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**Early exposure to synthetic estrogen puts “DES daughters”
at higher risk for breast cancer**

PHILADELPHIA – So-called “DES daughters,” born to mothers who used the anti-miscarriage drug diethylstilbestrol during pregnancy, are at a substantially greater risk of developing breast cancer compared to women who were not exposed to the drug *in utero*.

Reporting in the August issue of the journal *Cancer Epidemiology, Biomarkers & Prevention*, a nationwide team of researchers found that DES daughters over age 40 had 1.9 times the risk of developing breast cancer, compared to unexposed women of the same age. They also found that the relative risk of developing the cancer was even greater in DES daughters over age 50, but say the number of older women in their study group is, as yet, too small for a firm statistical comparison.

“This is really unwelcome news because so many women worldwide were prenatally exposed to DES, and these women are just now approaching the age at which breast cancer becomes more common,” said the study’s lead author, Julie Palmer, Sc.D., professor of epidemiology at the Boston University School of Public Health. She said an estimated one to two million women in the U.S. were exposed to DES, which was frequently prescribed to women from the 1940s through 1960s to prevent miscarriages.

The ongoing study suggests that DES-exposed women are developing the typical range of breast cancers after age 40 at a faster rate than non-exposed women of the same ages. The researchers also found that the highest relative risk of developing breast cancer was observed in study participants from the cohorts with the highest cumulative doses of DES exposure.

Because of the increased risk observed for DES daughters, the authors urge women who know they were exposed to DES to have regular screening mammograms, and to think twice about using supplemental female hormones.

“DES daughters often ask us about use of these hormones,” Palmer said. “It might be wise for exposed women to avoid such supplements. Use of hormone supplements is, in itself, an independent breast cancer risk factor, and women may choose not to compound their already increased risk.”

When DES, a synthetic estrogen, was developed in 1938, physicians believed that low levels of estrogen in pregnant women led to spontaneous abortions or premature deliveries. In 1953, a clinical trial indicated no benefit with regard to miscarriage prevention. However, use continued in the U.S. until 1971 when researchers determined that DES greatly increased the risk of developing rare cancers

of the vagina and cervix in DES daughters; the federal Food and Drug Administration subsequently banned use of the drug in pregnant women. Later research demonstrated that DES increased the risk of breast cancer development in the mothers who used it.

To see if DES daughters and sons were also at greater risk of cancer or other serious illnesses, in 1992 the National Cancer Institute (NCI) funded a long-term study that assembled all known “cohorts,” or groups of DES daughters that were already being studied (some since the 1970s), as well as a collection of unexposed women. This particular analysis included 4,817 exposed and 2,073 unexposed daughters, and, to date, 102 cases of invasive breast cancer have occurred in the combined group.

Factoring out other breast cancer risk variables such as the age when these women first gave birth, or their number of children, did not change DES daughters’ relative risk of developing breast cancer, Palmer said. She adds that the breast cancer cases “tracked the normal range” of breast cancer subtypes, so are expected to be neither more nor less lethal than is commonly seen. Only a few deaths have occurred in the combined group due to breast cancer, so survival statistics are not yet available, she said.

Scientifically, the study may be the first to provide direct evidence that prenatal exposure to excess estrogen may be a risk factor for development of breast cancer, Palmer said. “That theory has been around, but it has been difficult to study. The DES tragedy offers us a direct way to test the hypothesis,” she said.

Although researchers do not know how DES may increase breast cancer risk, Palmer said some scientists believe the excess estrogen increases the number of breast tissue stem cells available at birth – cells which could malignantly transform into cancer.

If true that excess estrogen *in utero* impacts breast cancer risk later in life, “there is a concern that other environmental factors that increases fetal exposure to estrogenic compounds may do the same thing,” Palmer said. “This study suggests that such environmental exposures may deserve more serious consideration.”

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