DES Action VOICE

A Focus On Diethylstilbestrol

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DES Son's Research Review

Why Different Studies Yield Conflicting Results

"Urogenital Abnormalities in Men Exposed to Diethylstilbestrol *In Utero*: A Cohort Study," Julie R. Palmer et al. *Environmental Health 2009*, 8:37-1-6, 2009. (http://www.ehjournal.net/content/8/1/37)

Reviewed by Fran Howell

This study confirms that DES Sons are at increased risk for cryptorchidism (undescended testicles), epididymal cysts (benign but painful), and testicular inflammation and infection. It also helps unravel the mystery as to why earlier studies presented conflicting results.

Using information collected by the on-going National Cancer Institute (NCI) DES Follow-up Study, researcher Julie Palmer, Sc.D., from Boston University's Slone Epidemiology Center, analyzed data from three studies of DES Sons. They were done with mailed questionnaires (1994, 1997 and 2001), which asked about abnormalities of the urogenital tract.

> The earlier the exposure, the higher the prevalence of anomalies, which holds true for DES Sons because genitalia are most susceptible to harm caused by exposures during the early weeks of gestation.

One study was of a group of DES Sons born at the University of Chicago's hospital; the second was of DES Sons born after their mothers were treated at a private infertility clinic near Boston, and the third was of DES Sons born at the Mayo Clinic in Rochester, MN.

Two of the studies found a link between DES exposure and a higher prevalence of genital tract abnormalities in DES Sons. But the Mayo Clinic results showed no such correlation.

For all three groups, mothers' medical records were available. Upon close examination, Palmer came to understand that the risk for undescended testicles, epididymal cysts and testicular inflammation/infection was the highest for men who were first exposed to DES before the 11th week of gestation, and whose mothers had been given the large cumulative dose of more than five grams of DES.

As it turns out, the protocol for handling so-called problem pregnancies at the Mayo Clinic was generally more conservative than elsewhere. According to Palmer, "The Mayo Clinic cohort differs from the other cohorts in two major ways: only 48% were

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exposed before the 11th week of gestation and very few were exposed to 5 grams or more" of DES.

Palmer's dose and timing analysis of the three studies answers the mystery as to why the Mayo Clinic's results regarding DES Sons conflicted with the others. Dose and timing matter.

Also, Palmer points out that according to animal studies, when the synthetic estrogen DES was given during pregnancy, the male offspring had higher than expected incidences of undescended testicles and epididymal cysts. Researchers theorize from those studies that normal descent of the testes is, at least in part, under hormonal control. So getting the same results in human studies was not a surprise to Palmer, since animal work is often a predictor of the human experience.

She also notes that interestingly, "timing of in utero exposure to DES has been shown to be a predictive factor for structural anomalies of the cervix and vagina in DES-exposed daughters." The earlier the exposure, the higher the prevalence of anomalies, which holds true for DES Sons because genitalia are most susceptible to harm caused by exposures during the early weeks of gestation.

Palmer was particularly interested in the association between prenatal DES exposure and the increased risk for inflammation/infection of the testes. She speculates that some DES Sons may have been born with a small structural abnormality, such as a minor obstruction that could explain their greater testicular inflammation/infection risk. Palmer calls for follow-up on this point.

Findings in this study, Palmer says, can be extended to current concerns of endocrine disruptors in the environment. She notes an increase in the prevalence of undescended testicles being seen in recent years in the general population. Some scientists are looking at both genetics and environmental factors for a cause. According to Palmer, these research results regarding DES appear to lean toward the possibility that genital anomalies may have something to do with increased estrogen exposure before birth.

Palmer notes the importance of continuing studies on these groups of DES Sons as they age. She says it makes sense to watch for an increased possibility of benign prostatic hypertrophy (enlargement of the prostate gland) and prostate cancer among DES Sons, because both conditions occur more often in men as they age. DES VOICE