CANCER FACTS

National Cancer Institute • National Institutes of Health
Department of Health and Human Services

DES: Questions and Answers

Key Points

- DES (diethylstilbestrol), a synthetic form of estrogen (a female hormone), was prescribed between 1940 and 1971 to help women with certain complications of pregnancy (see Question 1).
- DES has been linked to an uncommon cancer of the vagina or cervix (called clear cell adenocarcinoma) in a small number of daughters of women who had used DES during pregnancy (see Question 2).
- Women who used DES may have a slightly increased risk of breast cancer (see Question 4).
- It is important for DES-exposed daughters to be aware of the possible health effects of DES and inform their doctor of their exposure (see Question 6).
- Resources are available for people who were exposed to DES (see Question 12).
- References (see page 7).

1. What is DES?

DES (diethylstilbestrol) is a synthetic form of estrogen, a female hormone. It was prescribed between 1940 and 1971 to help women with certain complications of pregnancy. Use of DES declined in the 1960s after studies showed that it is not effective in preventing pregnancy complications. When given during the first 5 months of a pregnancy, DES can interfere with the development of the reproductive system in a fetus. For this reason, although DES and other estrogens may be prescribed for some medical problems, they are no longer used during pregnancy.

2. What health problems might DES-exposed daughters have?

In 1971, DES was linked to an uncommon cancer (called clear cell adenocarcinoma) in a small number of daughters of women who had used DES during pregnancy. This cancer of the vagina or cervix usually occurs after age 14, with most cases found at age 19 or 20

in DES-exposed daughters. Some cases have been reported in women in their thirties and forties. The risk to women older than age 40 is still unknown, because the women first exposed to DES *in utero* are just reaching their fifties, and information about their risk has not been gathered. The overall risk of an exposed daughter to develop this type of cancer is estimated to be approximately 1/1000 (0.1 percent). Although clear cell adenocarcinoma is extremely rare, it is important that DES-exposed daughters be aware of the risk and continue to have regular physical examinations.

Scientists found a link between DES exposure before birth and an increased risk of developing abnormal cells in the tissue of the cervix and vagina. Physicians use a number of terms to describe these abnormal cells, including dysplasia, cervical intraepithelial neoplasia (CIN), and squamous intraepithelial lesions (SIL). These abnormal cells resemble cancer cells in appearance; however, they do not invade nearby healthy tissue as cancer cells do. These abnormal cellular changes usually occur between the ages of 25 and 35, but may appear in exposed women of other ages as well. Although this condition is not cancer, it may develop into cancer if left untreated. DES-exposed daughters should have a yearly Pap test and pelvic exam to check for abnormal cells. DES-exposed daughters also may have structural changes in the vagina, uterus, or cervix. They also may have irregular menstruation and an increased risk of miscarriage, tubal (ectopic) pregnancy, infertility, and premature births.

3. What health problems might DES-exposed sons have?

There is some evidence that DES-exposed sons may have testicular abnormalities, such as undescended testicles or abnormally small testicles. The risk for testicular or prostate cancer is unclear; studies of the association between DES exposure *in utero* and testicular cancer have produced mixed results. In addition, investigations of abnormalities of the urogenital system among DES-exposed sons have not produced clear answers.

4. What health problems might DES-exposed mothers have?

Women who used DES may have a slightly increased risk of breast cancer. Current research indicates that the risk of breast cancer in DES-exposed mothers is approximately 30 percent higher than the risk for women who have not been exposed to this drug. This risk has been stable over time, and does not seem to increase as the mothers become older. Additional research is needed to clarify this issue and whether DES-exposed mothers are at higher risk for any other types of cancer.

5. How can people find out if they took DES during pregnancy or were exposed to DES *in utero*?

It has been estimated that 5 to 10 million people were exposed to DES during pregnancy. Many of these people are not aware that they were exposed. A woman who was pregnant between 1940 and 1971 and had problems or a history of problems during pregnancy may have been given DES or a similar drug. Women who think they used a hormone such as DES during pregnancy, or people who think that their mother used DES during

pregnancy, can contact the attending physician or the hospital where the delivery took place to request a review of the medical records. If any pills were taken during pregnancy, obstetrical records should be checked to determine the name of the drug. Mothers and children have a right to this information.

However, finding medical records after a long period of time can be difficult. If the doctor has retired or died, another doctor may have taken over the practice as well as the records. The county medical society or health department may know where the records have been stored. Some pharmacies keep records for a long time and can be contacted regarding prescription dispensing information. Military medical records are kept for 25 years. In many cases, however, it may be impossible to determine whether DES was used.

6. What should DES-exposed daughters do?

It is important for women who believe they may have been exposed to DES before birth to be aware of the possible health effects of DES and inform their doctor of their exposure. It is important that the physician be familiar with possible problems associated with DES exposure, because some problems, such as clear cell adenocarcinoma, are likely to be found only when the doctor is looking for them. A thorough examination may include the following:

- *Pelvic examination*—A physical examination of the reproductive organs. An examination of the rectum also should be done.

- *Palpation*—As part of a pelvic examination, the doctor feels the vagina, uterus, cervix, and ovaries for any lumps. Often palpation provides the only evidence that an abnormal growth is present.

- *Pap test*—A routine cervical Pap test is not adequate for DES-exposed daughters. The cervical Pap test must be supplemented with a special Pap test of the vagina called a "four-quadrant" Pap test, in which cell samples are taken from all sides of the upper vagina.

- *Iodine staining of the cervix and vagina*—An iodine solution is used to temporarily stain the linings of the cervix and vagina to detect adenosis (a noncancerous but abnormal growth of glandular tissue) or other abnormal tissue.

- *Colposcopy*—In colposcopy, a magnifying instrument is used to view the vagina and cervix. Some doctors do not perform colposcopy routinely. However, if the Pap test result is not normal, it is very important to check for abnormal tissue.

- *Biopsy*—Small samples of any tissue that appears abnormal on colposcopy are removed and examined under a microscope to see whether cancer cells are present.

- *Breast examinations*—Researchers are studying whether DES-exposed daughters have a higher risk of breast cancer than unexposed daughters; therefore, DES-exposed daughters should continue to follow the routine breast cancer screening recommendations for their age group.

7. What should DES-exposed mothers do?

A woman who took DES while pregnant (or suspects she may have taken it) should inform her doctor. She should try to learn the dosage, when the medication was started, and how it was used. She also should inform her children who were exposed before birth so that this information can be included in their medical records. DES-exposed mothers should have regular breast cancer screening and yearly medical checkups that include a pelvic examination and a Pap test.

8. What should DES-exposed sons do?

DES-exposed sons should inform their physician of their exposure and be examined periodically. While the level of risk of developing testicular cancer is unclear among DES-exposed sons, males with undescended testicles or unusually small testicles have an increased risk of developing testicular cancer, whether or not they were exposed to DES.

9. Is it safe for DES-exposed daughters to use oral contraceptives or hormone replacement therapy?

Each woman should discuss this important question with her doctor. Although studies have not shown that the use of birth control pills or hormone replacement therapy are unsafe for DES-exposed daughters, some doctors believe these women should avoid these medications because they contain estrogen. Structural changes in the vagina or cervix should cause no problems with the use of other forms of contraception, such as diaphragms or spermicides.

10. Do DES-exposed daughters have unusual problems with fertility and pregnancy?

A 1980 study of DES-exposed and unexposed daughters participating in the National Cooperative Diethylstilbestrol Adenosis Study (DESAD) found that fertility did not differ between the two groups. However, this study found an increased risk of premature births, miscarriage, and ectopic pregnancy associated with DES exposure.

A followup study published in 2001 examined DES-exposed and unexposed daughters from the DESAD project and DES-exposed and unexposed daughters from another study group known as the Chicago cohort. The Chicago cohort consisted of daughters whose mothers participated in an early clinical trial (research study) that tested the effectiveness of DES during pregnancy. The clinical trial was conducted at the University of Chicago. The followup study found that DES-exposed daughters have a higher risk of infertility than unexposed women, and the increased risk of infertility is mainly due to uterine or tubal problems. The researchers suggested that the difference in the findings between the

two studies may be attributed to the age of the participants. The earlier study evaluated data from women who were primarily between ages 25 and 30. The followup study not only analyzed data from a larger number of participants but also covered a longer time period, so the women were closer to the end of their reproductive years.

In another analysis of data published in 2000, researchers evaluated the long-term pregnancy experiences of DES-exposed daughters compared with unexposed daughters. They found that DES daughters were more likely to have had premature births, miscarriage, or ectopic pregnancy. Full-term infants were delivered in the first pregnancies of 64.1 percent of exposed women compared with 84.5 percent of unexposed women.

Though there is evidence that the risk of ectopic pregnancy, miscarriage, and premature birth is increased for DES-exposed daughters, most DES-exposed daughters do not experience DES-related problems during pregnancy. If a DES-exposed daughter becomes pregnant, the doctor should be told of the DES exposure and should monitor the pregnancy closely.

11. What is the focus of current research on DES exposure?

Researchers continue to study DES-exposed daughters as they move into the menopausal years. The cancer risks for exposed daughters and sons are also being studied to determine if they differ from the unexposed population. In addition, researchers are studying possible health effects on the grandchildren of mothers who were exposed to DES during pregnancy (also called third-generation daughters or DES granddaughters).

Two published studies have examined DES granddaughters for possible abnormalities. A 1995 study found that the age menstruation began was not affected by the mother's exposure to DES. In a 2002 study, researchers compared DES granddaughters' pelvic exams to the results of their mothers' first pelvic exams. None of the granddaughters' pelvic exams showed changes usually associated with DES exposure. The researchers concluded that third-generation effects of *in utero* DES exposure are unlikely.

Researchers are also studying the theory that *in utero* exposure to DES may lead to an increased risk of breast cancer. A 2002 analysis found that DES exposure *in utero* was associated with a slightly increased risk of breast cancer. The experience of the women thus far suggested that increased risk might be restricted to women age 40 or older, and to tumors that have estrogen receptors (need the hormone estrogen to grow), but both observations are uncertain at this point because of the relatively small number of women diagnosed to date. The researchers concluded that more followup of women exposed to DES *in utero* is needed to further clarify these findings.

A study published in 2003 found little support for the hypothesis that *in utero* exposure to DES influences the psychosexual characteristics (the likelihood of ever having been married, age at first intercourse, number of sexual partners, and having had a same-sex sexual partner in adulthood) of adult men and women.

12. Where can DES-exposed people get additional information?

Resources for people who were exposed to DES include the following:

Organization:	**Centers for Disease Control and Prevention (CDC)**
Address:	CDC's DES Update Mailstop F–29 4770 Buford Highway, NE. Atlanta, GA 30341–3724
Telephone (toll-free):	1–888–232–6789
E-mail:	ncehinfo@cdc.gov
Internet Web site:	http://www.cdc.gov/des/index.html

The CDC's DES Update Web page provides consumers, health care providers, and DES Update partners with up-to-date information about the health effects of DES, and screening and treatment options for DES-exposed groups. The Interactive DES Self-Assessment Guide is designed to help consumers determine whether they might have been exposed to DES between 1938 and 1971. Research on the children of DES daughters is also available on the site.

Organization:	**DES Action USA**
Address:	Suite 301 610 16th Street Oakland, CA 94612
Telephone:	510–465–4011 1–800–DES–9288 (1–800–337–9288)
Fax number:	510–465–4815
E-mail:	desaction@earthlink.net
Internet Web site:	http://www.desaction.org

DES Action USA is a consumer group organized by individuals who were exposed to DES. It provides information, referrals, and support for DES-exposed people and health professionals.

Organization:	**DES Cancer Network**
Address:	Suite 400 514 10th Street, NW. Washington, DC 20004–1403
Telephone:	202–628–6330 1–800–DES–NET4 (1–800–337–6384)
Fax number:	202–628–6217
E-mail:	DESNETWRK@aol.com
Internet Web site:	http://www.descancer.org

The DES Cancer Network is a national organization for DES-exposed women and their family and friends. It offers education, support, and research advocacy, with a special focus on DES cancer issues.

Organization:	**The Registry for Research on Hormonal Transplacental Carcinogenesis (Clear Cell Cancer Registry)**
Address:	Department of Obstetrics and Gynecology The University of Chicago Room 321 5841 South Maryland Avenue, MC 2050 Chicago, IL 60637
Telephone:	773–702–6671
Fax number:	773–702–0840
E-mail:	danderso@babies.bsd.uchicago.edu
Internet Web site:	http://obgyn.bsd.uchicago.edu/registry.html

The Registry for Research on Hormonal Transplacental Carcinogenesis (also called the Clear Cell Cancer Registry) is a worldwide registry for individuals who developed clear cell adenocarcinoma as a result of exposure to DES. Staff members also answer questions from the public.

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Wilcox AJ, Umbach DM, Hornsby PP, Herbst AL. Age at menarche among diethylstilbestrol granddaughters. *American Journal of Obstetrics and Gynecology* 1995; 173(3 Pt 1):835–836.

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1–800–4–CANCER (1–800–422–6237)
TTY (for deaf and hard of hearing callers): 1–800–332–8615

NCI Online

Internet

Use http://cancer.gov to reach the NCI's Web site.

LiveHelp

Cancer Information Specialists offer online assistance through the *LiveHelp* link on the NCI's Web site.

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