significantly lower amount of estradiol in exposed fetuses than fetuses not exposed to DES (controls). However, when pregnant mice were given a much lower 0.1 mg/kg dose of DES, the unexpected result was a significant increase in serum estradiol levels in the fetuses relative to controls. These results show that the response of the endocrine system in a mouse fetus to low doses of estrogenic chemicals is opposite to that of an adult mouse, possibly due to a positive feedback effect in fetuses. The consequence is that the fetus is exposed to not only the estrogenic chemical, but also to the increased estradiol that is produced. This will result in the effect of the low dose of DES being greater than what would be predicted based on only its activity in the fetus. In addition, this finding shows that low and high doses of chemicals can cause opposite effects on the fetal endocrine system, lead to inverted-U dose-response relationships.