

SUMMER 2015

Report of the DES Follow-up Study from the National Cancer Institute

Message from the Principal Investigators



Our lives are very busy these days and we want to thank you for taking the time to complete our most recent questionnaire. The information you and other participants in the follow-up study provide helps us to better understand the effects of DES exposure. In fact, because of the information you've provided, we have learned and published findings about the adverse health outcomes that occur over a lifetime among women exposed to DES in-utero in the *New England Journal of Medicine*. In addition, the links between prenatal DES exposure and the risk of cardiovascular disease, diabetes, osteoporosis and other related conditions have been published in the journal *Epidemiology*. You can find the full list of publications on the DES website (www.desfollowupstudy.org). As we analyze the latest data, we will continue to monitor potential health risks and report the results of our findings to you.

Your support through the years has been remarkable, and we hope that we can count on you again as we carry on this important research. The information you provide allows us to continue to explore how DES has impacted your lives.

Robert Hoover, M.D., Sc.D.
Rebecca Troisi, Sc.D., M.A.

Prenatal Diethylstilbestrol Exposure and Risk of Obesity in Adult Women

Some studies in animals suggest that prenatal DES exposure is linked to obesity and to abnormal metabolism of glucose. Using data from the National Cancer Institute DES Follow-Up Study, we evaluated the association between prenatal DES exposure and adult obesity. To do this, we looked at factors like weight gain, body mass index (BMI – a measure of body fatness) and waist circumference among 2,871 women exposed to DES before their birth and also among 1,352 who were not exposed to DES.

We conducted statistical analyses to see if exposed women had a higher risk of being obese, and whether there were differences between exposed and unexposed women in BMI, weight gain, waist circumference and height. Other factors possibly related to obesity such as age, educational level and whether the woman smoked, were accounted for in the analysis. We also considered whether the mother smoked during the pregnancy with the daughter, the daughter's use of postmenopausal hormones, her

menopausal status, and how many children she had.

DES-exposed women had a 9% greater overall risk of being obese compared with unexposed women, but these findings could have been due to chance. Compared with unexposed women, the risk of obesity was 23% greater for women who were exposed prenatally to a low DES dose and 5% greater for women exposed to a high dose. Overall, most women gained around 30 pounds between the ages of 20 and the mid-fifties, and DES-exposed women gained slightly more (about 1.5 pounds) than those not exposed, although this was not statistically significant. Height and waist circumference were very similar among DES-exposed and unexposed women. This study suggests that prenatal DES exposure may be associated with a small increase in adult obesity but not the larger differences that have been observed in some animal studies.

Hatch EE, et al., *J Dev Orig Health Dis.* 2015;6:201-7

Research in Progress

We continually examine both the information that you provide on the questionnaires and the medical records that you allow us to obtain from your doctors to learn more about the health conditions that you report. We are currently focusing on prenatal DES exposure to determine:

- The risk of cancer and other medical conditions, such as cardiovascular disease in women and men;
- The risk of cervical dysplasia, mammographic density, benign breast disease, and breast carcinoma in situ in women; and
- The risk of benign prostatic hypertrophy (BPH) in men.

DES RESEARCH UPDATE

Study of Genetic Markers in DES Exposed Daughters – A Pilot Study



In May 2014, researchers at the National Cancer Institute and Boston University began a small pilot study that is attempting to understand how prenatal DES exposure affects a person's biology and influences health conditions. The researchers are asking women (both DES exposed and unexposed) in the greater Boston area to provide a small blood sample at Boston University's General Clinical Research Center. The samples will be used to compare levels of hormones between exposed and unexposed

women and to find out if there are any DES-related epigenetic changes in cells. Epigenetic changes occur in the cells during fetal development. These changes can turn genes on or off. So far, 47 women have provided samples and we are truly grateful for their help. If this pilot study is successful we hope to study this question in a larger group of women. The findings may have important implications for the ways in which hormonal exposures in the fetus influence human health in later life.

Update on Third Generation Study

In the first study of the third generation, 793 granddaughters were enrolled. Some of their mothers were prenatally exposed to DES and some were not. In that study, a higher percentage of DES exposed granddaughters reported having irregular periods, and experiencing regular periods at a later age. Two DES-exposed granddaughters reported ovarian cancer occurring in their early 20s, and one exposed mother reported that her daughter was diagnosed with ovarian cancer when she was 9 years old. These findings were very preliminary and require confirmation. We also saw an excess of leukemia among the unexposed granddaughters, which underscores the concept of chance findings. Associations with DES can occur by chance when there are small numbers of cancer cases. Continued follow-up of the granddaughters is necessary to determine if there are health effects related to DES.

A second study was conducted and included 661 of the previously enrolled granddaughters, and an additional 472 granddaughters who were enrolled in the study for the first time. The information from this study is currently being analyzed to determine if the findings on menstrual cycles and on ovarian cancer remain.

It's important that we have your correct address and contact information to send you future newsletters and questionnaires. Please call or email any updates to your Study Contact.

Slone Epidemiology Center at Boston University

Boston, Massachusetts
Study Contact: Helen Bond
(617) 206-6220
desstudy@bu.edu

Cedars-Sinai Medical Center

Los Angeles, California
Study Contact: Phyllis Lopez
310-423-3302
Phyllis.Lopez@cshs.org

University of Chicago

Chicago, IL 60637
Study Contact: Diane Anderson
773-702-6670/1
chicagodesprogram@babies.bsd.uchicago.edu

Dartmouth-Hitchcock Medical Center

Lebanon, New Hampshire
Study Contact: Suzanne Lenz
603-653-3699 or 877-295-0030
Suzanne.B.Lenz@hitchcock.org

Mayo Clinic

Rochester, Minnesota
507-284-2747
desstudy@mayo.edu

The Methodist Hospital-Research Institute

Houston, Texas
Study Contact: Jaya Kamath
(713) 441-3198
desresearch@tmhs.org

The next questionnaire is scheduled to be sent in the spring of 2016. If you would like to complete the questionnaire on-line, please send your email address to your Study Contact.