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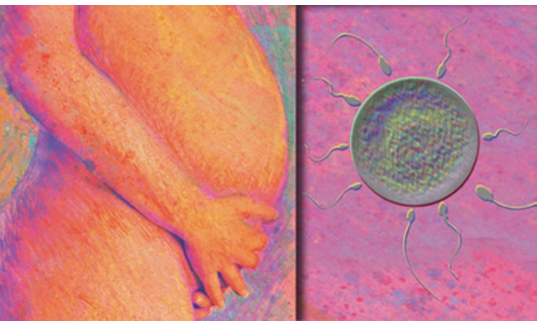
REPRODUCTIVE ENDOCRINOLOGY

DES—adverse health outcomes after *in utero* exposure

Women exposed to diethylstilbestrol (DES) *in utero* have an increased lifetime risk of a number of adverse health outcomes, including reproductive outcomes, new data reveal.

The synthetic estrogen DES started to be prescribed to pregnant women for the prevention of adverse pregnancy outcomes in the late 1940s. The drug was withdrawn from use in this group of women in the early 1970s, after evidence from the 1950s onwards had shown that DES had no effect on pregnancy outcomes and was associated with adverse health outcomes in daughters of exposed women. Specifically, clusters of cases of rare vaginal and cervical clear-cell adenocarcinomas and reproductive tract abnormalities were reported in young women exposed to DES *in utero*.



The new study involved the long-term follow-up of women who had participated in three cohort studies initiated in the 1970s, which enabled the researchers to shed light on the cumulative effects of DES exposure. The researchers assessed the risk of 12 adverse health outcomes that had previously been shown to be linked to DES. The study included 4,653 women with documented *in utero* exposure to DES and 1,927 unexposed women.

Women exposed to DES *in utero* had increased risks of all 12 adverse health outcomes compared with women without DES exposure, with hazard ratios ranging from 1.4 to 8.1. Among the nine reproductive outcomes analyzed, hazard ratios were greater than 3.70 for ectopic pregnancy, preterm delivery, loss of second trimester pregnancy and neonatal death in the DES-exposed women.

Cumulative risks, assessed until the age of 45 years for reproductive outcomes and 55 years for other outcomes, were also increased in DES-exposed women. The risk attributable to DES (the excess risk) was particularly high for preterm delivery, being 35.4%.

Importantly, DES-exposed women who had vaginal epithelial changes—a marker of high DES dose and/or exposure to DES early in gestation—at entry examination had significantly increased risks of seven of the 12 adverse outcomes compared with DES-exposed women without such changes.

The high lifetime risk of a range of adverse health outcomes prompt the researchers to conclude that continued monitoring of daughters of DES-exposed women is appropriate.

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Original article Hoover, R. N. *et al.* Adverse health outcomes in women exposed *in utero* to diethylstilbestrol. *N. Engl. J. Med.* **365**, 1304–1314 (2011)