

DES: Questions and Answers

Key Points

- DES (diethylstilbestrol), a synthetic form of estrogen (a female hormone), was prescribed between 1938 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 used DES during pregnancy (see Question 2).
- Daughters of women who took DES during pregnancy may have a slightly increased risk of breast cancer after age 40 (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).

1. What is DES?

DES (diethylstilbestrol) is a synthetic form of estrogen, a female hormone. It was prescribed between 1938 and 1971 to help women with certain complications of pregnancy (1). Use of DES declined following studies in the 1950s that showed it was 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 clear cell adenocarcinoma in a small number of daughters of women who had used DES during pregnancy. This uncommon cancer of the vagina or cervix is usually diagnosed between age 15 and 25 in DES-exposed daughters (1). 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 in 1,000 (0.1 percent) (1). Although clear cell adenocarcinoma is extremely rare, it is important that DES-exposed daughters be aware of the risk and 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, and squamous intraepithelial lesions (1). These abnormal cells resemble cancer cells in appearance; however, they do not invade nearby healthy tissue as cancer cells do. Although these conditions are not cancer, they 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 may also have structural changes in the vagina, uterus, or cervix, as well as irregular menstruation and an increased risk of miscarriage, ectopic (tubal) pregnancy, infertility, and premature births (1).

Evidence from a recent study suggests that daughters of women who took DES during pregnancy may have a slightly increased risk of breast cancer after age 40. The risk of breast cancer for DES-exposed women over age 40 was 1.9 times the risk of breast cancer for unexposed women of the same ages. The increased risk association was present for all breast cancer risk factors examined, and did not differ by tumor receptor status, tumor size, or lymph node involvement (2).

Although this evidence suggests that prenatal DES exposure increases the risk of breast cancer, breast cancer is still a relatively rare event among DES-exposed women. For every 1,000 DES-exposed women aged 45 to 49, 4 new cases of breast cancer per year would be expected, compared with 2 new cases per year in every 1,000 unexposed women (3).

While the greater risk above age 40 is statistically significant, i.e., is more than would be expected to happen by chance alone, it is still based on relatively small numbers. The actual risk could be quite a bit lower or higher. Therefore, additional research is needed to be sure that the increased risk was caused by DES (2).

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 (1).

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 (1). 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 (1). A woman who was pregnant between 1938 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 doctor performs 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 continuing to study whether DES-exposed daughters have a higher risk of breast cancer than unexposed daughters; therefore, DES-exposed daughters should continue to rigorously 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 screenings 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?

Multiple studies have found an increased risk of premature births, miscarriage, and ectopic pregnancy associated with DES exposure (1). In an analysis of data published in 2000, researchers found that DES daughters were three times more likely to have had premature births and four times more likely to have had a miscarriage or ectopic pregnancy than unexposed daughters. Full-term infants were delivered in the first pregnancies of 64.1 percent of exposed women compared with 84.5 percent of unexposed women (4).

Early studies investigating a possible link between DES exposure and infertility produced conflicting results. However, a study published in 2001 that compared DES-exposed and unexposed daughters 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 (5).

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) (6).

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 (7). 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 (6).

A recent and larger study using questionnaires to daughters of mothers who were exposed *in utero* to DES (granddaughters), however, shows a slight effect on menstrual periods—later attainment of menstrual regularization and more irregular periods—in the exposed granddaughters compared with the unexposed granddaughters. Also, there was a suggestion that infertility was greater among the exposed, and the exposed tended to have fewer births. Because a number of these associations are based on small numbers of events, researchers will continue to study these women to further clarify these findings (8).

Researchers are also following up on the observation that exposure to DES may lead to an increased risk of breast cancer. A 2006 analysis found that DES exposure *in utero*

was associated with a slightly increased risk of breast cancer. The experience of the women thus far suggests that increased risk might be restricted to women age 40 or older. Further follow-up is needed to confirm this and to characterize risk as the women age.

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 (9).

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
Mail Stop E-29
1600 Clifton Road, NE.
Atlanta, GA 30333
Telephone: 1-800-232-4636 (toll-free)
E-mail: cdcinfo@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: 158 South Stanwood Road
Columbus, OH 43209
Telephone: 1-800-DES-9288 (1-800-337-9288)
E-mail: desaction@columbus.rr.com
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: The Registry for Research on Hormonal Transplacental Carcinogenesis (Clear Cell Cancer Registry)

Address: The University of Chicago
Department of Obstetrics and Gynecology
5841 South Maryland Avenue
Chicago, IL 60637

Telephone: 773-702-6671

Fax number: 773-834-2341

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 diagnosed with clear cell adenocarcinoma of the vagina and/or cervix. Staff members also answer questions from the public.

Selected References

1. National Cancer Institute. *DES Research Update 1999: Current Knowledge, Future Directions*. National Cancer Institute, 1999.
2. Palmer JR, Wise LA, Hatch EE, et al. Prenatal diethylstilbestrol exposure and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2006; 15(8):1509-1514.
3. Ries LAG, Eisner MP, and Kosary CL, et al. (eds). *SEER Cancer Statistics Review, 1975-2002*. Bethesda, MD: National Cancer Institute, 2005. Retrieved November 3, 2006, from http://seer.cancer.gov/csr/1975_2002/.
4. Kaufman RH, Adam E, Hatch EE, et al. Continued follow-up of pregnancy outcomes in diethylstilbestrol-exposed offspring. *Obstetrics and Gynecology* 2000; 96(4):483-489.
5. Palmer JR, Hatch EE, Rao RS, et al. Infertility among women exposed prenatally to diethylstilbestrol. *American Journal of Epidemiology* 2001; 154(4):316-321.
6. Kaufman RH, Adam E. Findings in female offspring of women exposed in utero to diethylstilbestrol. *Obstetrics and Gynecology* 2002; 99(2):197-200.
7. 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.
8. Titus-Ernstoff L, Troisi R, Hatch EE, et al. Menstrual and reproductive characteristics of women whose mothers were exposed in utero to diethylstilbestrol (DES). *International Journal of Epidemiology* 2006; 35(4):862-868.
9. Titus-Ernstoff L, Perez K, Hatch EE, et al. Psychosexual characteristics of men and women exposed prenatally to diethylstilbestrol. *Epidemiology* 2003; 14(2):155-160.

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Related Resources

Publications (available at <http://www.cancer.gov/publications>)

- *What You Need To Know AboutTM Breast Cancer*
- *What You Need To Know AboutTM Cancer of the Cervix*

National Cancer Institute (NCI) Resources

Cancer Information Service (toll-free)

Telephone: 1-800-4-CANCER (1-800-422-6237)

TTY: 1-800-332-8615

Online

NCI's Web site: <http://www.cancer.gov>

LiveHelp, NCI's live online assistance:

<https://cissecure.nci.nih.gov/livehelp/welcome.asp>

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