

<https://www.cdc.gov/des/consumers/about/history.html>

Diethylstilbestrol History

Diethylstilbestrol (DES) is an estrogen that was first manufactured in a laboratory in 1938, so it is called a "synthetic estrogen." During 1938-1971, U.S. physicians prescribed DES to pregnant women to prevent miscarriages and avoid other pregnancy problems. As a result, an estimated 5-10 million pregnant women and the children born of these pregnancies were exposed to DES. Physicians prescribed DES to pregnant women on the theory that miscarriages and premature births occurred because some pregnant women did not produce enough estrogen naturally. At the time, physicians thought DES was safe and would prevent miscarriages and pre-term (early) births.

In 1953, published research showed that DES did not prevent miscarriages or premature births. However, DES continued to be prescribed until 1971. In that year, the Food and Drug Administration (FDA) issued a Drug Bulletin advising physicians to stop prescribing DES to pregnant women. The FDA warning was based on a study published in 1971 that identified DES as a cause of a rare vaginal cancer in girls and young women who had been exposed to DES before birth (in the womb).

The news that DES could be harmful led to a national effort to find women prescribed DES while pregnant and notify them of the potential DES-related health problems. Physicians reviewed patients' medical records and notified women who had been prescribed DES. As a result of this effort, many women were made aware of the DES health risk known at that time, known as clear cell adenocarcinoma (CCA), a rare vaginal cancer. Women were encouraged to have their DES-exposed daughters screened regularly by a gynecologist because CCA was found in girls as young as 8 years old.

Women contacted during the 1970s, along with their children, formed the core of large study groups that researchers call "cohorts." Researchers studied the health of these DES-exposed cohorts for more than 20 years. Much of what is known about DES-related health risks is the result of these long-term studies. For more information on these cohort studies, [click here](#).

Despite earlier efforts to identify DES-exposed women and men, many persons exposed to DES were not located. These persons may not realize that they were exposed to DES. Unfortunately, no medical test (such as blood, urine, or skin analysis) can detect DES exposure. However, to assess whether you may have been exposed to DES and to learn what you can do about DES, refer to the [Interactive DES Self-Assessment Guide](#), and [What You Can Do About DES](#).

All DES-exposed persons are at an increased risk for developing some health problems when compared with persons who were not exposed to DES. All of the health problems related to DES exposure also can occur in persons who were not exposed to DES. CDC's DES update provides information on [DES-related health effects](#).

Many companies manufactured DES and similar synthetic drugs. In 1976, the *Journal of the American Medical Association (JAMA)* published a list of the most commonly used names and spellings for DES and similar drugs.

DES Type-Drugs That May Have Been Prescribed to Pregnant Women

(Source: NCI. Exposure in utero to diethylstilbestrol and related synthetic hormones. JAMA (Sept. 6, 1976) - Vol 236 No. 10, pp. 1107-1109.)

Nonsteroidal Estrogens:	Fonatot	Palestrol	Nonsteroidal Estrogen-Androgren Combination: Amperone
Benzestrol	Gynben	Restrol	
Chlorotrianisene	Gyneben	Stil-Rol	
Comestrol	Hexestrol	Stilbal	
Cyren A	Hexoestrol	Stilbestrol	
Cyren B	Hi-Bestrol	Stilbestronate	
Delvinal	Menocrin	Stilbetin	
DES	Meprane	Stilbinol	
DesPlex	Mestilbol	Stilboestroform	
Dibestil	Microest	Silboestrol	
Diestryl	Methallenestrol	Stilboestrol DP	
Dienestrol	Mikarol	Stilestrate	
Dienoestrol	Mikarol forti	Stilpalmitate	
Diethylstilbestrol dipalmitate	Milestrol	Stilphostrol	
Diethylstilbestrol diphosphate	Monomestrol	Stilronate	
Diethylstilbestrol dipropionate	Neo-Oestrinol I	Stilrone	
Diethylstilbenediol	Neo-Oestrinol II	Stils	
Digestil	Nulabort	Synestrin	
Domestrol	Oestrogenine	Synestrol	Vaginal Cream Suppositories with Nonsteroidal Estrogens: AVC Cream w/ Dienestrol Dienestrol Cream
Estilben	Oestromenin	Synthosestrin	
Estrobene	Oestromon	Tace	
Estrobene DP	Orestol	Vallestril	
Estrosyn	Pabestrol D	Willestrol	

National Cancer Institute

Diethylstilbestrol (DES) and Cancer

What is DES?

Diethylstilbestrol (DES) is a synthetic form of the female hormone estrogen. It was prescribed to pregnant women between 1940 and 1971 to prevent miscarriage, premature labor, and related complications of pregnancy (1). The use of DES declined after studies in the 1950s showed that it was not effective in preventing these problems.

In 1971, researchers linked prenatal (before birth) DES exposure to a type of cancer of the cervix and vagina called clear cell adenocarcinoma in a small group of women (2). Soon after, the Food and Drug Administration (FDA) notified physicians throughout the country that DES should not be prescribed to pregnant women (3). The drug continued to be prescribed to pregnant women in Europe until 1978 (4). DES is now known to be an endocrine-disrupting chemical, one of a number of substances that interfere with the endocrine system to cause cancer, birth defects, and other developmental abnormalities. The effects of endocrine-disrupting chemicals are most severe when exposure occurs during fetal development.

What is the cancer risk of women who were exposed to DES before birth?

The daughters of women who used DES while pregnant—commonly called DES daughters—have about 40 times the risk of developing clear cell adenocarcinoma of the lower genital tract than unexposed women. However, this type of cancer is still rare; approximately 1 in 1,000 DES daughters develops it.

The first DES daughters who were diagnosed with clear cell adenocarcinoma were very young at the time of their diagnoses (2). Subsequent research has shown that the risk of developing this disease remains elevated as women age into their 40s (5).

DES daughters have an increased risk of developing abnormal cells in the cervix and the vagina that are precursors of cancer (dysplasia, cervical intraepithelial neoplasia, and squamous intraepithelial lesions) (6). These abnormal cells resemble cancer cells, but they do not invade nearby healthy tissue and are not cancer. They may develop into cancer, however, if left untreated. Scientists estimated that DES-exposed daughters were 2.2 times more likely to have these abnormal cell changes in the cervix than unexposed women. Approximately 4% of DES daughters developed these conditions because of their exposure (7). It has been recommended that DES daughters have a yearly Pap test and pelvic exam to check for abnormal cells (6).

DES daughters may also have a slightly increased risk of breast cancer after age 40. A 2006 study from the United States suggested that, overall, breast cancer risk is not increased in DES daughters, but that, after age 40, DES daughters have approximately twice the risk of breast cancer as unexposed women of the same age and with similar risk factors (8). However, a 2010 study from Europe found no difference in breast cancer risk between DES daughters and unexposed women and no difference in overall cancer risk (5). A 2011 study found that about 2% of a large cohort of DES daughters has developed breast cancer due to their exposure (7).

DES daughters should be aware of these health risks, share their medical history with their doctors, and get regular physical examinations.

Do DES daughters have problems with fertility and pregnancy?

Several studies have found increased risks of premature birth, miscarriage, and ectopic pregnancy associated with DES exposure. An analysis of updated data published in 2011 is outlined in the table below.

Fertility Problems in DES Daughters (7)			
Fertility Complication	<u>Hazard Ratio</u>	Percent Cumulative Risk* to Age 45, DES-exposed Women	Percent Cumulative Risk* to Age 45, Unexposed Women
Premature delivery	4.68	53.3	17.8
Stillbirth	2.45	8.9	2.6
Neonatal death	8.12	7.8	0.6
Ectopic pregnancy	3.72	14.6	2.9
Miscarriage (second trimester)	3.77	16.4	1.7
Preeclampsia	1.42	26.4	13.7
Infertility	2.37	33.3	15.5

*The total risk (probability) that a certain problem will occur.

Some studies suggest that the increased risk of infertility is mainly due to uterine or fallopian tube problems (9).

What other health problems might DES daughters have?

Concerns have been raised that DES daughters may have problems with their immune system. However, research thus far suggests that DES daughters do not have an increased risk of autoimmune diseases. Researchers found no difference in the rates of lupus, rheumatoid arthritis, optic neuritis, and idiopathic thrombocytopenia purpura between DES-exposed and unexposed women (10).

Studies examining the risk of depression among DES daughters have had conflicting results. One study found a 40% increase in risk of depression, whereas another found no increased risk for these women (11, 12). A study published in 2003 found little support for the possibility that prenatal exposure to DES influences certain psychological and sexual characteristics of adult men and women, such as the likelihood of ever having been married, age at first sexual intercourse, number of sexual partners, and having had a same-sex sexual partner in adulthood (12).

DES daughters have more than twice the risk of early menopause (menopause that begins before age 45) as unexposed women. Scientists estimate that 3% of DES-exposed women have experienced early menopause due to their exposure to DES (7).

What health problems might DES-exposed sons have?

Some studies have found that men whose mothers used DES during pregnancy have an increased risk of testicular abnormalities, including undescended testicles or development of cysts in the epididymis (13). There is also some evidence of increased risks of inflammation or infection of the testicles (13).

Whether DES-exposed sons have increased risks of testicular or prostate cancer is unclear; studies to date have produced mixed results. As the cohort of these men gets older, more data will be available to help answer this question.

Research has shown that men who were exposed to DES through their mothers do not have an increased risk of infertility, even when they have genital abnormalities (13).

What health problems might women who took DES during pregnancy have?

Women who used DES may have a slight increase in the risk of developing (14) and dying from (15) breast cancer compared with women who did not use DES. No evidence exists to suggest that women who took DES are at higher risk for any other type of cancer (4).

What health problems might DES-exposed grandchildren have?

Researchers are also studying possible health effects among women and men who are the children of DES daughters. These groups are called DES granddaughters and DES grandsons, or the third generation. Researchers are studying these groups because studies in animal models suggest that DES may cause DNA changes (i.e., altered patterns of methylation) in mice exposed to the chemical during early development (16). These changes can be heritable and have the potential to affect subsequent generations. A comparison of the results of DES granddaughters' pelvic exams with those of their mothers' first pelvic exams found none of the changes that had been associated with prenatal DES exposure in their mothers (9). However, another analysis showed that DES granddaughters began their menstrual periods later and were more likely to have menstrual irregularities than other women of the same age. The data also suggested that infertility was greater among DES granddaughters, and that they tended to have fewer live

births (17). However, this association is based on small numbers of events and was not statistically significant. Researchers will continue to follow these women to study the risk of infertility. Recent studies have found that DES granddaughters and DES grandsons may have a slightly higher risk of cancer (18) and birth defects (19), including hypospadias in DES grandsons (20). However, because each of these associations is based on small numbers of events, researchers will continue to study these groups to clarify the findings.

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

It is estimated that 5 to 10 million Americans—pregnant women and the children born to them—were exposed to DES between 1940 and 1971 (4). DES was given widely to pregnant women between 1940 and 1971 to prevent complications during pregnancy. DES was provided under many different product names and also in various forms, such as pills, creams, and vaginal suppositories (6). The table below includes examples of products that contained DES.

DES Product Names		
Nonsteroidal Estrogens		
Benzestrol	Gynben	Stil-Rol
Chlorotrianisene	Gyneben	Stilbal
Comestrol	Hexestrol	Stilbestrol
Cyren A.	Hexoestrol	Stilbestronate
Cyren B.	Hi-Bestrol	Stilbetin
Delvinal	Menocrin	Stilbinol
DES	Meprane	Stilboestroform
Desplex	Mestilbol	Silboestrol
Dibestil	Microest	Stilboestrol DP
Diestryl	Methallenestril	Stilestrate
Dienostrol	Mikarol	Stilpalmitate
Dienoestrol	Mikarol forti	Stilphostrol
Diethylsteilbestrol	Milestrol	Stilronate
dipalmitate	Monomestrol	Stilrone
Diethylstilbestrol	Neo-Oestranol I	Stils
diphosphate	Neo-Oestranol II	Synestrin
Diethylstilbestrol	Nulabort	Synestrol
dipropionate	Oestrogenine	Synthosestrin
Diethylstilbenediol	Oestromenin	Tace
Digestil	Oestromon	Vallestril
Dinestrol	Orestol	Willestrol
Domestrol	Pabestrol D	
Estilben	Palestrol	
Estrobene	Restrol	

Estrobene DP
Estrosyn
Fonatul

Nonsteroidal Estrogen-Androgen Combinations

Amperone	Teserene
Di-Erone	Tylandril
Estan	Tylostereone
Metystil	

Nonsteroidal Estrogen-Progesterone Combinations

Progravidium

Vaginal Cream Suppositories with Nonsteroidal Estrogens

AVC Cream with Dienestrol
Dienestrol Cream

Women who think they used DES during pregnancy, or people who think that their mother used DES during pregnancy, can try contacting the physician or institution where they received their care to request a review of their medical records. If any pills were taken during pregnancy, obstetrical records could be checked to determine the name of the drug.

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 most cases, however, it may be impossible to determine whether DES was used.

What should DES-exposed daughters do?

Women who know or believe they were exposed to DES before birth should be aware of the health effects of DES and inform their doctor about their possible exposure. It has been recommended that exposed women have an annual medical examination to check for the adverse health effects of DES (6). A thorough examination may include the following:

- Pelvic examination
- Pap test and colposcopy—A routine cervical Pap test is not adequate for DES daughters. The Pap test must gather cells from the cervix and the vagina. It is also good for a clinician to see the cervix and vaginal walls. They may use a colposcope to follow-up if there are any abnormal findings.
- Biopsy
- Breast examinations—It is recommended that DES daughters continue to rigorously follow the routine breast cancer screening recommendations for their age group. The NCI fact sheet Mammograms includes information about these guidelines.

What should DES-exposed mothers do?

A woman who took DES while pregnant or who 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.

It is recommended that DES-exposed mothers have regular breast cancer screenings and yearly medical checkups that include a pelvic examination and a Pap test.

What should DES-exposed sons do?

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

Is it safe for DES daughters to use hormone replacement therapy?

Each woman should discuss this question with her doctor. Studies have not shown that hormone replacement therapy is unsafe for DES daughters. However, some doctors believe that DES daughters should avoid these medications because they contain estrogen (21).

What is the focus of current research on DES exposure?

In 1992, NCI, together with collaborators at five research centers, began a long-term study of individuals exposed to DES, the DES Follow-up StudyExit Disclaimer. Participants were initially drawn from eight different medical centers and consisted of five individual cohorts of people. In order for the study findings to be valid, enrollment in the study is limited to participants who have been part of existing cohorts. It is not currently possible for the DES Follow-up Study to accept new participants.

Researchers continue to study DES daughters as they move into their menopausal years. The cancer risks for exposed sons are also being studied to determine whether they differ from those for unexposed men.

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).

The National Institute of Environmental Health Sciences (NIEHS) is leading laboratory studies to investigate DES exposure and its effects on health. NIEHS researchers developed a rodent model of prenatal DES exposure that has been useful in replicating and predicting adverse health effects in prenatally exposed men and women. This experimental model has been used worldwide to study mechanisms involved in DES-related toxicity and the adverse effects of less potent environmental estrogens.

Where can DES-exposed people get additional information?

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

National Cancer Institute

DES Follow-up Study

<http://www.desfollowupstudy.org>Exit Disclaimer

Since 1992, the NCI, in collaboration with research centers throughout the United States, has been conducting the DES Follow-up Study of more than 21,000 mothers, daughters, and sons, to better understand the long-term health effects of exposure to DES.

Registry for Research on Hormonal Transplacental Carcinogenesis (Clear Cell Cancer Registry)

The University of Chicago
Department of Obstetrics and Gynecology
MC 2050
5841 South Maryland Avenue
Chicago, IL 60637
773-702-6671
773-834-2341 (Fax)
danderso1@babies.bsd.uchicago.edu

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.

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