

Effects of DES Exposure Follow Women for Decades

By Charles Bankhead, Staff Writer, MedPage Today
October 05, 2011

MedPage Today Action Points

- Explain that the teratogenic effects of diethylstilbestrol have continued to exact a heavy toll throughout the lifetime of women who were exposed to the drug in utero.
- Point out that DES-exposed women had significantly higher rates of multiple adverse outcomes including increases in infertility, spontaneous abortion, preterm delivery, early menopause, grade 2 or higher cervical intraepithelial neoplasia, and breast cancer.

Review

The teratogenic effects of diethylstilbestrol (DES) have continued to exact a heavy toll throughout the lifetime of women who were exposed to the drug in utero, investigators reported.

The lingering effects of DES encompassed a broad spectrum of health disorders, ranging from infertility and a variety of pregnancy complications to a significantly elevated risk of breast and cervical cancer, according to Robert N. Hoover, MD, ScD, of the National Cancer Institute in Bethesda, Md., and colleagues.

All comparisons of women exposed to DES with an unexposed control group demonstrated statistically significant differences, most of which were at least twice as high in exposed women, they reported in the Oct. 6 issue of the *New England Journal of Medicine*.

"Our study linked 12 adverse health outcomes in women to their exposure to DES in utero, with most risks increased by a factor of more than two as compared with the risks among unexposed women," Hoover and co-authors wrote in their summation.

"For most outcomes, risks were higher among women with vaginal epithelial changes, a histologic marker of high-dose DES exposure, than for women without this condition," they continued.

"Although DES has not been prescribed for pregnant women in the U.S. for 40 years, adverse outcomes continue to occur in women exposed in utero, and continued monitoring, as is ongoing in this cohort, for established and unexpected adverse

outcomes seems prudent."

Developed in 1938 as the first synthetic estrogen, DES was used almost immediately to prevent pregnancy complications. The use continued until clinical trials conducted in the 1950s showed no pregnancy-associated efficacy for the hormone.

In the 1960s, an unusual cluster of vaginal and cervical adenocarcinoma was identified in adolescent girls and young women. Subsequent investigation revealed a strong association between the cancers and in utero exposure to DES, the authors wrote in their introduction.

Additional studies of women exposed to DES showed developmental defects in the genital tract and an increased rate of several complications of pregnancy, they continued.

Concern about the clinical significance and magnitude of the findings led to longer-term studies of women exposed to DES in utero.

In the early 1990s, investigators at NIH and multiple collaborating institutions combined participants in three large cohort studies begun in the 1970s and contacted all of the surviving women and enrolled them in a systematic assessment and follow-up study.

Investigators compared the exposed and unexposed women with respect to 12 adverse outcomes associated with DES exposure, including cumulative risk to age 45 for reproductive outcomes and to 55 for other outcomes.

The final analysis included 4,653 DES-exposed women and 1,955 women who were not exposed. The average age at follow-up was 48.

The comparisons showed significantly higher rates of adverse outcomes in the DES-exposed women.

- Infertility: 33% versus 15.5%, HR 2.37, 95% CI 2.05 to 2.75
- Spontaneous abortion: 50.3% versus 38.6%, HR 1.64, 95% CI 1.42 to 1.88
- Preterm delivery: 53.3% versus 17.8%, HR 4.68, 95% CI 3.74 to 5.86
- Loss of second-trimester pregnancy: 16.4% versus 1.7%, HR 3.77, 95% CI 2.56 to 5.54
- Ectopic pregnancy: 14.6% versus 2.9%, HR 3.72, 95% CI 2.58 to 5.38
- Preeclampsia: 26.4% versus 13.7%, HR 1.42, 95% CI 1.07 to 1.89
- Stillbirth: 8.9% versus 2.6%, HR 2.45, 95% CI 1.33 to 4.54
- Early menopause: 5.1% versus 1.7%, HR 2.35, 95% CI 1.67 to 3.31
- Grade 2 or higher cervical intraepithelial neoplasia: 6.9% versus 3.4%, HR 2.28, 95% CI 1.59 to 3.27
- Breast cancer: 3.9% versus 2.2%, HR 1.82, 95% CI 1.04 to 3.18

Hazard ratios for the adverse outcomes tended to be higher among women with vaginal epithelial changes, consistent with high-dose DES exposure.

The study was supported by the National Cancer Institute.

Co-author Stanley J. Robboy disclosed a relationship with UCB, Belgium. Co-author Beth Y. Karlan disclosed a relationship with IRIS International.

Primary source: New England Journal of Medicine

Source reference:

Hoover RN, et al "Adverse health outcomes in women exposed in utero to diethylstilbestrol" *N Engl J Med* 2011; 365: 1304-1313.

Disclaimer

The information presented in this activity is that of the authors and does not necessarily represent the views of the University of Pennsylvania School of Medicine, MedPage Today, and the commercial supporter. Specific medicines discussed in this activity may not yet be approved by the FDA for the use as indicated by the writer or reviewer. Before prescribing any medication, we advise you to review the complete prescribing information, including indications, contraindications, warnings, precautions, and adverse effects. Specific patient care decisions are the responsibility of the healthcare professional caring for the patient. Please review our Terms of Use.