DES UPDATE

For you, your family, and your health care provider

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

DEPARTMENT OF HEALTH & HUMAN SERVICES • USA

CDC

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CDC'S DES UPDATE

Diethylstilbestrol (DES) is a synthetic estrogen that was developed in 1938 to supplement a woman's natural estrogen production. Prescribed by physicians during 1938–1971 for women who experienced miscarriages or premature deliveries, DES was originally considered effective and safe for both the pregnant woman and the developing baby.

In the United States, an estimated 5–10 million persons were exposed to DES during 1938–1971, including women who were prescribed DES while pregnant and the female and male children born of these pregnancies.

The Centers for Disease Control and Prevention (CDC) has developed CDC's DES Update so the public and health care providers have the latest, most comprehensive, and accurate information about DES. CDC is working with consumer organizations and health care provider partners around the country to distribute information about DES.

CDC's DES Update includes:

- **Fact Sheets –** Information on the history of DES, known health effects, recent and on-going research, tips for working with your health care provider, and steps to take for protecting your health and the health of your family.
- **DES Self-Assessment –** A guide to help you determine if you might have been exposed to DES.
- **DES Health Information Record –** A form to help you keep track of your DES health information.

CDC's DES Update also includes a Web site (www.cdc.gov/DES) from which you can print and download information and a toll-free number (1-888-232-6789) that you can call for free printed materials. The DES Update is a resource for you, your family, and your health care provider, and is designed to help persons who think they may have been exposed to DES stay up-to-date.

— Centers for Disease Control and Prevention

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Milestones

1938

Diethylstilbestrol (DES), a synthetic estrogen, first prescribed to supplement a pregnant woman's natural estrogen production.

1940's-1950's

DES prescription expanded nationally through medical publications and physician communication about its therapeutic value and administration.

Smith OW et al., American Journal of Obstetrics and Gynecology

1953

DES found to be *not effective* in preventing miscarriages and premature birth, but continued to be prescribed.

Dieckmann WJ et al., American Journal of Obstetrics and Gynecology

1971

DES found to be *not safe*...linked to rare vaginal cancer in young DES Daughters.

Herbst AL et al., New England Journal of Medicine

FDA Drug Bulletin warned physicians about potential harmful effects of prescribing DES to pregnant women.

1974

Research project to locate and follow DES Daughters begun.

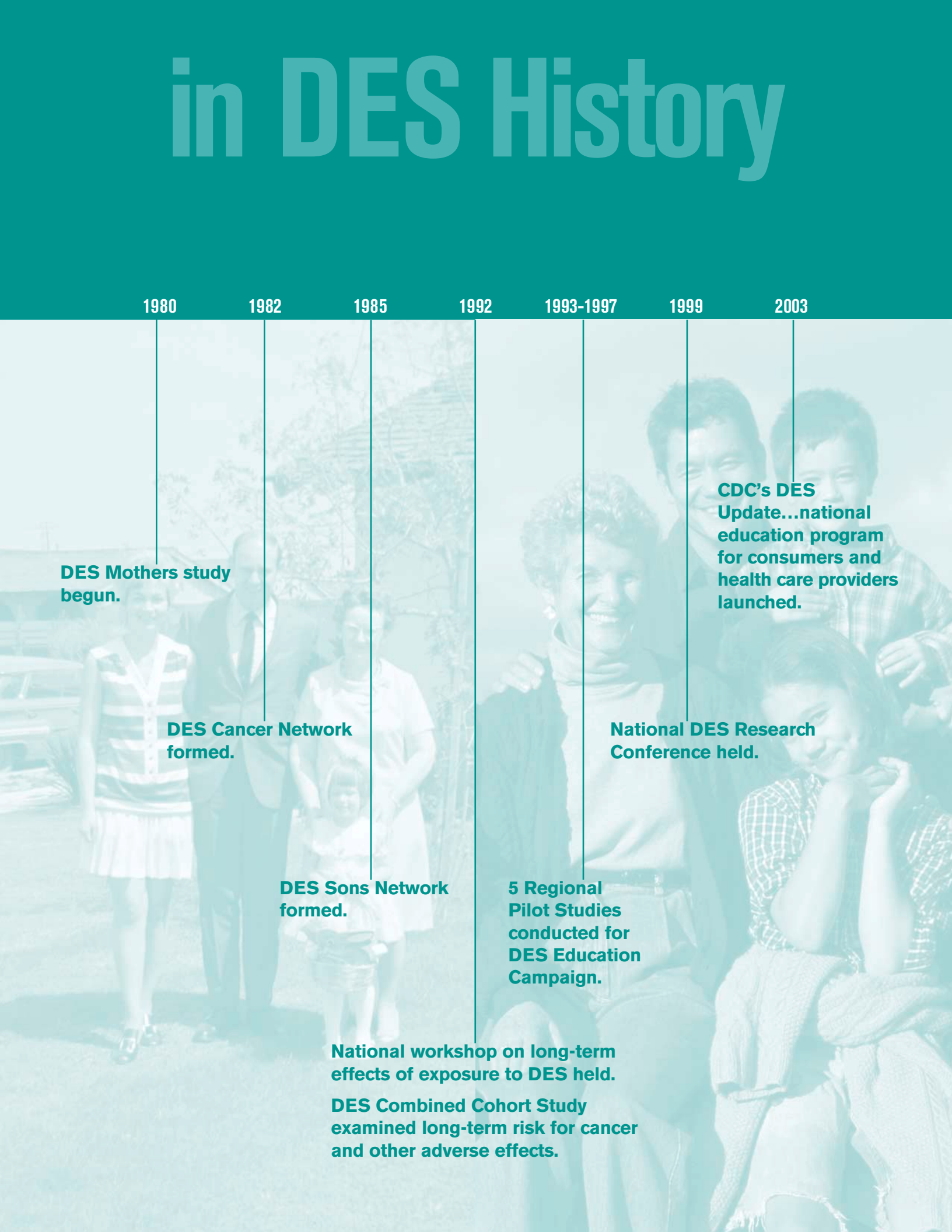
1978

National DES Task Force issued Physician Advisory; recommended all physicians personally notify their DES-exposed patients, start national public information campaign.

1979

DES Action formed.

in DES History



1980

DES Mothers study begun.

1982

DES Cancer Network formed.

1985

DES Sons Network formed.

1992

National workshop on long-term effects of exposure to DES held.

DES Combined Cohort Study examined long-term risk for cancer and other adverse effects.

1993-1997

5 Regional Pilot Studies conducted for DES Education Campaign.

1999

National DES Research Conference held.

2003

CDC's DES Update…national education program for consumers and health care providers launched.

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Tab 4: Additional DES Resources

- **Partner and Government Organizations –** A list of the names and contact information for organizations that provide useful DES resources.
- **DES Glossary –** A list of terms and definitions relevant to the topic of DES.
- **DES Bibliography –** A list of published research and other sources of DES information grouped by main topic.
- **Notes –** A section for your notes.

Binder Pocket

- **DES SELF-ASSESSMENT: A Guide to Understanding Your Risk for DES Exposure –** A guide to help you determine if you might have been exposed to DES.

TAB 1: WHAT WE KNOW ABOUT DES

Overview

Diethylstilbestrol (DES) is a synthetic estrogen that was developed to supplement a woman's natural estrogen production. First prescribed by physicians in 1938 for women who experienced miscarriages or premature deliveries, DES was originally considered effective and safe for both the pregnant woman and the developing baby. In the United States, an estimated 5–10 million persons were exposed to DES during 1938–1971, including women who were prescribed DES while pregnant and the female and male children born of these pregnancies. In 1971, the Food and Drug Administration (FDA) issued a Drug Bulletin advising physicians to stop prescribing DES to pregnant women because it was linked to a rare vaginal cancer in female offspring.

More than 30 years of research have confirmed that health risks are associated with DES exposure. However, not all exposed persons will experience the following DES-related health problems.

- Women prescribed DES while pregnant are at a modestly increased risk for breast cancer.
- Women exposed to DES before birth (in the womb), known as DES Daughters, are at an increased risk for clear cell adenocarcinoma (CCA) of the vagina and cervix, reproductive tract structural differences, pregnancy complications, and infertility. Although DES Daughters appear to be at highest risk for clear cell cancer in their teens and early 20s, cases have been reported in DES Daughters in their 30s and 40s (Hatch, 1998).
- Men exposed to DES before birth (in the womb), known as DES Sons, are at an increased risk for non-cancerous epididymal cysts.

Researchers are still following the health of persons exposed to DES to determine whether other health problems occur as they grow older.

Whether you know for sure or suspect you were exposed to DES, you can use CDC's DES Update to learn more about what DES exposure means and what you can do about DES. This section of CDC's DES Update includes the following information.

- **DES: Yesterday, Today, Tomorrow –** A history of DES and what to look for about DES in the future.
- **CDC's DES Update –** An overview of CDC's DES health education program, including a timeline of the history of DES and a list of partner organizations.
- **CDC's DES Update in Brief –** A summary card to help start a discussion about DES. Take this card to your health care provider and share it with family and friends.
- **Known DES Health Effects –** In-depth information about the health effects found in women prescribed DES while pregnant, DES Daughters, and DES Sons.
- **Understanding DES Research –** Information on DES research, including how to decide whether a source of information is reliable, what can be learned about human health risks from laboratory animal studies, and the role of cohort studies in DES research.

DES: YESTERDAY, TODAY, TOMORROW

DES: Yesterday

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, refer to the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research.

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 sections of CDC's DES Update titled DES SELF-ASSESSMENT: A Guide to Understanding Your Risk for DES Exposure, 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. To learn more, refer to the section of CDC's DES Update titled WHAT WE KNOW ABOUT DES: Known DES 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

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

Nonsteroidal Estrogen-Androgren Combination

Amperone
Di-Erone
Estan
Metystil
Teserene
Tylandril
Tylostereone

Nonesteroidal Estrogen-Progesterone Combination

Progravidium

Vaginal Cream Suppositories with Nonsterioidal Estrogens

AVC Cream w/ Dienestrol
Dienestrol Cream

DES: Today

Over the years, research has shown that exposure to DES puts both women and men at an increased risk for certain health problems. This means that some, but not all, of the women and men who were exposed to DES will experience one or more DES-related health problems.

Research confirms the following increased health risks associated with DES:

Women Prescribed DES While Pregnant are at a modestly increased risk for

- Breast cancer

DES Daughters are at an increased risk for

- Clear cell adenocarcinoma (CCA), a rare kind of vaginal and cervical cancer

  Increased risk for clear cell cancer appears to be highest for DES Daughters in their teens and early 20s. However, case have been reporter for DES Daughters in their 30s and 40s (Hatch, 1998).

- Reproductive tract structural differences (for example, T-shaped uterus)
- Pregnancy complications, including ectopic (tubal) pregnancy and pre-term (early) delivery
- Infertility

DES Sons are at an increased risk for

- Non-cancerous epididymal cysts (growths on the testicles)

To learn more about DES-related health risks, refer to the section of CDC's DES Update titled WHAT WE KNOW ABOUT DES: Known DES Health Effects.

No medical test (such as a blood, urine, or skin analysis) can detect DES exposure. Tracing old medical records that prove DES exposure is difficult. Understandably, many women do not remember whether they were prescribed DES while pregnant. Physicians who prescribed DES may have retired or passed away. Their records may have been destroyed. All these factors make it difficult for persons to determine their DES-exposure status with certainty.

We do know that women who were not under a physician's care during their pregnancy likely did not receive DES, because it required having a physician's prescription. However, sometimes physicians gave DES pills or injections directly to their patients. We also know that most women who were prescribed DES had a history of miscarriage or giving birth prematurely.

For help deciding whether you might have been exposed to DES, refer to the section of CDC's DES Update titled DES SELF-ASSESSMENT: A Guide to Understanding Your Risk for DES Exposure.

DES: Tomorrow

Although some questions about the long-term risks of DES exposure remain unanswered, related health effects have taken a heavy toll on many families. As research continues, we might learn about new DES health risks that have not yet been identified.

Fortunately, DES-exposed persons can take action to protect their health. They can work with their health care providers to learn about and follow appropriate preventive health behaviors. They can get regular screenings, and they can stay up-to-date on risks associated with DES exposure.

CDC's DES Update can help you take action. It is designed to give you the most complete, up-to-date information on DES, including how to evaluate exposure and make informed decisions to protect the health of you and your family.

CDC'S DES UPDATE

Overview

The Centers for Disease Control and Prevention (CDC) have developed CDC's DES Update so the public and health care providers have the latest, most comprehensive, and accurate information about diethylstilbestrol (DES).

CDC's DES Update was funded by the U.S. Congress and developed in conjunction with the National Cancer Institute (NCI) and many partner organizations. Researchers have been studying the effects of DES exposure for more than 30 years. However, not all persons who were exposed to DES nor their health care providers have always known the latest information about DES.

A key goal of CDC's DES Update is to provide the most comprehensive information about DES, including findings from continuing studies on the health effects of DES exposure. CDC has also designed and distributed DES Update educational materials that give health care providers the latest research and tools they can use to learn more about DES. Ultimately, we want to help patients and health care providers have good discussions about DES and make the right choices to protect patients' health.

CDC'S DES UPDATE

How Can CDC's DES Update Help Me?

CDC's DES Update includes information for persons who want to

- assess whether they might have been exposed to DES;
- know more about how exposure to DES could affect them, their family, and friends;
- stay up-to-date on research about the effects of exposure to DES;
- get advice about talking with health care providers about DES;
- share information about DES with others; and
- contact the DES Update's partner organizations.

CDC's DES Update is a resource for you, your family, and your health care provider. CDC's DES Update includes a Web site (www.cdc.gov/DES) from which you can print and download information, and a toll-free number (1-888-232-6789) that you can call for free printed materials.

CDC's DES Update can help persons who think they may have been exposed to DES. To assess whether you may have been exposed to DES and to learn what you can do about DES exposure, refer to the section of CDC's DES Update titled DES SELF-ASSESSMENT: A Guide to Understanding Your Risk for DES Exposure.

CDC will also sponsor a series of teleconferences, during which researchers and clinicians will present the latest research on DES exposure. The public is invited to call in, and DES researchers and clinicians will be available to answer questions from callers. Summaries of the teleconferences will be posted on CDC's DES Update Web site. For more information about these teleconferences, refer to the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: DES Teleconferences.

Is this the first DES educational effort?

CDC's DES Update is the first comprehensive health education program. However, this is not the first effort to reach out to persons who have been affected by DES. In 1971, Dr. Arthur L. Herbst published a study identifying a rare cancer of the vagina, clear cell adenocarcinoma (CCA), as a health risk for females exposed to DES before birth (in the womb). Since then, government agencies and advocacy organizations have been working to inform the public and health care providers about the effects of DES exposure. Following is a timeline of the history of DES:

- **1971:** The Food and Drug Administration (FDA) issued a Drug Bulletin warning physicians that giving DES to a pregnant woman could harm the developing baby in her womb.
- **1972:** Registry of DES Daughters diagnosed with clear cell adenocarcinoma (CCA) was established.
- **1974:** National Cooperative Diethylstilbestrol and Adenosis (DESAD) project began. This project was designed to locate DES Daughters and monitor their health over time.
- **1978:** The National DES Task Force issued a Physician Advisory recommending that all physicians review their medical records and notify women who were prescribed DES while pregnant. The Task Force also recommended the initiation of a public health information campaign. In addition, reports about DES appeared in many newspapers, magazines, and television programs.
- **1979:** DES Action USA, a national consumer advocacy group, was started by women who had been prescribed DES while pregnant, and their families.
- **1980:** The research study, DES Mothers, began.
- **1982:** DES Cancer Network, an advocacy and support group for DES Daughters diagnosed with CCA, was formed.
- **1985:** The DES Sons Network was formed in conjunction with DES Action USA.
- **1992:** The National Institutes of Health (NIH) held a national workshop on long-term health effects of exposure to DES. The DES Combined Cohort Study joined five existing study groups to examine the long-term risk for cancer and other adverse effects by studying thousands of people together in one study.
- **1993–1997:** The National Cancer Institute (NCI) conducted regional DES education program pilot studies in five sites, including California, Massachusetts, New York, Texas, and Wisconsin. The results of the pilot studies provided a foundation for CDC's DES Update.
- **1999:** The National Institutes of Health (NIH) held a National DES Research Conference.
- **2003:** CDC launched its national DES Update for consumers and health care providers.

What is CDC's DES Update doing to get the word out?

CDC is working with advocacy and health care provider partners around the country to distribute information about DES. For example, DES advocacy organizations (such as DES Action, DES Cancer Network, and DES Sons Network) are channels to reach people who know they have been exposed to DES. In addition, the National Centers of Excellence in Women's Health developed materials to update health care providers.

The following government and non-government organizations worked with CDC to produce the DES Update:

American Academy of Physician Assistants
American College of Nurse-Midwives
American College of Obstetricians and Gynecologists
American Medical Association
American Medical Women's Association
American Nurses Association
Association of Reproductive Health Professionals
DES Action USA
DES Cancer Network
DES Sons Network
Mennonite College of Nursing at Illinois State University
National Association of Nurse Practitioners in Women's Health
National Cancer Institute, National Institutes of Health
National Centers of Excellence in Women's Health
National Women's Health Network
Office on Women's Health, Department of Health and Human Services
Registry for Research on Hormonal Transplacental Carcinogenesis, University of Chicago
RESOLVE: The National Infertility Association
Y-ME Indianapolis
Y-ME Chattanooga

KNOWN DES HEALTH EFFECTS

Overview

Research has confirmed that several health risks are associated with DES exposure. Risks have been identified for women prescribed DES while pregnant; women exposed to DES before birth (in the womb), known as DES Daughters; and men exposed to DES before birth (in the womb), known as DES Sons. These risks include:

Women Prescribed DES While Pregnant are at a modestly increased risk for

- Breast cancer

DES Daughters are at an increased risk for

- Clear cell adenocarcinoma (CCA), a rare kind of vaginal and cervical cancer
- Reproductive tract structural differences (for example, T-shaped uterus)
- Pregnancy complications, such as ectopic (tubal) pregnancy and pre-term delivery
- Infertility

DES Sons are at an increased risk for

- Non-cancerous epididymal cysts (growths on the testicles)

Research continues on the health risks for women and men exposed to DES. For more information, refer to the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research.

KNOWN DES HEALTH EFFECTS

Women Prescribed DES While Pregnant

This section addresses questions about increased health risks for women prescribed DES while pregnant, including information on

- their increased risk of breast cancer, and
- steps that should be taken for detecting breast cancer early.

I was prescribed DES during my pregnancy. Am I at an increased risk for any health problems?

Women prescribed DES while pregnant are at a modestly increased risk for developing breast cancer. Studies have consistently reported an increased risk of approximately 30% for women prescribed DES while pregnant. The most recent study, published in the *British Journal of Cancer* (Titus-Ernstoff, 2001), included more than 6,000 women and compared breast cancer rates of women exposed to DES with rates among women who were not exposed. This study followed participants over a longer period of time than earlier research on breast cancer risks associated with DES. The researchers' findings were consistent with earlier studies, confirming an increased breast cancer risk of approximately 30% for women prescribed DES while pregnant. That means when considering breast cancer risks across a lifetime, one in six women prescribed DES during pregnancy will get breast cancer. In comparison, only one in eight unexposed women will get breast cancer across their lifetime.

Why haven't I heard about a connection between DES and breast cancer?

Early studies of women prescribed DES while pregnant were inconclusive. Even now, not all researchers agree that there is a link between DES exposure and breast cancer. Despite differences of opinion, the 2001 *British Journal of Cancer* study is important for two reasons. First, it is the largest study of its kind. Second, participants in the 2001 study were older than participants in previous studies; as women grow older, their chances for developing breast cancer increase, regardless of whether they were exposed to DES. Because participants were older, many more women had breast cancer in the 2001 study than in earlier studies. This provides the 2001 study with more "power" to detect meaningful differences between the rates of breast cancer among women who were and were not exposed to DES. In other words, the more women included in a study, the less likely that the results of the study can be considered chance. Now researchers can confirm with a higher degree of certainty that women prescribed DES while pregnant have a modestly increased risk of breast cancer.

How does being prescribed DES while pregnant compare with other risk factors for breast cancer?

Exposure to DES while pregnant is just one of many factors that can increase a woman's chance of developing breast cancer. Several other factors can further increase the risk for breast cancer, including personal and family history of breast cancer, genetics, diet and lifestyle choices, use of hormone replacement therapy (HRT), and having children later in life. In addition, as women grow older, their chances of developing breast cancer increase, regardless of whether they were exposed to DES. The following chart explains the increasing risk for breast cancer as a woman ages. This chart illustrates breast cancer risk for women who were not exposed to DES while pregnant.

A woman's chance of being diagnosed with breast cancer:	
from age 30 to age 40	1 out of 257 women
from age 40 to age 50	1 out of 67 women
from age 50 to age 60	1 out of 36 women
from age 60 to age 70	1 out of 28 women
from age 70 to age 80	1 out of 24 women
Ever	1 out of 8 women

* Source: National Cancer Institute Surveillance, Epidemiology, and End Results Program, 1995-1997.

If I was prescribed DES while pregnant, what can I do now to increase my chances for early detection of breast cancer?

You should follow a regular schedule for breast cancer screening recommended by your health care provider. The types and timing of the screening should be based on your risk factors for breast cancer. Talk with your health care provider about when you should start screenings for breast cancer and how often you should be checked. Your health care provider may recommend that you learn and practice breast self-examination as a way to detect any lumps in your breasts, discharge from the nipples, or skin changes (such as dimpling or puckering). Most health care providers will recommend that women 40 years of age and older have a mammogram (an X-ray of the breast) every 1–2 years. In addition, most health care providers perform clinical breast examinations (visual and manual examination of the breast) during routine physical examinations.

For more information about breast cancer causes and prevention, visit the NCI Web site at www.cancer.gov or call the Cancer Information Service (CIS) toll-free 1-800-4-CANCER (1-800-422-6237). For more information about DES exposure and related health risks, visit CDC's DES Update Web site at www.cdc.gov/DES or call toll-free 1-888-232-6789.

To learn more about the risk of breast cancer for women prescribed DES while pregnant, refer to the sections of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research and ADDITIONAL DES RESOURCES: DES Bibliography.

KNOWN DES HEALTH EFFECTS

Women Exposed To DES Before Birth (In The Womb), Known As DES Daughters

This section addresses general and specific questions about increased health risks for DES Daughters, including information on

- clear cell adenocarcinoma (CCA) of the vagina and cervix;
- pregnancy complications and infertility;
- steps to take with your health care provider to minimize your health risks; and
- what to tell your siblings about DES.

General Questions about Health Risks

My mother was prescribed DES while pregnant with me. Am I at an increased risk for any health problems?

Recent research has confirmed that women exposed to DES before birth (in the womb), known as DES Daughters, are at an increased risk for the following health problems:

- **Clear cell adenocarcinoma (CCA)** – A rare type of vaginal and cervical cancer. Approximately one in 1,000 (0.1 %) DES Daughters might be expected to develop CCA. The risk is virtually non-existent among premenopausal women not exposed to DES.
- **Reproductive tract structural differences** – Including T-shaped uterus, hooded cervix, cervical cockscomb, and pseudopolyp.
- **Pregnancy complications** – Ectopic (tubal) pregnancy and pre-term (early) delivery.
- **Infertility** – Difficulty becoming pregnant.

The amount of risk for each of these problems varies, and all of these health effects also can occur in women not exposed to DES. The following information provides more detail about each of these health problems.

Clear Cell Adenocarcinoma (CCA) of the Vagina and Cervix

CCA, a rare form of vaginal and cervical cancer, was the first health problem identified as being associated with DES exposure (Herbst, 1971; Noller, 1972). CCA of the vagina and cervix occurs more frequently in DES Daughters than in women not exposed to DES. DES Daughters are 40 times more likely to develop CCA of the vagina and cervix than women not exposed to DES. This means that approximately one of every 1,000 women exposed to DES before birth (in the womb) might be expected to develop CCA of the vagina and/or the cervix.

Before the use of DES, CCA of the vagina and cervix only occurred in women past childbearing age. In contrast, DES Daughters have been diagnosed with CCA of the vagina and cervix at as early as age 8 and up to their late teens and early 20s. In addition, recent studies have indicated that some DES Daughters have been diagnosed with CCA of the vagina and cervix in their 30s and 40s (Hatch, 1998). **Therefore, DES Daughters should have regular cancer screenings as they grow older.**

Reproductive Tract Structural Differences

Some studies have shown that up to one third of DES Daughters were born with or developed some form of reproductive tract abnormality of the cervix, uterus, or fallopian tubes, including vaginal adenosis or cervical changes (such as collars, hoods, septae, and cockscombs) (Jeffries, 1984; Herbst, 1984). Many of these changes are harmless and had no effect on physical development, risk of disease, or ability to conceive a child. However, some DES Daughters experienced health problems as a result of reproductive tract abnormalities. DES Daughters should talk with their health care providers about the possibility of reproductive tract structural differences so they can work together to identify and treat any potential problems.

Pregnancy Complications and Infertility

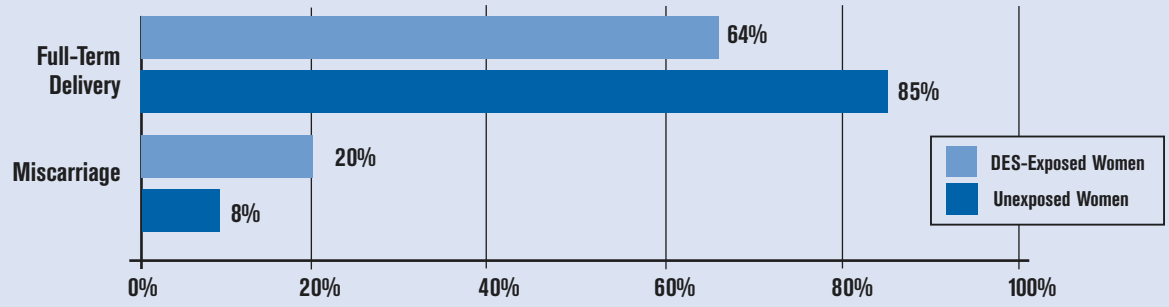
Most DES Daughters will be able to conceive and carry a healthy baby to term. However, DES Daughters are at an increased risk of reproductive problems, including complications during pregnancy and infertility.

- **Premature Delivery.** Consistently, research shows that DES Daughters are at an increased risk for problems during pregnancy. These problems are primarily associated with an increased risk for premature (early) delivery. Of DES Daughters, 64% deliver a full-term baby in their first pregnancy, compared with 85% of unexposed women. Approximately 20% of DES Daughters experience pre-term labor, compared with 8% of unexposed women (Kaufman, 2000).

Important Note on Fertility

If you are a DES Daughter, it is critical that you tell your health care provider when you begin planning your pregnancy. Many of the risk factors associated with DES exposure during pregnancy are preventable or treatable if you take action. Any pregnancy of a DES Daughter should be treated as "high risk" by health care providers.

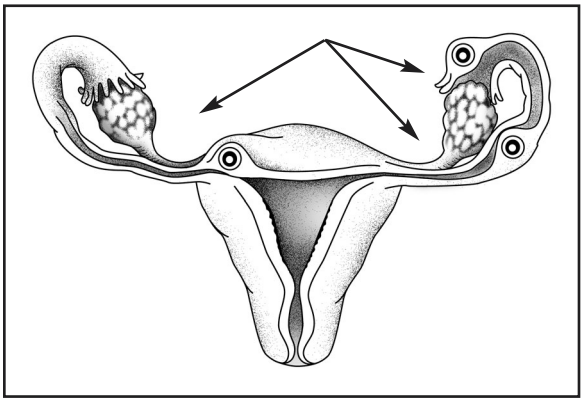
Comparison of Full-term Delivery and Miscarriage Rates for First Pregnancies of DES-Exposed Women vs. Unexposed Women*



* Kaufman, 2000

- **Other Pregnancy Complications.** DES Daughters are also at an increased risk for other complications during pregnancy, including ectopic (tubal) pregnancy, and miscarriage. Estimates of a DES Daughter's risk for an ectopic pregnancy range from 3–5 times higher than the risk for a woman not exposed to DES. DES Daughters are also more likely to experience miscarriage than are unexposed women. The most recent study found almost 20% of DES Daughters had a miscarriage during their first pregnancy. About 10% of unexposed women had a miscarriage during their first pregnancy. The risk of miscarriage during the second trimester is slightly higher than the risk of miscarriage during the first trimester. Overall, 82%–85% of DES Daughters were able to deliver at least one healthy baby, compared to 87% of unexposed women. DES Daughters were less likely than unexposed women to have more than one child (Kaufman, 2000).

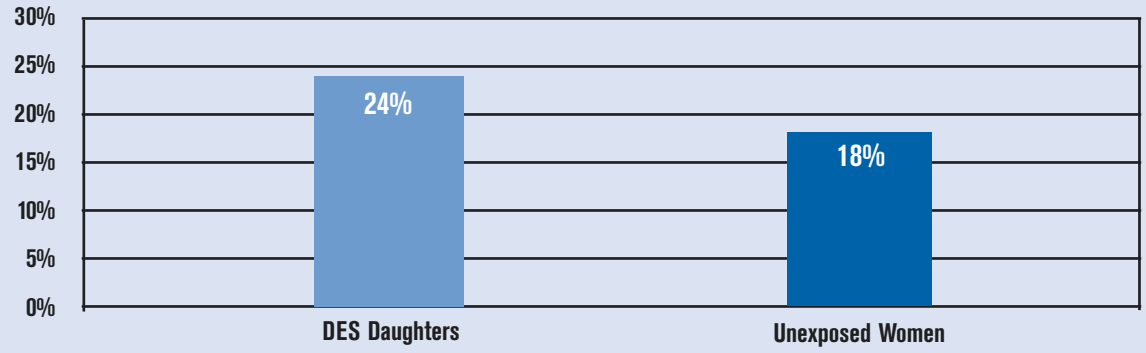
Three Possible Sites of an Ectopic Pregnancy in DES Daughters



The risk of an ectopic pregnancy is 3 to 5 times higher for a DES Daughter.

- **Infertility.** The most recent and comprehensive infertility study reported that 24% of DES Daughters were unable to become pregnant, compared with 18% of women not exposed to DES. Additionally, 28% of DES Daughters had tried for 12 months to become pregnant without success, compared with 16% of women not exposed to DES. DES exposure was most strongly associated with infertility caused by uterine problems (such as the shape of the uterus) (Palmer, 2001).

Infertility Rates for DES Daughters vs. Unexposed Women*



* Palmer, 2001

Specific Questions about Clear Cell Adenocarcinoma (CCA) of the Vagina and Cervix

I'm in my 40s. Am I still at risk for CCA of the vagina and cervix?

So far, most DES-related cases of CCA of the vagina and cervix have occurred in women in their late teens and early 20s. However, a small number of DES-related clear cell cancers have been diagnosed in women in their 30s and 40s (Hatch, 1998; Herbst, 2000). In the general population, CCA of the vagina and cervix is rare and when found, it occurs in women past childbearing age. Because DES Daughters now range in age from their early 30s to early 60s, many have not reached or are just approaching menopause. Currently, researchers do not know whether DES exposure will make CCA more common when DES Daughters are past menopause. **Therefore, DES Daughters should continue to receive regular cancer screening throughout their lifetimes.**

Are women who were prescribed DES while pregnant at an increased risk for CCA of the vagina and cervix?

No. The increased risk for CCA of the vagina and cervix only applies to DES Daughters and not to women prescribed DES while pregnant.

What should I expect from my health care provider in terms of detecting and monitoring CCA of the vagina and cervix?

CCA of the vagina and cervix is treatable when detected early. Therefore, the most important step that any woman can take is to continue to receive regular gynecological examinations throughout her lifetime. The National Cancer Institute (NCI) published a description of appropriate pelvic examinations for DES Daughters. In this publication, recommendations regarding pelvic examinations for DES Daughters were similar to those recommended for unexposed women. Special steps included

- Careful visual examination and palpation (feeling) of the vagina and cervix with rotation of the speculum so that all vaginal walls can be inspected;
- Pap smears from the cervix and the surfaces of the upper vagina; and
- Iodine staining of the vagina and cervix or a colposcopy if abnormalities are detected during the examination.

  Iodine staining allows your health care provider to distinguish healthy tissues from abnormal ones.

  A colposcopy uses a device that works like a magnifying glass, allowing your health care provider to carefully check the vagina and cervix. Your provider may take photographs using the colposcope so that any changes in your condition can be monitored during future examinations (Kaufman, 1995).

Questions about Reproduction and Infertility

How likely am I to have problems with fertility if I was exposed to DES?

Although most DES Daughters can successfully conceive and carry a baby to full term, they experience infertility more than unexposed women. The most recent study of infertility among DES Daughters reported that 24% had never become pregnant, compared with 18% of unexposed women. Of DES Daughters, 28% had tried without success to become pregnant over a period of 12 months, compared with 16% of unexposed women (Palmer, 2001).

Why does DES increase my risk for infertility?

Reasons for DES-related infertility vary. Recent research indicates that the primary reason for an increased risk of infertility among DES Daughters results from abnormalities in the uterus or fallopian tubes that are associated with exposure to DES before birth (in the womb) (Palmer, 2001).

What can I do as a DES Daughter to protect my health during pregnancy?

If you are planning a pregnancy, or if you are already pregnant, tell your health care provider about your DES exposure. Before you become pregnant, you may want to discuss your increased risks with your health care provider, including the risk of infertility, ectopic (tubal) pregnancy, miscarriage, and pre-term (early) delivery.

Once you become pregnant, your health care provider likely will classify you as having a "high-risk" pregnancy. This means you should be closely monitored for DES-related complications during your pregnancy. Again, most DES Daughters have no problems becoming pregnant or carrying a baby to full term. Although all women should have good prenatal care, it is particularly important for DES Daughters.

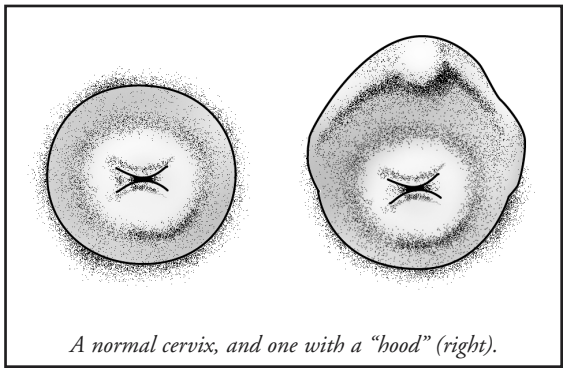
If I have structural differences in my reproductive tract, will that influence my ability to conceive and bear children?

Your risk of experiencing infertility or pregnancy complications depends on what reproductive tract structural difference you have. An "abnormal" structure is not necessarily a faulty one; it could just mean that an organ is shaped differently or has an additional feature that is not usually present (such as a "collar" on the cervix). By itself, an abnormality does not necessarily cause infertility or complicate a pregnancy. In one study, for example, researchers found that women with DES-related changes in the vagina or cervix achieved the same rate of pregnancy as women without those abnormalities (Cousins, 1980). However, other research has indicated that abnormalities in the uterus have been associated with an increased rate of ectopic (tubal) pregnancy and miscarriage (Kaufman, 1980, 1984).

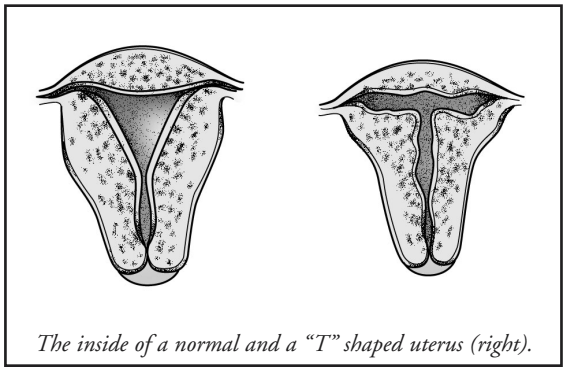
What are some examples of physical differences?

Most physical or structural differences associated with exposure to DES are found in the reproductive tract, including a "hood" or collar on the cervix, T-shaped uterus, and non-cancerous vaginal adenosis. Vaginal adenosis, one of the most common changes experienced by DES Daughters, occurs when the vagina has an unusual type of tissue on its surface. Adenosis is often associated with excess mucous in the vagina and can be mistaken for a vaginal infection. Vaginal adenosis, like many DES-related physical changes, is harmless and requires no special treatment. However, health care providers should monitor all DES-related abnormalities for changes over time (Kaufman, 1995).

Reproductive Tract Differences in DES Daughters



A normal cervix, and one with a "hood" (right).



The inside of a normal and a "T" shaped uterus (right).

What steps should my health care provider and I take in terms of special screenings or tests based on my DES exposure?

Any pregnant woman who is classified as being "high-risk" because of DES exposure or any other reason should work with her health care provider to establish a plan of action based on her increased health risks. Preconception counseling with your OB/GYN will help you learn about the risks of infertility and pregnancy complications including ectopic (tubal) pregnancy, miscarriage, premature labor, and premature birth. No single test, treatment, or screening is needed because of your exposure to DES, but your health care provider may recommend that you undergo certain tests or screenings appropriate for your risks. Some example procedures given to "high-risk" women during pregnancy and preconception examinations include

- a pelvic examination to check for any cervical changes such as collars, hoods, septae, and cockscombs; and
- if you have experienced infertility, a hysterosalpingogram, which is an X-ray that can check for structural differences and physical alterations in your upper genital tract.

My younger sisters/brothers are worried that they were exposed to DES, even though my mom was only prescribed DES when she was pregnant with me. What can I tell them?

Only children who were in the womb at the time their mother was prescribed DES are considered to have been exposed to DES.

To learn more about the increased health risks for DES Daughters, refer to the sections of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research and ADDITIONAL DES RESOURCES: DES Bibliography.

KNOWN DES HEALTH EFFECTS

Men Exposed To DES Before Birth (In The Womb), Known As DES Sons

This section addresses questions about increased health risks for DES Sons, including information on

- non-cancerous epididymal cysts (growths on the testicles);
- other genital abnormalities;
- infertility;
- ongoing follow-up studies;
- steps for obtaining screenings and tests; and
- what to tell your siblings about DES.

My mother was prescribed DES while pregnant with me. Am I at an increased risk for any health problems?

Only a few studies have focused on health problems experienced by men exposed to DES before birth (in the womb), known as DES Sons. The research has focused on the following health concerns among DES Sons.

- **Non-Cancerous Epididymal Cysts**
  The most consistent research finding for DES Sons indicates that they have an increased risk for non-cancerous epididymal cysts, which are growths on the testicles (Bibbo, 1977; Gill, 1979; Conley, 1983; Niculescu, 1985; Wilcox, 1995). In one study, 21% of DES Sons had non-cancerous epididymal cysts compared with 5% of unexposed men (Gill, 1979).

- **Other Genital Abnormalities**
  Whether DES increases the risk for other genital abnormalities in men remains unclear. A few studies have reported that DES Sons experience a greater likelihood of being born with undescended testicles (cryptorchidism), a misplaced opening of the penis (hypospadias), or a smaller than normal penis (microphallus). These studies estimated that 15%–32% of DES Sons experience one or more of these structural differences compared with 5%–8% of unexposed men (Gill, 1979; Wilcox, 1995). Other studies, however, have not identified an increased risk of structural differences (Leary, 1984; Vessey, 1983). Because findings have been inconsistent, researchers cannot say with certainty that DES causes these types of genital abnormalities in DES-exposed men.

- **Infertility**
  DES Sons are not at an increased risk for infertility. Some DES Sons have been concerned that DES exposure might be linked to infertility. Although one study found a lower sperm count in men exposed to DES compared with unexposed men (Gill, 1979), a 40-year follow-up study of DES Sons found no increased risk of infertility among men exposed to DES before birth (Wilcox, 1995).

Are there any ongoing follow-up studies of DES Sons?

The National Cancer Institute's DES Combined Cohort Study began in 1992. This study follows men and women exposed to DES before birth (in the womb), known as DES Sons and Daughters, to monitor their health patterns compared with the general population. These cohort studies will continue to follow DES Sons regarding a range of health issues (such as cancer, heart disease, and autoimmune disease).

Cohort studies are designed to follow the same group of people over long periods of time. This means that new participants cannot be added to the study. To learn more about cohort studies, refer to the section of CDC's DES Update titled WHAT WE KNOW ABOUT DES: Understanding DES Research.

What steps should I take with my health care provider in terms of special screenings or tests based on my DES exposure?

Although no special screenings or tests are necessary for DES Sons, for more information about how to work with your health care provider, refer to the section of CDC's DES Update titled WHAT YOU CAN DO ABOUT DES: Working with Your Health Care Provider.

My younger brothers/sisters are worried that they were exposed to DES, even though my mom was only prescribed DES when she was pregnant with me. What can I tell them?

Only children who were in the womb at the time their mother was prescribed DES are considered to have been exposed to DES.

To learn more about the increased health risks for DES Sons, refer to the sections of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research and ADDITIONAL DES RESOURCES: DES Bibliography.

UNDERSTANDING DES RESEARCH

Overview

Researchers have been studying DES and its health effects for many years. However, sometimes the data and results are difficult for non-researchers to understand. It may also be difficult for people to figure out how research can be applied to their own health.

This section of CDC's DES Update will help you understand and use research about DES and includes the following information:

- **Understanding Scientific Research –** Tips for interpreting and understanding scientific research.
- **Deciding Whether a Source is Reliable –** Criteria for assessing whether a source is providing accurate and reliable information.
- **Role of Laboratory Animal Studies –** A basis for learning about human health risks from laboratory animal studies.
- **Role of DES Cohort Studies –** An explanation for understanding how studies of the DES cohorts (groups of DES-exposed persons who are included in follow-up research on DES-related health effects) fit into the DES research picture.

UNDERSTANDING DES RESEARCH

Understanding Scientific Research

Several journal article citations are provided in CDC's DES Update fact sheets. How do I read a citation?

Knowing how to read a citation for a journal article will help you find it either at the library or on a Web site. The following is an example citation for a journal article about DES:

Hatch EE, Palmer JR, Titus-Ernstoff L, Noller KL, Kaufman RH, et al. Cancer risk in women exposed to diethylstilbestrol in utero. JAMA 1998;280(7):630-4.

The authors who wrote the article are listed first. If there are several authors, only the first few authors' names will be listed, followed by "et al." The complete title comes next. The name of the journal where the study was published follows. Oftentimes, the name of the journal will be an acronym. For example, in this case, JAMA stands for *Journal of the American Medical Association.* The year the study was published is next. A new issue of this journal is printed each week, so the citation includes the volume (280) and issue number (7). The citation also includes the page numbers (630-4) of the article.

If you have difficulty reading a citation or finding an article, ask a librarian for help.

Where can I find copies of scientific journal articles?

Community libraries often have copies of well-known scientific journals. Hospital or university libraries may have a wider range and older issues of these journals. Some journals also have articles available on their Web sites. Some Web sites offer the articles free of charge, but others may require you to register with the site and pay a nominal fee. You will need the citation for the article to find it either at the library or on a Web site. See the answer to the previous question for an example citation.

What does it mean if an article or journal is "peer reviewed?"

Scientific journals require research articles to go through a process called "peer review." During peer review, scientific experts who were not connected to the study review the article and decide whether it was done properly and whether the findings have merit. Only studies that pass peer review get published.

What does it mean when researchers say that results are "statistically significant?"

Because health problems occur for a variety of reasons, including chance, researchers must determine if a health effect they are studying may have occurred in study participants as a result of chance alone. Specifically, "statistical significance" refers to a finding in a research study that is larger or smaller than would be expected by chance alone.

Statistical significance is expressed in scientific journals by a probability value (p-value). P-values are calculated using a statistical formula that includes the number of people and health effects being studied and is designed to answer the question, "Could a group of this many people, who all experienced a common exposure, have had this health problem in common by chance alone?" A finding is considered statistically significant if there is less than a 5% probability (p=.05 or less) that the findings resulted from chance. Conversely, if there is greater than a 5% probability (p=.06 or greater) that a finding resulted from chance, the finding is not statistically significant.

How do I interpret statistics in research about DES-related health risks?

Understanding research about DES-related health risks without knowing how to interpret statistics can be difficult. The following table offers some examples of how scientific studies present risk information.

Different Ways that Studies Describe Risks	Statistical Phrase	Risks Presented as Ratios	Risks Presented as Decimals or Percentages	Type of Risk
In the general population, a woman's lifetime risk of developing breast cancer is about one in eight. That means that, over a lifetime, in a group of eight women, one of those women would be expected to be diagnosed with breast cancer.	One in eight	1:8	.13 or 13%	Absolute risk*
For women prescribed DES while pregnant, lifetime risk of developing breast cancer is one in six. That means that, over a lifetime, in a group of six women exposed to DES during pregnancy, one of those women would be expected to be diagnosed with breast cancer.	One in six	1:6	.16 or 16%	Absolute risk
For women prescribed DES while pregnant, the risk for breast cancer is approximately 30% higher than for women who were not exposed to DES during pregnancy.	Approximately 30%	From 1:8 to 1:6	.30 or 30%	Relative risk**

Source of risk information in this chart: Titus-Ernstoff L, et al. Long term cancer risk in women given diethylstilbestrol (DES) during pregnancy. Br J Cancer 2001;84:126-33.

* The absolute risk is a number that represents the probability that an individual with a special risk factor (such as exposure to DES) will experience a health effect (e.g., breast cancer).

** Relative risk is the comparison of disease rates (e.g., breast cancer) between persons with higher risks and those in the general population (who have no special exposure).

What is a "cohort" study?

A "cohort" is a group of people who share common characteristics or experiences. By compiling and summarizing data from a cohort, scientists can observe whether disease conditions develop at higher rates in a cohort group than they would expect in the general population.

In this case, a DES cohort is a group of people who were exposed to DES. Scientists have been following DES cohorts for several years, to evaluate their medical conditions and disease rates. Researchers are trying to determine whether DES-exposed women and men are at an increased risk for certain health problems compared with the general population. For instance, one cohort study revealed that one in six women prescribed DES while pregnant can be expected to develop breast cancer in her lifetime, compared with an expected rate of one in eight women in the general population (Titus-Ernstoff, 2001).

Deciding Whether a Source is Reliable

Many sources of information about DES are available. Knowing if the information can be trusted can be difficult. The following are some criteria to help you consider the reliability of a source.

Where was the research published?

Health care providers trust and use research published in credible, peer-reviewed scientific journals because experts have reviewed studies published in these journals to make sure they are of high quality. Some examples of credible, peer-reviewed journals are *JAMA*, the *Journal of the National Cancer Institute*, the *New England Journal of Medicine*, and *Science*. If you have any questions about whether a journal is peer-reviewed, ask a librarian or your health care provider.

How does the new information fit with what is already known?

Each research study contributes to an existing body of knowledge. Usually, more weight can be given to study findings that support and build on the findings of other research. If the findings of one study contradict the findings of previous studies, months or several years may pass before more information becomes available to support the contradictory study. In other words, one study alone is never enough to make a case – it simply gives direction about what new research is needed.

How does funding influence research?

Objectivity, the ability to report study results without personal bias, is an important consideration. The source of funding for a research project may bias the reporting of results. The funding source is usually included in the journal article. When reading an article from a funded research project, you must consider whether the funders of this research had anything to gain by the results. When research is paid for by a source that does not have an interest in the results, funders' expectations or preferences were less likely to have influenced the results.

Can I trust information from television, magazines, or brochures?

Many health reports in the media are based on articles published in peer-reviewed journals; however, some reports are not. When you see a report on television, in a magazine, or in a brochure, you must consider where this information came from, who provided the information, whether the source is credible, who did the study, and whether it is consistent with other research. If you are unsure, ask your health care provider.

Also remember that news stories focus on what is "new." So when a new study is published in a scientific journal, reporters may highlight the results in their stories as being conclusive. However, a single study is never enough to make a case; new research requires other studies to support the results before a study's findings are considered applicable to medical practice.

I get a lot of my information on the Internet. Is that okay?

More and more, health-related Web sites and newsletters are available to people with Internet access. Use the preceding guidelines to think about the credibility, expertise, bias, and funding of the source of information. The most credible Internet sites come from recognized experts, like health agencies and reputable health and medical organizations. If you are unsure, ask your health care provider for credible Web sites. CDC's DES Update has a Web site for health care providers and the public (www.cdc.gov/DES).

For a list of credible health information sources refer to the section of CDC's DES Update titled ADDITIONAL DES RESOURCES: Partner and Government Organizations.

I've heard lots of stories about DES exposure that aren't in the research. Why is that?

Personal stories, sometimes called "anecdotal evidence," refer to individual experiences. They may or may not be consistent with scientific research. An important element of studying large populations (like the DES cohort studies) is that individual experience is included in the reported data. Even though you may have heard details from persons that are not consistent with findings from scientific research, those experiences have been averaged into the population data. Scientific evidence from large studies (like the DES cohort studies) is reliable, because the studies are rigorous and better reflect the experiences of the population that is being studied.

Role of Laboratory Animal Studies

DES can no longer be prescribed to pregnant women, even for use in clinical studies. To project future health risks of DES exposure, scientists are conducting animal studies with laboratory mice. Scientists administer DES to pregnant female mice and then study the results. Because mice age more quickly than humans, these studies can be used to explore future health risks. Using laboratory animal models allows scientists to pursue hypotheses that are not possible to research in humans. Results from these animal studies can also guide them on the types of diseases and health effects to look for in humans. Although laboratory animal studies can often predict human health effects, because of differences between humans and mice, the results of laboratory animal studies are not always transferable to humans. In addition, studies of humans rely on tracking the outcomes of DES cohorts (women and men already exposed to DES).

Role of DES Cohort Studies

The National Cancer Institute's (NCI) DES Combined Cohort Follow-up Study was formed in 1992. NCI researchers brought together a large group of mothers and their children who had been exposed to DES, as well as a group of similar (in age, medical history, etc.), but unexposed persons. NCI recruited for this study primarily from previously studied groups and their family members. These cohort groups were followed over a long period of time. For this reason, new people cannot be added to the study.

Following is a list and brief description of the DES Cohort Studies.

- **Diethylstilbestrol Adenosis Project (DESAD) –** The DESAD began in 1974 at Baylor College of Medicine, Gundersen Clinic, Massachusetts General Hospital, the Mayo Clinic, and the University of Southern California. The DESAD, the largest DES cohort, included 4,014 DES Daughters and 1,033 unexposed women. Exposed women had documented evidence of DES exposure through review of prenatal records or by physician referral. The DESAD was assembled to conduct studies to determine if DES Daughters were at an increased risk for health problems related associated with their exposure to DES (Labarthe, 1978).

- **DES Mothers Study –** The DES Mothers Study began in 1980. The participant group (cohort) included approximately 3,000 women exposed to DES while pregnant and 3,000 unexposed women. These participants had delivered babies during 1940–1960 at Boston Lying-In Hospital, the Mayo Clinic, Dartmouth Medical School, and a private practice in Portland, Maine. Exposure status was determined through review of medical records. The cohort was created to determine if women exposed to DES during pregnancy were at increased risk for cancer (Greenberg, 1984).

- **Mayo Clinic Sons Study –** The Sons Study included approximately 800 men exposed to DES before birth (in the womb) and 600 unexposed men. This cohort was identified by review of medical records of women who gave birth at Mayo Clinic hospitals (Leary, 1984).

- **Connecticut Mothers Study –** The participants included women who delivered babies during 1946–1965 at medical offices in Fairfield and New Haven Counties, Connecticut. The participants included 1,706 DES-exposed mothers and 1,405 unexposed mothers. The participants are now included in the DES Combined Cohort Studies (Hadjimichael, 1984).

- **Dieckmann Cohort –** Participants in the group, assembled in 1974 to study DES-related health risks, included approximately 800 women exposed to DES while pregnant and 800 unexposed mothers; approximately 400 women exposed to DES before birth (in the womb) and 400 women in a control group; and approximately 400 men exposed to DES before birth and 400 unexposed men. The 1974 group comprised the second Dieckmann cohort; the first included mothers who were participants in a study at the University of Chicago in the early 1950s. Results based on the initial study indicated that DES was not effective in preventing miscarriages (Dieckmann, 1953).

- **British Research Medical Council (BRMC) Study –** Participants included pregnant diabetic women enrolled in clinical trial and DES Daughters and DES Sons identified through follow-up study, for a total of 151 participants (79 DES-exposed and 72 unexposed people) (Reid, 1955).

- **British Randomized Trial –** A group assembled to study DES-related health effects. Participants included women exposed to DES during pregnancy and men and women exposed before birth (in the womb). The DES-exposed group included 379 mothers, 144 daughters, and 177 sons. A control group of unexposed included 371 mothers, 170 daughters, and 163 sons (Guisti, 1995).

- **Registry for Research on Hormonal Transplacental Carcinogenesis –** The Registry was established at Massachusetts General Hospital in 1971 to track the incidence of clear cell adenocarcinoma (CCA) of the vagina or cervix. The registry originally numbered 21 cases; however, by 2002, approximately 750 cases had been recorded at the registry. Most of the information on treatment outcome and recurrence rates of CCA has come from the study of patients in the registry. The registry is now located at the University of Chicago (Department of Obstetrics and Gynecology, The University of Chicago, 5841 South Maryland Avenue, Mail Code 2050, Chicago, IL, 60637. Phone: 773-702-6671. Fax: 773-702-5161) (Herbst, 1972).

What kinds of research are still going on?

Researchers continue to monitor the health status of 15,000 members of the combined cohort study. Many of the health problems being monitored are health problems that may be influenced by exposure to DES before birth (in the womb). These health problems include breast cancer in women, testicular cancer in men, and the potential interaction of hormone replacement therapy with DES exposure.

Researchers also are monitoring rates of health problems that appear to have no relationship to DES exposure (such as heart disease and diabetes). Scientists have no hypothetical or other reason to believe there is any link between DES and these diseases. These studies are being done to evaluate the overall health of DES-exposed persons.

Why don't we have final answers about DES health risks?

The health risks associated with DES exposure change over a person's lifetime. Consequently, research is ongoing to learn how health risks change as DES-exposed persons age.

For instance, DES Daughters who are still in their 30s may not have yet faced their risk for infertility, ectopic pregnancy, or other pregnancy complications. Older DES Daughters and their mothers could be just reaching the stage of life where they must make an informed decision about estrogen replacement therapy. Age of DES-exposed persons is particularly relevant when thinking about DES exposure and cancer risk. Most cancer diagnoses do not begin to emerge until people are well into their fifth decade of life. Men and women who were exposed to DES before birth (in the womb) are just beginning to reach that age. Only continued research will show whether people who were exposed to DES before birth are at an increased risk for breast cancer, prostate cancer, and other diseases.

TAB 2: WHAT WE ARE LEARNING ABOUT DES

Overview

Between the time that diethylstilbestrol (DES) was first manufactured in 1938 and the discovery of related health problems in 1971, approximately 5–10 million pregnant women and their children were exposed to the drug. In 1971, the Food and Drug Administration (FDA) issued a warning to physicians advising them not to prescribe DES to pregnant women. The warning was based on a discovery the same year that exposure to DES before birth (in the womb) increased the risk of clear cell adenocarcinoma (CCA) of the vagina (Herbst, 1971) and cervix (Noller, 1972). Since the time that DES was linked to CCA, researchers have been monitoring the health problems of women prescribed DES during pregnancy and their children exposed to DES before birth (in the womb). For more information on the confirmed health risks, refer to the section of CDC's DES Update titled WHAT WE KNOW ABOUT DES: Known DES Health Effects.

Researchers are currently working to learn more about DES. It is possible that they will learn about new health risks as individuals who were exposed to DES grow older. Health risks that are currently being investigated and related concerns that may not be confirmed by research are discussed in this section. Staying informed about DES is important, giving you the knowledge to ask your health care provider appropriate questions to protect your health and the health of your family.

This section of CDC's DES Update includes the following information.

- **Recent DES Research –** A review of current DES research.
- **Related Concerns –** A discussion of potential, but unconfirmed, health risks and other related health issues.
- **DES Teleconferences –** A series of conversations with DES researchers and clinical experts.

To learn more about how DES research is conducted, refer to the section of CDC's DES Update titled WHAT WE KNOW ABOUT DES: Understanding DES Research.

RECENT DES RESEARCH

Overview

This section of CDC's DES Update contains brief summaries of recently published research regarding the health of women and men who were exposed to DES. Each summary includes highlights from the study and a citation so you can look up the journal article if you want more information. Reading the entire article may give you a better understanding of the study. For help interpreting or understanding research results, refer to the section of CDC's DES Update titled WHAT WE KNOW ABOUT DES: Understanding DES Research.

Although many DES studies have been published since 1971, only the most recent are summarized in this section. Following are the titles of the DES research summaries in this section.

- Cancer Risk in Women Exposed to Diethylstilbestrol In Utero
- Continued Follow-Up of Pregnancy Outcomes in DES-Exposed Offspring
- Cancer Risk in Men Exposed In Utero to Diethylstilbestrol
- Long-term Cancer Risk in Women Given Diethylstilbestrol During Pregnancy
- Infertility Among Women Exposed Prenatally to Diethylstilbestrol
- Incidence of Squamous Neoplasia of the Cervix and Vagina in Women Exposed Prenatally to Diethylstilbestrol (United States)
- Findings in Female Offspring of Women Exposed In Utero to Diethylstilbestrol
- Hypospadias in Sons of Women Exposed to Diethylstilbestrol In Utero: A Cohort Study
- Risk of Breast Cancer in Women Exposed to Diethylstilbestrol In Utero: Preliminary Results (United States)

The research summarized in this section can be considered trustworthy and was selected because

- each study had data from a substantial number of persons whose DES exposure was confirmed;
- the study was published in a journal that uses the peer-review process; and
- the researchers were considered objective and highly qualified to conduct the research.

As you read these research summaries, remember that researchers work with groups and averages. Situations exist in which a person's health does not fit the average experience represented in the research.

RECENT DES RESEARCH

Cancer Risk in Women Exposed to Diethylstilbestrol In Utero (Hatch et al., 1998)

In this study, the researchers wanted to learn whether women exposed to DES before birth (in the womb), known as DES Daughters, were more likely to develop cancer than unexposed women. Cancer rates of DES Daughters were also compared with cancer rates among women in the general population whose DES exposure status was unknown. At the time of this study, researchers accepted that DES exposure before birth increased a woman's risk of developing clear cell adenocarcinoma (CCA) of the vagina and cervix. However, researchers were not certain whether the risk for other types of cancer also increased.

Over a 16-year period, the researchers compared the medical histories of 3,650 DES Daughters with those of 1,202 unexposed women. The researchers then compared cancer rates from the two study groups to cancer rates for women in the general population whose DES exposure status was not known.

The researchers found that for DES Daughters, the rate for all types of cancer (other than CCA) was similar to the rates for unexposed women and women in the general population. In addition, DES Daughters were 40 times more likely than women in the general population to develop CCA.

Although this study was one of the largest of its kind, the study had some limitations. For example, the average age of DES Daughters who participated was 24 at the start of the study and 38 at last follow-up. The researchers suggested continued study of these DES Daughters for any increased cancer risks during menopausal years.

Another limitation of this study concerned breast cancer. Many studies have demonstrated that women exposed to estrogen in high doses or over a long period of time have an increased risk for breast cancer. However, breast cancer is most likely to occur in older women. Thus, the women in this study will have to be monitored over the next several decades to determine whether DES Daughters develop breast cancer at higher rates than do unexposed women.

Citation: Hatch EE, Palmer JR, Titus-Ernstoff L, Noller KL, Kaufman RH, et al. Cancer risk in women exposed to diethylstilbestrol in utero. JAMA 1998;280:630-4.

RECENT DES RESEARCH

Continued Follow-Up of Pregnancy Outcomes in Diethylstilbestrol-Exposed Offspring (Kaufman et al., 2000)

Health care providers and researchers who work with pregnant women have known for years that women exposed to DES before birth (in the womb), known as DES Daughters, often have difficulty conceiving and carrying a pregnancy to full term. Although the reasons for increased pregnancy complications among DES Daughters are not fully understood, the researchers of this study hypothesized that structural abnormalities in the cervix may account for increased miscarriages. The researchers compared the pregnancy histories of 3,373 DES Daughters with those of 1,036 unexposed women; these women comprised the largest study of pregnancy among DES Daughters to date.

The researchers found that DES Daughters had more negative outcomes during first pregnancies than unexposed women. Of DES Daughters, 64% delivered a full-term baby during their first pregnancy compared with 85% of unexposed women. Approximately 20% of DES Daughters experienced a miscarriage compared with 10% of unexposed women. Ectopic (tubal) pregnancy occurred in 4%–7% of DES Daughters, but less than 1% of unexposed women experienced this problem.

When considering all pregnancies, DES Daughters suffered more reproductive complications than unexposed women. Approximately 84% of DES Daughters had delivered at least one live birth compared with 87% of unexposed women. Approximately 30% of DES Daughters experienced a miscarriage compared with 24% of unexposed women. Of DES Daughters, 7%–11% had ectopic pregnancies, whereas only 1.9% of unexposed women had such a pregnancy. Premature births and miscarriages during the second trimester of pregnancy were also more common among DES Daughters than among unexposed women. Approximately 25% of DES Daughters had never been pregnant compared with approximately 19% of unexposed women.

Although many DES Daughters are now beyond their childbearing years, many younger DES Daughters still plan to have children. DES Daughters and their health care providers should be aware that these women are at an increased risk for a range of pregnancy complications. Extensive prenatal care may be needed for a pregnant woman exposed to DES or a woman trying to become pregnant who knows she was exposed to DES.

Citation: Kaufman RH, Adam E, Hatch EE, Noller KL, Herbst AL, et al. Continued follow-up of pregnancy outcomes in diethylstilbestrol-exposed offspring. Obstet Gynecol 2000;96:483-9.

RECENT DES RESEARCH

Cancer Risk in Men Exposed In Utero to Diethylstilbestrol (Strohsnitter et al., 2001)

Since the discovery of an increased cancer risk among DES Daughters in 1971, some researchers have investigated whether men exposed to DES before birth (in the womb), known as DES Sons, also have an increased risk of cancer. Researchers hypothesized that DES exposure could increase the risk for testicular cancer because prenatal exposure to abnormal levels of other types of estrogen have been associated with this cancer. Previous studies of the relationship between exposure to DES before birth and an increased risk of testicular cancer were inconclusive. Some studies showed an increased rate of testicular cancer for DES Sons compared with unexposed men, and other studies indicated no differences.

The authors of this study conducted a follow-up study comparing the cancer rates of DES Sons with the cancer rates of unexposed men. A total of 2,759 men participated in the study, including 1,365 DES-exposed men and 1,394 unexposed men. The study included a review of death certificates for 48 men who died during 1978–1994 from any type of cancer. Researchers also reviewed the men's medical histories for 1978–1994, including any cancer risk factors (such as smoking or a previous history of cancer). The researchers compared the number of cancer cases in the DES-exposed men with the number of cancer cases in unexposed men. These rates also were compared with cancer rates for men in the general population (whose DES exposure status was not known).

The researchers found that the overall rate of cancer in DES Sons was not higher than the rate of cancer in the general population. However, the researchers did find that slightly more cases of testicular cancer occurred in DES-exposed men than in unexposed men, or than would be expected in the general population. Seven DES Sons were diagnosed with testicular cancer at ages 23–41, compared with two unexposed men ages 28 and 40.

Even with the higher rates of testicular cancer among DES Sons, the study did not prove an association between exposure to DES before birth and testicular cancer. The number of DES Sons diagnosed with testicular cancer was not large enough to prove an association. In other words, the higher rate of testicular cancer among DES Sons could have resulted from chance rather than exposure to DES. In addition, researchers did not know the amount of DES taken by mothers of the DES Sons in the study, or the timing of DES prescriptions during pregnancy. Dosage and timing could result in different cancer risks.

Citation: Strohsnitter WC, Noller KL, Hoover RN, Robboy SJ, Palmer JR, et al. Cancer risk in men exposed in utero to diethylstilbestrol. Journal of the Natl Cancer Inst 2001;93:545-51.

RECENT DES RESEARCH

Long-Term Cancer Risk in Women Given Diethylstilbestrol (DES) During Pregnancy (Titus-Ernstoff et al., 2001)

Since the late 1970s, research has assessed the health risks for women prescribed DES while pregnant. Several studies conducted in the 1970s and 1980s demonstrated a modestly increased risk for breast cancer among DES-exposed women. However, not all findings were statistically significant, meaning that the higher rate of breast cancer among DES-exposed women could have resulted from chance rather than DES exposure. Other studies suggested that higher risks of endometrial (uterine) and ovarian cancer occurred in women prescribed DES while pregnant. Researchers were concerned about DES exposure and the increased risk for all three types of cancer because cancer of the breast, uterus, and cervix are all affected by exposure to hormones.

The researchers designed this study as a follow-up to evaluate long-term cancer risks, especially breast cancer, for women prescribed DES while pregnant. The medical records of women who participated in other research on DES exposure during pregnancy were studied. Information was gathered from 2,019 women prescribed DES while pregnant and 1,978 women who were not prescribed DES while pregnant. In addition, researchers studied the medical records of women from earlier studies who had died and determined how many of those deaths were the result of cancer. Using both sets of medical records, researchers were able to examine the medical records of 3,844 DES-exposed women and 3,716 unexposed women. With this information, the researchers compared the cancer rates of DES-exposed women to the cancer rates of unexposed women; they also compared the rates of cancer for these women in the study to the rates of cancer in the general population of women whose DES exposure status was not known.

The researchers found that women prescribed DES while pregnant had a 20%–30% higher risk of developing breast cancer than unexposed women and women in the general population. The researchers found no increased risk for any other cancers, including endometrial or ovarian cancer.

The findings of this study indicated that approximately 16% of women who were prescribed DES while pregnant developed breast cancer. In comparison, approximately 13% of women who were not prescribed DES while pregnant developed breast cancer. In other words, one in six women exposed to DES while pregnant are likely to develop breast cancer, compared with one in eight women not exposed to DES while pregnant. The increased risk of breast cancer did not appear to be interactive with other risk factors (such as use of hormone replacement therapy (HRT), use of birth control bills, or family history of breast cancer). That means that DES exposure, in addition to HRT or family history, did not increase the risk of breast cancer higher than that caused by DES exposure alone.

Citation: Titus-Ernstoff L, Hatch EE, Hoover RN, Palmer JR, Greenberg ER, et al. Long-term cancer risk in women given diethylstilbestrol (DES) during pregnancy. Br J Cancer 2001;84:125-33.

RECENT DES RESEARCH

Infertility Among Women Exposed Prenatally to Diethylstilbestrol (Palmer et al., 2001)

For several decades, researchers have tried to determine whether exposure to DES before birth (in the womb) affects a woman's ability to become pregnant. Two earlier studies provided conflicting results that may have occurred because the women were in their early childbearing years when the studies were conducted and because their fertility histories were incomplete. In this study, the average age was 42; so these women had had many more reproductive years than women included in the two earlier studies.

This study compared the reproductive history of 1,753 DES Daughters with the reproductive history of 1,050 women not exposed to DES. The researchers found that compared with unexposed women, a greater number of DES Daughters had never become pregnant. Similarly, a greater number of DES Daughters, compared with unexposed women, tried for a year or more to become pregnant without success. In addition, researchers found that the timing of DES exposure in the womb (the trimester(s) during which exposure to DES took place) had some effect on infertility rates.

Specifically, 24% of DES Daughters had never become pregnant compared with 18% of unexposed women. Most DES Daughters who never became pregnant had been exposed to DES during the first 9 weeks in the womb. This finding supports earlier research, which found that structural abnormalities that affect fertility (such as endometriosis, abnormalities of the fallopian tubes, and inadequate production of cervical mucus) were more common among women whose DES exposure occurred during their mothers' first trimester of pregnancy.

Despite problems with becoming pregnant, 76% of DES Daughters eventually became pregnant compared with 82% of unexposed women.

Citation: Palmer JR, Hatch EE, Rao RS, Kaufman RH, Herbst AL, et al. Infertility among women exposed prenatally to diethylstilbestrol. Am J Epidemiol 2001;154:316-21.

RECENT DES RESEARCH

Incidence of Squamous Neoplasia of the Cervix and Vagina in Women Exposed Prenatally to Diethylstilbestrol [United States] (Hatch et al., 2001)

Women exposed to DES before birth (in the womb), known as DES Daughters, are at increased risk for clear cell adenocarcinoma (CCA) of the vagina and cervix, but the effect of in-utero DES exposure on later development of squamous neoplasia in the cervix and vagina is uncertain. This combined follow-up study of 3,899 DES Daughters (median age 38) and 1,374 unexposed daughters (median age 39) was followed 1982–1995. Subjects were drawn from three previously studied cohorts (DESAD, Dieckmann, and Horne). The purpose was to examine the long-term risk of developing high-grade squamous intraepithelial neoplasia (HSIL) of the genital tract in DES Daughters compared with unexposed daughters.

The study found a small but significant increase in HSIL among DES Daughters in all age groups, including those over age 40. A total of 111 pathology-confirmed HSIL cases occurred, including five of the vagina, one of the vulva and two cases of invasive cervical cancer. The overall relative risk was 2.1 among DES-exposed versus unexposed. The relative risk among those whose mothers were prescribed DES within 7 weeks of the last menstrual period was 2.8 compared with 1.35 among women exposed for the first time at 15 weeks or later. Women with documented high-grade neoplasia before 1982 were excluded because prior treatment of the cervix may lower the subsequent finding of intraepithelial neoplasia. Researchers could not rule out that more frequent and intensive screening among DES-exposed women played a role in these findings.

Neoplasia is abnormal and uncontrolled cell growth; a neoplasm is new growth of benign or malignant tissue. Squamous cells are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the passages of the respiratory and digestive tracts. These flat cells look like fish scales under a microscope. Squamous intraepithelial lesion (SIL) is a general term for the abnormal growth of squamous cells on the surface of the cervix. The changes in the cells are described as low grade or high grade, depending on how much of the cervix is affected and how abnormal the cells appear. Cervical intraepithelial neoplasia (CIN) is a general term for the growth of abnormal cells on the surface of the cervix. Numbers from 1 to 3 may be used to describe how much of the cervix contains abnormal cells. High-grade squamous intraepithelial lesion (HSIL) is a precancerous condition in which the cells of the uterine cervix are moderately or severely abnormal. In this study, grades 2 and 3 were considered high. (Adapted from National Cancer Institute Dictionary, available at URL: http://cancer.gov/dictionary/.)

Citation: Hatch EE, Herbst AL, Hoover RN, Noller KL, Adam E, Kaufman RH, et al. Incidence of squamous neoplasia of the cervix and vagina in women exposed prenatally to diethylstilbestrol [United States]. Cancer Causes Control 2001;12:837–45.

RECENT DES RESEARCH

Findings in Female Offspring of Women Exposed In Utero to Diethylstilbestrol (Kaufman et al., 2002)

Although previous laboratory animal studies found cancer of the uterus and cervix in female offspring of DES Daughters, thus far, few studies have focused on health problems in third-generation humans (the offspring of DES Daughters and Sons). This article is a preliminary report from an ongoing study of third-generation DES health effects.

The researchers recruited DES Daughters who participated in the National Collaborative Diethylstilbestrol Adenosis (DESAD) cohort study. Twenty-six DES Daughters agreed to participate with their daughters. Each of the 28 third-generation daughters filled out a questionnaire and had a gynecological examination, during which the pelvis, abdomen, breasts, and cervix were inspected, a colposcopy of the cervix and vagina was performed, a cervical-vaginal smear was obtained from the upper vagina and the cervix, and an iodine staining of the vagina and cervix was performed. The results of this examination were compared with the same type of examination performed on their mothers (DES Daughters) during the earlier DESAD study.

In the previous DESAD study, researchers found that 16 of the 26 DES Daughters had cervical or vaginal changes. In the current study of third-generation daughters, no abnormalities of the lower genital tract were detected. However, the researchers cautioned that the sample size of 26 DES Daughters and 28 third-generation daughters was too small to detect an increased risk of genital tract abnormalities.

A second limitation of this study was the age of the participants. A mean age for the third-generation daughters of 20.1 years (age range: 15–28 years) may have been too young to detect clear cell adenocarcinoma (CCA) of the vagina and cervix, which is more often found in older unexposed women. A third limitation of this study was the possibility that results were biased by the self-selection of participants. Only 26 of 70 eligible DES Daughters and 28 of their third-generation daughters participated in this study. These women may not be representative of all eligible participants. However, most women who did not participate declined because they were unavailable or had been told by a gynecologist that they did not have abnormalities.

Citation: Kaufman RH, Adam E. Findings in female offspring of women exposed in utero to diethylstilbestrol. Obstet Gynecol 2002;99:197-200.

RECENT DES RESEARCH

Hypospadias in Sons of Women Exposed to Diethylstilbestrol In Utero: A Cohort Study (Klip et al., 2002)

Although laboratory animal studies have reported third-generation (offspring of DES Daughters and Sons) health effects of DES exposure, little is known about human health effects in the children of the women exposed to DES before birth. The goal of this study was to examine the risk of hypospadias (abnormality of the penis) in the sons of women exposed to DES before birth.

This Dutch cohort study consisted of a questionnaire of 16,284 women with diagnosed fertility problems. The researchers compared the prevalence of the rate of hypospadias between the sons of mothers who had been exposed to DES before birth with sons whose mothers had not been exposed to DES. The mothers of 205 sons reported DES exposure, and four of these sons had confirmed hypospadias; eight sons of the remaining 8,729 sons in the study had hypospadias. Risk of hypospadias was not affected by maternal age, fertility treatment, or use of assisted reproductive techniques.

Results suggested that although absolute risk was small, the third-generation health effects of DES exposure warrant additional studies.

Citation: Klip H, Verloop J, van Gool JD, Koster META, Burger CW, van Leeuwen FE. Hypospadias in sons of women exposed to diethylstilbestrol in utero: a cohort study. Lancet 2002; 359:1102-7.

RECENT DES RESEARCH

Risk of Breast Cancer in Women Exposed to Diethylstilbestrol In Utero: Preliminary Results (United States). (Palmer et al., 2002)

In this prospective follow-up study, researchers wanted to learn whether women exposed to DES before birth (in the womb), known as DES Daughters, were more likely to develop breast cancer than unexposed women. Information on reproductive factors, behavioral risk factors and health problems, including breast cancer, was gathered in 1994 from 4,821 DES Daughters and 2,095 unexposed women. Three years later, 3,916 DES Daughters and 1,746 unexposed women completed a short follow-up questionnaire that asked about new occurrences of disease. The researchers confirmed results of the surveys by checking medical reports or death certificates. The data revealed that 43 cases of breast cancer occurred among DES Daughters and 15 cases occurred among the unexposed.

Findings of the study are not definitive, but suggest that exposure to DES before birth (in the womb) may be associated with an increased risk of breast cancer. The risk of breast cancer for DES Daughters as a whole group is slightly higher than estimated in earlier studies (Hatch, 1998), but is not a statistically significant increase (that means the higher incidence of breast cancer could be the result of chance, rather than being associated with exposure to DES).

The study findings were different, depending upon the age of the study participants.

DES Daughters under age 40 did not have a higher risk of breast cancer than unexposed women under 40. However, DES Daughters who were over 40 years old who participated in the study were 2½ times more likely to experience breast cancer than were unexposed women over age 40. The increased risk was statistically significant (not due to chance, but increased risk was more likely to be related to association with DES exposure).

It is important to note that the findings from this study are viewed as preliminary due to some limitations of the research. Although participants had been followed for an average of 19 years, the median age of the study group in 1997 was 43 years, an age when breast cancer incidence is still relatively low in the general population. Continued investigation as the group of DES Daughters grow older is necessary to have enough data to determine if DES exposure is indeed linked to an increased risk of breast cancer among women exposed before birth (in the womb).

In addition, while the DES Daughters and unexposed women in the study were similar in most respects, they differed in some important areas. DES Daughters in the study were more likely to be older when they gave birth to their first child or to have had fewer or no children than were unexposed women. Both these characteristics have been associated with increased incidence of breast cancer and raise questions about whether DES exposure or other characteristics might be responsible for increased risks.

Citation: Palmer JR, Hatch EE, Rosenberg CL, Hartge P, Kaufman RH, Titus-Ernstoff L, et al. Risk of breast cancer in women exposed to diethylstilbestrol in utero: preliminary results (United States). Cancer Causes Control 2002;13:753-8.

RELATED CONCERNS

Overview

Although scientists have answered many questions about health risks associated with exposure to DES, other questions remain unanswered. This section addresses unresolved issues that have been raised about other health problems or decisions that might be related to DES exposure.

Women prescribed DES while pregnant, DES Daughters, and DES Sons wonder if DES exposure is related to health risks that have not been confirmed by science. The following are common concerns.

- **Cancer:** Are DES Daughters at an increased risk for any cancers besides clear cell adenocarcinoma (CCA) of the vagina or cervix? Are DES Sons at risk for any type of cancer?
- **Health problems other than cancer:** Does exposure to DES increase risks for any other health problems (such as autoimmune diseases, osteoporosis, psychological problems, and sexual dysfunction)?
- **Hormone replacement therapy (HRT):** Women considering estrogen or hormone replacement therapy (HRT) may wonder if their DES exposure should affect their decision about HRT decisions.
- **Who is DES Exposed?:** Women prescribed DES for a pregnancy wonder whether the children of their other pregnancies were affected. DES Daughters and Sons wonder whether their siblings are considered DES exposed. Should the children of DES Daughters and Sons be considered DES exposed? Are there health risks for the third generation?

Remember that none of the questions addressed in this section have definitive answers. Generally, you can protect your health by staying informed and talking with a health care provider about your concerns.

RELATED CONCERNS

Potential Health Risks: Women Prescribed DES While Pregnant

If I was prescribed DES while pregnant, should I consider hormone replacement therapy (HRT)?

The decision to take HRT is personal and should be made in consultation with your health care provider. Some women prescribed DES while pregnant are concerned about whether they should take hormone replacement therapy (HRT) because they are worried about exposure to additional estrogen. Although both taking DES while pregnant and HRT have been independently associated with an increased risk of breast cancer, research has not found an interactive effect of DES exposure and HRT (Titus-Ernstoff, 2001). The lack of an interactive effect means that the combination of exposure to DES and HRT does not increase the risk of breast cancer beyond the risk associated with either DES exposure or HRT alone. Also, the risk of breast cancer for a woman with a close relative with breast cancer (Pharaoh, 1997) is greater than the modestly increased risk of breast cancer from exposure to DES while pregnant or exposure to five or more years of HRT (Collaborative Group on Hormonal Factors in Breast Cancer, 1996).

For more information on hormone replacement therapy (HRT), refer to the following sources.

- CDC Information About Hormone Replacement Therapy Web site (www.cdc.gov/nccdphp/hrt.htm) or CDC's toll-free number (1-888-8 PUEBLO [1-888-878-3256]).
- The section of CDC's DES Update titled ADDITIONAL DES RESOURCES: DES Bibliography.

During my first pregnancy, my physician prescribed DES, but did not when I was pregnant with my other children. Were my other children exposed to DES?

Only children who were in the womb at the time their mother was prescribed DES are considered to have been exposed to DES.

RELATED CONCERNS

Potential Health Risks: Women Exposed To DES Before Birth (In The Womb), Known As DES Daughters

Are DES Daughters at an increased risk for cancer or other health problems?

Ongoing research has confirmed health risks for DES Daughters including increased incidence of clear cell adenocarcinoma (CCA), structural abnormalities in the reproductive organs, infertility, and pregnancy complications. (To read more about confirmed health risks, refer to the section of CDC's DES Update titled KNOWN DES HEALTH EFFECTS: Women Exposed to DES Before Birth (In the Womb), Known as DES Daughters.) However, recent research findings raise additional concerns about health problems associated with DES exposure for women exposed before birth. Although research has not provided definitive answers for these questions, DES Daughters and their health care providers should be aware of these emerging issues and remain up-to-date on current research in these areas.

Age of Diagnosis for CCA in DES Daughters

Early studies of this health risk suggested that CCA was primarily a risk for DES Daughters in their teens and 20s. More recent information from the CCA registry at the University of Chicago shows that DES Daughters in their 30s and 40s have been diagnosed with CCA (Hatch, 1998). No one knows how common CCA may be as the majority of DES Daughters enter their 50s and 60s. As a result, CCA is now considered a lifetime risk for DES Daughters.

Cervical Intraepithelial Neoplasia (CIN)

Scientists are also investigating if DES Daughters have an increased risk of a condition called cervical intraepithelial neoplasia. Cervical intraepithelial neoplasia (CIN) is a general term for the growth of abnormal cells on the surface of the cervix. One recent study found that DES Daughters are twice as likely to experience CIN as unexposed women (Hatch, 2001). An earlier study found that DES Daughters are two to four times more likely than unexposed women to have abnormal cells changes on the cervix or to experience cervical carcinoma in situ (CIS). CIS involves only the cells in which the cancer begins, but does not spread to nearby tissues (Robboy, 1984). More recently, researchers analyzed experiences of women from the Netherlands DES Information Center. DES Daughters registered at the Information Center reported three times the incidence of cervical cancer as did unexposed women (Verloop, 2000).

Breast Cancer

Exposure to estrogen before birth has been linked to increased risk for breast cancer (Trichopoulous, 1990; Potischman, 1999). As a result, concerns have been raised about whether DES Daughters have an increased risk of breast cancer.

Until recently the majority of DES Daughters were too young to determine whether DES exposure increased their risk of breast cancer. However, a recent study provides initial results linking exposure to DES before birth with increased rates of breast cancer (Palmer, 2002). The study found that among study participants, DES Daughters were more likely to experience breast cancer than were unexposed women. DES Daughters had a relative risk of 1.4 (40% higher incidence of breast cancer). However, the finding was not statistically significant, which means that the increased rate

of breast cancer could have been the result of chance. The study did find that, in study participants over 40, DES Daughters were two-and-a-half times more likely than unexposed women to be diagnosed with breast cancer. The results for women over 40 were statistically significant (not likely to be due to chance). DES Daughters under 40 years of age did not experience an increased risk of breast cancer. The findings from this study are considered preliminary until confirmed and refined by other research. However, DES Daughters and their health care providers should be aware of this research and follow breast cancer screening guidelines recommended by the American Cancer Society (ACS) or the National Cancer Institute (NCI). Guidelines for breast cancer screening can be found at the ACS Web site (www.cancer.org) or at the NCI Web site (www.cancer.gov).

Research on additional health concerns is ongoing because as DES Daughters experience menopause, a time during which certain conditions (such as osteoporosis, breast cancer, and cervical cancer) become more common in the population, continued monitoring is necessary. While research continues, you should protect your health by staying informed and talking with a health care provider about screenings for age-related cancers.

For more information about protecting your health, refer to the section of CDC's DES Update titled WHAT YOU CAN DO ABOUT DES: Protecting Your Health and the Health of Your Family.

Considering that I was exposed to DES before birth (in the womb), is it all right for me to take birth control pills?

Some DES Daughters wonder whether they should use birth control pills. The decision about birth control methods is a very personal one. Women should talk with their health care providers about the best method for each woman based on medical conditions and health history. Research can also help women make informed medical decisions. Research has not found DES Daughters to be at risk for any cancers except clear cell cancer of the vagina and cervix (Hatch, 1998). The largest study of DES Daughters to date found that use of birth control pills by DES Daughters did not increase the risk for breast cancer or any other type of cancer (Hatch, 1998). The recently published Women's Contraceptive and Reproductive Experience Study found that use of birth control pills did not increase women's risk of breast cancer (Marchbanks, 2002). The study included more than 9,000 women, but did not include information about their DES exposure status.

Should DES Daughters consider hormone replacement therapy (HRT)?

Research on DES Daughters and HRT has been limited because many DES Daughters were born in the 1950s and 1960s and have yet to reach menopause—the time when replacing estrogen is typically considered. Studies are ongoing and researchers continue to evaluate any possible links between exposure to DES before birth (in the womb) and risks associated with HRT. The decision to take HRT is a personal one and should be made in consultation with your health care provider.

For more information on hormone replacement therapy (HRT), refer to the following sources.

- CDC Information About Hormone Replacement Therapy Web site (www.cdc.gov/nccdphp/hrt.htm) or CDC's toll-free number (1-888-8 PUEBLO [1-888-878-3256]).
- The section of CDC's DES Update titled ADDITIONAL DES RESOURCES: DES Bibliography.

RELATED CONCERNS

Potential Health Risks: Men Exposed To DES Before Birth (In The Womb), Known As DES Sons

Are DES Sons at an increased risk for cancer?

Research established that DES Sons were at an increased risk of non-cancerous epididymal cysts, which are growths on the testicles (Bibbo, 1977; Gill, 1979; Wilcox, 1995). Research has not found that DES Sons are at an increased risk for any type of cancer (Strohsnitter, 2001).

However, questions have been raised because laboratory animal studies demonstrated a relationship between DES exposure and an increased rate of a rare type of testicular cancer (rete testis) and prostate cancer (Newbold, 1985, 1987; McLaughlan, 1998). In addition, testicular cancer has been linked with exposure to abnormal levels of estrogen before birth (in the womb) (Panagiotopolou, 1990; Kappel, 1985; Rosing, 1984; Braun, 1995; Petridou, 1997), and testicular cancer is an increased health risk for men with undescended testicles – a condition shown by some studies to be associated with DES exposure (Moller, 1997).

Early studies on the link between testicular cancer and DES exposure produced mixed results. Several studies found an increased risk of testicular cancer among DES Sons (Henderson, 1979; Depue, 1983; Moss, 1986; Schottenfeld, 1980), but two other studies found no relationship between DES exposure and an increased risk for testicular cancer (Brown, 1986; Gershman, 1988). The most recent study found an increased rate of testicular cancer among DES-exposed men compared with unexposed men. However, the increased rate was not statistically significant, which means the higher rate of testicular cancer among DES Sons could have resulted from chance rather than exposure to DES (Strohsnitter, 2001).

Generally, the risk of prostate cancer increases as men grow older. While research continues, you should protect your health by staying informed and talking with a health care provider about screenings for age-related cancers.

Are DES Sons at an increased risk for any other health problems?

Some studies have associated exposure to DES before birth with genital abnormalities in males. These include undescended testicles (cryptorchidism), misplaced opening of the penis (hypospadias), a small penis (microphallus), and growths on testicles (testicular neoplasia). Other studies have not found these abnormalities to be associated with DES exposure. No other health effects, with the exception of epididymal cysts, have been consistently found in DES Sons. However, ongoing studies sponsored by the National Cancer Institute (NCI) continue to monitor health problems among DES Sons. Future follow-up studies may uncover other health risks as DES Sons age.

RELATED CONCERNS

Potential Health Risks: Third Generation (the Offspring of DES Daughters and Sons)

Do the children of DES Daughters and Sons have any health risks?

Third-generation children (the offspring of DES Daughters and Sons) are just beginning to reach the age when relevant health problems (such as reproductive tract problems), can be studied.

A study of the health risks for the daughters of DES daughters, or third-generation daughters, was published in 2002. The researchers compared findings of pelvic examinations of 28 daughters with findings noted in their mothers (DES Daughters). Even though abnormalities were present in more than 60% of DES Daughters, no abnormalities were found in their daughters (Kaufman, 2002).

Sons of DES Daughters are being studied at the Netherlands Cancer Institute. Early research reported that hypospadias, misplaced opening of the penis, occurred 20 times more frequently among sons of DES Daughters (Klip, 2002).

What is known about a third-generation health risks from laboratory animal studies?

In laboratory animal studies of elderly third-generation DES-exposed, female mice, an increased risk of uterine cancers, benign ovarian tumors, and lymphomas was found. Elderly third-generation DES-exposed male mice were at an increased risk of certain reproductive tract tumors. Both the female and male mice studied were the offspring of female mice exposed to DES before birth (in the womb). While DES research about third-generation health risks continues, you should protect your health by staying informed and talking with a health care provider about your concerns.

RELATED CONCERNS

Potential Health Risks: General Questions

What is known about DES and autoimmune diseases?

Although laboratory animal studies of mice exposed to DES before birth (in the womb) suggested an increased risk of autoimmune disease in female mice, studies among humans have reported mixed results. One study indicated that autoimmune diseases occurred more often in women exposed to DES before birth (in the womb), known as DES Daughters, than in the general population. However, no one autoimmune disease (such as rheumatoid arthritis or lupus) occurred more often than others (Noller, 1988). Researchers will continue to explore this issue.

What other health risks have been studied?

No studies of humans have documented consistent findings linking DES exposure to any psychological condition or sexual dysfunction. However, some laboratory animal studies suggested links between exposure to estrogens before birth (in the womb) and cognitive abilities. For more information refer to topic "Psychology" in the section of CDC's DES Update titled ADDITIONAL DES RESOURCES: DES Bibliography.

DES TELECONFERENCES

Overview

CDC's DES Update will host a series of telephone conferences on current DES research. Several studies have been published in the past few years, and each teleconference will focus on a particular topic of current DES research. Each teleconference will begin with a brief presentation by a DES researcher with a response by an expert clinician. Following the presentation and response, call-in participants are invited to ask questions about the research discussed and how it applies to health risks.

The DES teleconferences are scheduled throughout 2003. The following topics will be discussed.

- Research Findings on Health Risks for DES Sons
- Breast Cancer and DES Exposure: The Latest Research on Women Exposed to DES While Pregnant and DES Daughters
- Cancer Risks for DES Daughters
- Infertility and Reproductive Health Risks for DES Daughters: The Latest Research
- What Does the Animal Research Tell Us about Future DES Health Effects?

The DES teleconferences will be advertised on CDC's DES Update Web site (www.cdc.gov/DES) and through our DES partner Web sites, listserves, and newsletters. In addition, the conferences will be summarized and posted on CDC's DES Web site (www.cdc.gov/DES).

If you would like to participate in a DES teleconference, call the toll-free number provided in the advertisements.

To read summaries of current DES research, see the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research.

TAB 3: WHAT YOU CAN DO ABOUT DES

Overview

You can take steps to protect your health and the health of your family. Whether you were prescribed DES while pregnant or exposed to DES before birth (in the womb), the information and resources in this section will help you

- work with your health care provider;
- protect your health and the health of your family; and
- keep a DES health information record.

WORKING WITH YOUR HEALTH CARE PROVIDER

How to Work Effectively with Your Health Care Provider

To stay informed about DES and protect your health, you should communicate regularly with your health care provider (for instance, your physician, physician's assistant, nurse, or nurse practitioner). Talking with your health care provider is not always easy; some patients hesitate to ask questions during regular office visits or check-ups because it is difficult for them to ask about complex issues such as DES. Others may be reluctant to contact their health care provider between office visits unless it is an emergency. But your health care provider needs to know your questions and concerns. Addressing your questions and concerns is the best way your health care provider can work with you to protect your health. You must take the initiative and help your health care provider give you the most effective care – the care that is right for you.

This section of CDC's DES Update addresses some of the most common questions and concerns that patients ask about how to work with a health care provider.

My health care provider has never talked with me about DES exposure.

If your health care provider has not talked with you about DES exposure, you can initiate the conversation. Most health care providers only have a few patients who have been exposed to DES, so they rarely have patients ask about the topic. Although CDC's DES Update is designed to give health care providers current information and resources for working with patients, if you do not mention your DES exposure, your health care provider will likely remain unaware.

I know (or have strong reason to suspect) that I was exposed to DES. What should I expect my health care provider to do?

Once your health care provider knows or suspects you were exposed to DES, certain screenings to check for DES health effects may be recommended. You and your health care provider can work together to set up a screening schedule that may minimize your risk of health problems. For a list of recommended screenings, see the section of CDC's DES Update titled WHAT YOU CAN DO ABOUT DES: Protecting Your Health and the Health of Your Family.

Are there materials I can take to my health care provider to help us talk about DES?

The following are some DES resources that you can take to your health care provider.

- CDC's DES Update summary card titled WHAT YOU CAN DO ABOUT DES: CDC'S DES Update in Brief.
- Downloadable materials from CDC's DES Update Web site at www.cdc.gov/DES.
- Recent DES research summarized in the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research.

What can I do if I want or need to change health care providers?

If you do not have a health care provider, or if your health care provider does not meet your needs, ask for recommendations from family, friends, or other health care providers. Be sure to check with your health care plan about any network or referral requirements.

You can also contact the consumer advocacy group, DES Action USA. DES Action has compiled a National Physician Referral List that includes physicians who have experience working with DES-exposed patients. This referral list can be obtained free of charge. Other health care providers in your area also may know about DES, but this referral list is a good place to start. Contact DES Action by telephone (1-800-DES-9288) or by e-mail (desaction@earthlink.net).

My gynecologist knows about my DES exposure. Do I need to tell my other health care providers?

Yes. Your DES exposure is a part of your health history, and all of your health care providers should know about it. The more your health care providers know about your health history, the more you can work together to protect your health.

In addition, you should keep copies of your medical records, especially if you see more than one physician. To help you keep track of your DES health history, including DES-related health problems, refer to the section of CDC's DES Update titled WHAT YOU CAN DO ABOUT DES: DES Health Information Record.

The American College of Obstetricians and Gynecologists is a resource for names of obstetricians, gynecologists, and maternal-fetal medicine specialists. Contact the Resource Center at The American College of Obstetricians and Gynecologists at 202-863-2518, P. O. Box 96920, Washington, D.C., 20090-6920, or www.acog.org.

I am a DES Son. Who should be aware of my DES exposure?

DES Sons should tell their primary care provider about their DES exposure. If you already have a urologist, be sure he or she is aware of your DES exposure. If you do not have a urologist, your primary health care provider can refer you to one, if necessary.

What is CDC doing to help educate health care providers?

CDC's DES Update is working with health care providers around the country to increase awareness about recent DES research and to give them current information and resources for working with patients. You can also help with this effort. When you visit your health care provider, bring along the summary card in the section of CDC's DES Update titled WHAT YOU CAN DO ABOUT DES: CDC'S DES Update in Brief.

This card also includes a list of the resources available for health care providers. In addition, CDC's DES Update Web site (www.cdc.gov/DES) has information and resources specifically designed for health care providers, along with information and resources for people who were exposed to DES.

What else can I do to more effectively work with my health care provider?

The following are some actions you can take to work more effectively with your health care provider.

- **Keep track of your health history.** Keeping a record of your health care visits, writing down any test results, and keeping track of future screening appointments will help you work effectively with your health care provider. To assist you in organizing this information, refer to the section of CDC's DES Update titled WHAT YOU CAN DO ABOUT DES: DES Health Information Record.
- **Prepare for your office visit with your health care provider.** Refer to the list of suggested questions provided in the next section. Prepare the questions you would like to ask and take the list with you to your appointment.
- **Do not wait to ask questions that are on your mind right now.** Call your health care provider's office with specific questions. If your health care provider is not available, ask to have your call returned or talk with a nurse or physician's assistant.

WORKING WITH YOUR HEALTH CARE PROVIDER

Questions To Ask Your Health Care Provider About DES

The following are questions everyone should ask their health care provider.

- Have you treated women/men who were exposed to DES?
- I was/may have been exposed to DES. What would you recommend I do to protect my health?
- Do you know about CDC's DES Update?
- Do new DES research findings mean I should be doing anything different to protect my health?

The following are questions to ask your health care provider if you were prescribed DES while pregnant.

- I was prescribed DES while pregnant. DES research shows that women like me have about a 30% increased risk of developing breast cancer over their lifetime. How will we plan my mammogram schedule and other physical exams to manage my increased risk?
- I know that monthly breast self-exams may help protect my health. Will you show me how to do a breast self-exam correctly? Does it matter what time of the month I perform breast self-exams?
- I was prescribed DES while pregnant with my daughter/son. What health risks should I be discussing with her/him?
- Do new DES research findings mean I should be doing anything different to protect my health?

The following are questions to ask your health care provider if you are a woman who was exposed to DES before birth (in the womb), known as a DES Daughter.

- My mother was prescribed DES while pregnant with me. Current DES research shows that DES Daughters continue to be at a higher risk for clear cell adenocarinoma (CCA) of the vagina and cervix into their late 40s. I understand I should be monitored for CCA throughout my lifetime. What types of screenings and exams should I receive to manage my increased risk?
- Have you worked with any DES Daughters who were able to become pregnant?
- Do you work with high-risk pregnancies? If not, could you refer me to a health care provider who does?
- Research shows that DES Daughters have an increased risk for structural changes of the uterus and cervix (such as a T-shaped uterus, cockscomb on the cervix, and hooded cervix). Do I need to be examined for any of these differences? If so, when?
- DES research shows that DES Daughters have an increased risk of tubal pregnancies, miscarriages, and premature deliveries. What additional screenings or tests should we think about to protect my health during pregnancy?

- Preliminary results of DES research indicate that DES Daughters older than 40 are at higher risk for breast cancer. I know that monthly breast self-exams may help protect my health. Will you show me how to do a breast self-exam correctly? Does it matter what time of the month I perform breast self-exams?
- What health risks does my mother have because she was prescribed DES while she was pregnant with me?
- (If applicable) What health risks does my brother have because he was exposed to DES before birth (in the womb)?
- Do new DES research findings mean I should be doing anything different to protect my health?

The following are questions to ask your health care provider if you are a man who was exposed to DES before birth (in the womb), known as a DES Son.

- My mother was prescribed DES while pregnant with me. Researchers are exploring whether DES exposure is linked to testicular cancer. I know that testicular self-exams may help protect my health. Will you show me how to do a testicular self-exam correctly? How often should I do self-exams and what should I look for?
- What health risks does my mother have because she was prescribed DES while she was pregnant with me?
- (If applicable) What health risks does my sister have because she was exposed to DES before birth (in the womb)?
- Do new DES research findings mean I should be doing anything different to protect my health?

This handout can be shared with your health care provider, family, or friends.

Centers for Disease Control and Prevention's

DES UPDATE

DES in Brief: Known Health Risks and New Resources

Research published 1971-2001 associates DES exposure with increased health risks for:

WOMEN PRESCRIBED DES WHILE PREGNANT are at a modestly increased risk for

- **Breast cancer**

WOMEN EXPOSED TO DES BEFORE BIRTH (in the womb), known as DES Daughters, are at an increased risk for

- **Clear cell adenocarcinoma (CCA) of the vagina and cervix**
- **Reproductive tract structural differences**
- **Pregnancy complications**
- **Infertility**

MEN EXPOSED TO DES BEFORE BIRTH (in the womb), known as DES Sons, are at an increased risk for

- **Non-cancerous epididymal cysts**

CDC's DES Update offers several free educational resources for health care providers and patients/consumers. To order a CD-ROM with the resources for health care providers or to order the printed resources for patients and consumers, visit the web site at www.cdc.gov/DES or call toll-free 1-888-232-6789.

RESOURCES FOR HEALTH CARE PROVIDERS

- **DES Grand Rounds Presentations**
- **DES Case Studies for medical, nursing, physician assistant and nurse practitioner students**
- **DES Review Essays**
- **CME & CEU self-study modules**
- **DES Web Site**

RESOURCES FOR PATIENTS AND CONSUMERS

- **DES Fact Sheets**
- **DES Self-Assessment**
- **Personal Health Information Record**
- **DES Web Site**

An estimated 5-10 million people were exposed to diethylstilbestrol (DES) in the United States during 1938-1971. DES was thought to be a safe and effective way to prevent miscarriages or premature deliveries. However, later studies revealed that DES had harmful side effects. Many people are still unaware of their exposure to DES and the potential health effects.

DES *Health Record*

FOR MEN

This health information record can help you manage your health decisions and help you discuss questions about DES exposure with your health care provider.

Each family member exposed to DES should complete a DES Health Information Record. You can photocopy this record or print additional copies from the CDC's DES Update Web site at www.cdc.gov/DES.

General Information

Name _____ Social Security Number _____

Date of Birth_____ Blood Type _____

Primary health care provider(s) _____

Other Specialists _____

Insurance Carrier _____ Policy/Plan Number _____

Group#_____

Effective Date _____ Phone Number _____

Your DES Health History

My mother was prescribed DES while she was pregnant with me. Yes ____ No____ Don't Know ___

I am the son of a woman or man exposed to DES before birth (in the womb), also known as a DES grandchild. Yes ____ No____ Don't Know ___

The following chart helps you track your health checkups. Record the date and year of your most recent exam. Space is provided to track future exams.

	Date/Year	Date/Year	Date/Year	Date/Year	Date/Year
Physical Exam, including testicular exam					

Has a health care provider ever diagnosed you with:

	Year of Diagnosis
Undescended testicles	_____
Abnormal opening of the penis	_____
Non-cancerous epididydmal cysts	_____
Any other genital tract abnormalities	_____
Any urinary tract abnormalities (increased frequency of urination, difficulty urinating, blood in your urine)	_____
Cancer (specify type(s)_____)	_____

(Research on increased risks of cancers among DES Sons is not definitive. However, there are some ongoing concerns about DES exposure and men's cancers, such as testicular and prostate cancers.)

Notes from your health care provider:

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

DES *Health Record*

FOR WOMEN

This health information record can help you manage your health decisions and help you discuss questions about DES exposure with your health care provider.

Each family member exposed to DES should complete a DES Health Information Record. You can photocopy this record or print additional copies from the CDC's DES Update Web site at www.cdc.gov/DES.

General Information

Name _____ Social Security Number _____

Date of Birth_____ Blood Type _____

Primary health care provider(s) _____

Obstetrician/Gynecologist_____

Other Specialists _____

Insurance Carrier _____ Policy/Plan Number _____

Group#_____

Effective Date _____ Phone Number _____

Your DES Health History

I was prescribed DES while I was pregnant. Yes ____ No____ Don't Know ___

My mother was prescribed DES while she was pregnant with me. Yes ____ No____ Don't Know ___

I am the daughter of a woman or man exposed to DES before birth (in the womb), also known as a DES grandchild. Yes ____ No____ Don't Know ___

The following chart helps you track your women's health checkups. Record the date and year of your most recent gynecological exam and mammogram. Space is provided to track future exams.

	Date/Year	Date/Year	Date/Year	Date/Year	Date/Year
Record of Gynecological Exams/Pap Tests					
Follow Up and Treatment for Abnormal Pap Tests					
Record of Mammograms					
Follow Up and Treatment for Abnormal Mammograms					

Notes from your health care provider:

_____

_____

_____

_____

Record age/date of:

	Age	Date
First menstrual cycle		
Last menstrual cycle (onset of menopause)		

Record number of:

	Age	Date
Full-term pregnancies		
Premature births		
Ectopic pregnancies		
Miscarriages		

Record name of and dates taken:

	Name	Dates
Birth Control Pills		
Fertility Medications		
Hormone Replacement Therapy		

PROTECTING YOUR HEALTH AND THE HEALTH OF YOUR FAMILY

Women Prescribed DES While Pregnant

Women prescribed DES while pregnant are at a modestly increased risk for breast cancer. They should be screened for breast cancer with the same tests and at the same intervals as women in the general population. The following are action steps you can take to protect your health.

- **Have clinical breast exams and regular mammograms**
  Most health care providers recommend that women 40 years of age and older have a mammogram (an X-ray of the breast) every 1–2 years. In addition, most health care providers perform clinical breast examinations (visual and manual examination of the breast) during routine physical examinations. Additional guidelines for breast cancer screening can be found at the National Cancer Institute (NCI) Web site (www.cancer.gov) or the American Cancer Society (ACS) Web site (www.cancer.org). A description of mammography can be found at the ACS Web site by typing "mammography" in the search box on the home page and then clicking on the link to the Glossary and typing "mammography" in the cancer-related terms box.

- **Perform monthly breast self-exams**
  Most health care providers recommend that you learn and practice monthly breast self-examination as a way to detect any lumps in your breasts, discharge from the nipples, or skin changes (such as dimpling or puckering). Instructions for breast self-examination can be found at the ACS Web site by typing "breast self-exam" in the search box on the home page and then clicking on the link "How to Perform a Breast Self-Exam."

- **Talk with your family, especially your children, about DES**
  If you have not already discussed it, you may find it difficult to tell your children they were exposed to DES. However, many mothers feel a sense of relief after telling their children; family members need to know whether they were exposed to DES. Once your children know about their exposure, they can get proper medical care to protect their health now and in the future.

  - Encourage your children to notify their health care provider about their DES exposure before birth (in the womb).

  - Request copies of CDC's DES Update to share with your children. Visit CDC's DES Web site at www.cdc.gov/DES or call toll-free 1-888-232-6789.

- **Share the DES Self-Assessment**
  As you talk with others about DES, they may wonder whether they were exposed to DES. To assess whether they may have been exposed to DES, refer to the section of CDC's DES Update titled DES SELF-ASSESSMENT: A Guide to Understanding Your Risk for DES Exposure.

- **Stay up-to-date on DES research**
  Researchers continue to study DES and will learn more health information about DES exposure in follow-up studies. For more information refer to the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research.

- **For more information about**
  - DES exposure and related health risks, visit CDC's DES Update Web site at www.cdc.gov/DES or call toll-free 1-888-232-6789.
  - Breast cancer risk for women prescribed DES while pregnant, refer to the sections of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research, and ADDITIONAL DES RESOURCES: DES Bibliography.
  - Breast cancer causes and prevention, visit the National Cancer Institute (NCI) Web site at www.cancer.gov or call the Cancer Information Service (CIS) toll-free 1-800-4-CANCER (1-800-422-6237). The American Cancer Society (ACS) also provides detailed information about breast cancer screening at their Web site (www.cancer.org).

PROTECTING YOUR HEALTH AND THE HEALTH OF YOUR FAMILY

Women Exposed to DES Before Birth (in the Womb), known as DES Daughters

DES Daughters are at an increased risk for clear cell adenocarcinoma (CCA) of the vagina and cervix, cervical intraepithelial neoplasia (CIN), reproductive tract structural differences, pregnancy complications, pre-term delivery, and infertility and therefore should be monitored throughout their lifetimes. The following are steps you can take to protect your health.

- **Schedule regular gynecological exams, including Pap test and pelvic exam**
  The National Cancer Institute (NCI) published a description of appropriate pelvic examinations for DES Daughters. Pelvic examinations for DES Daughters should be performed in a similar manner as those performed among unexposed women.

  Pelvic examinations in DES Daughters should include

  - careful visual examination and palpation (feeling) of the vagina and cervix with rotation of the speculum so that all vaginal walls can be inspected;
  - Pap smears from the cervix and the surfaces of the upper vagina; and
  - iodine staining of the vagina and cervix or a colposcopy, depending on the detection of any abnormalities during the examination. Iodine staining allows your health care provider to evaluate changes in the cervix or vagina. A colposcopy uses a device that works like a magnifying glass, allowing your health care provider to carefully check the vagina and cervix. Your health care provider may take photographs using the colposcope so that any changes in your condition can be monitored during future examinations.

- **Schedule clinical breast exams and regular mammograms**
  Studies have not found a statistically significantly increased risk of breast cancer among DES Daughters of all ages. However, a recent study did find significantly increased risk among DES Daughters over age 40 (Palmer, 2002). Since this was the first study to identify a link, research will continue to see if results will be repeated and to determine if DES Daughters of other ages also have a greater risk of breast cancer. While research continues, DES Daughters should be screened for breast cancer with the same tests and at the same intervals as women in the general population. The following actions can help you protect your health.

  - Most health care providers recommend that women 40 years of age and older have a mammogram (an X-ray of the breast) every 1–2 years.
  - In addition, most health care providers perform a clinical breast examination (visual and manual examination of the breast) during routine physical examinations. Guidelines for breast cancer screening can be found at the National Cancer Institute (NCI) Web site (www.cancer.gov) or the American Cancer Society (ACS) Web site (www.cancer.org). A description of mammography can be found at the ACS Web site by typing "mammography" in the search box on the home page and then clicking on the link to the Glossary and typing "mammography" in the cancer-related terms box.

- **Perform monthly breast self-exams**
  Most health care providers suggest that, in addition to getting recommended mammograms, you learn and practice monthly breast self-examination as a way to detect any lumps in your breasts, discharge from the nipples, or skin changes (such as dimpling or puckering). Instructions for breast self-examination can be found at the ACS Web site by typing "breast self-exam" in the search box on the home page (www.cancer.org) and then clicking on the link "How to Perform a Breast Self-Exam."

- **Obtain information regarding low-cost or free screening**
  To find out where you can get a free or low-cost Pap test or mammogram, visit CDC's National Breast and Cervical Cancer Early Detection Program Web site at http://www.cdc.gov/cancer/nbccedp/index.htm or call toll-free 1-888-842-6355.

- **Seek infertility counseling if you have difficulty becoming pregnant**
  DES Daughters are at an increased risk of infertility. Your health care provider should be informed about your pregnancy plans so that he or she can communicate to you the risks of infertility. Although no single test, treatment, or screening is necessary because of your DES exposure, your health care provider may recommend that you undergo certain tests or screenings appropriate for your risk. For example, your health care provider may perform a hysterosalpingogram. This is an X-ray that can check for structural differences and physical alterations in your upper genital tract.

  - For more information about infertility, refer to the section of CDC's DES Update titled ADDITIONAL DES RESOURCES: Partner and Government Organizations.

- **Treat pregnancies as "high risk"**
  DES Daughters are at an increased risk of pregnancy complications and should be sure that their health care providers consider their pregnancies "high risk" and establish an appropriate plan of action. Your provider may suggest more frequent check-ups or tests to ensure that your pregnancy is progressing properly.

- **Talk with your family, especially your children, about DES**
  Research on the health risks of the third generation (the offspring of DES Daughters and Sons) is just beginning, and the results are preliminary. Research will continue as these children age. If future research identifies health risks for the third generation, informing them about their DES exposure will become even more important. To help protect your child's health, consider taking the following steps.

  - Note your DES exposure on your child's health record. For a DES health information form, refer to the section of CDC's DES Update titled WHAT YOU CAN DO ABOUT DES: DES Health Information Record.
  - Notify your child's health care provider about your exposure to DES.
  - To learn more about the ongoing research of the third generation, refer to the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research.
  - Request copies of CDC's DES Update to share with your children. Visit CDC's DES Update Web site at www.cdc.gov/DES or call toll-free 1-888-232-6789.

- **Share the DES Self-Assessment**
  As you talk with others about DES, they may wonder whether they were exposed to DES. To assess whether you or others may have been exposed to DES, refer to the section of CDC's DES Update titled DES SELF-ASSESSMENT: A Guide to Understanding Your Risk for DES Exposure. For additional copies of the DES Self-Assessment, visit CDC's DES Update Web site at www.cdc.gov/DES or call toll-free 1-888-232-6789.

- **Stay up-to-date on DES research**
  Researchers continue to study DES and may learn more about the health effects of DES exposure. For more information, refer to the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research.

- **For more information about**

  - DES exposure and related health risks, visit CDC's DES Update Web site at www.cdc.gov/DES or call toll-free 1-888-232-6789.

  - Health risks for DES Daughters, refer to the sections of CDC's DES Update titled WHAT WE KNOW ABOUT DES: Known DES Health Effects; WHAT WE ARE LEARNING ABOUT DES: Recent DES Research; and ADDITIONAL DES RESOURCES: DES Bibliography.

PROTECTING YOUR HEALTH AND THE HEALTH OF YOUR FAMILY

Men Exposed to DES Before Birth (in the Womb), Known as DES Sons

DES Sons have an increased risk of non-cancerous epididymal cysts (growths on the testicles). The following are steps you can take to protect your health.

- **Perform monthly testicular self-exams**
  Researchers continue to study whether DES exposure is linked with an increased risk of developing testicular cancer. Talk with your health care provider about whether monthly testicular self-examinations should be a part of your regular health activities. For information about how to do a testicular self-exam, refer to the American Cancer Society's (ACS) Web site (www.cancer.org).

- **Talk with your family, especially your children, about DES**
  Research on the health risks for the third generation (the offspring of DES Daughters and Sons) is just beginning. Research will continue on these children as they age. If future research identifies health risks to the third generation, informing them about their DES exposure will become even more important. To help protect your child's health, consider taking the following steps.

  - Note your DES exposure on your child's health record. For a health information form, refer to the section of CDC's DES Update titled WHAT YOU CAN DO ABOUT DES: DES Health Information Record.
  - Notify your child's health care provider about your exposure to DES.
  - To learn more about the ongoing research of the third generation, refer to the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research.
  - Request copies of CDC's DES Update to share with your children. Visit CDC's DES Update Web site at www.cdc.gov/DES or call toll-free 1-888-232-6789.

- **Share the DES Self-Assessment**
  As you talk with others about DES, they may wonder whether they were exposed to DES. To assess whether you or others may have been exposed to DES, refer to the section of CDC's DES Update titled DES SELF-ASSESSMENT: A Guide to Understanding Your Risk for DES Exposure.

  For additional copies of the DES Self-Assessment, visit CDC's DES Update Web site at www.cdc.gov/DES or call toll-free 1-888-232-6789.

- **Stay up-to-date on DES research**
  Researchers continue to study DES and may learn more about the health effects of DES exposure. For more information refer to the section of CDC's DES Update titled WHAT WE ARE LEARNING ABOUT DES: Recent DES Research.

- **For more information about**
  - DES, visit CDC's DES Update Web site at www.cdc.gov/DES or call toll-free 1-888-232-6789; and
  - Health risks for DES Sons, refer to the sections of CDC's DES Update titled WHAT WE KNOW ABOUT DES: Known DES Health Effects; WHAT WE ARE LEARNING ABOUT DES: Recent DES Research; and ADDITIONAL DES RESOURCES: DES Bibliography.

TAB 4: ADDITIONAL DES RESOURCES

Overview

Other resources are available to help you learn more about DES research, health risks, and support system.

This section of CDC's DES Update includes the following information.

- **Partner and Government Organizations –** A list of the names and contact information for organizations that provide useful DES resources.
- **DES Glossary –** A list of terms and definitions relevant to the topic of DES.
- **DES Bibliography –** A list of published research and other sources of DES information grouped by main topic.
- **Notes –** A place to record your thoughts and questions about DES.

PARTNER AND GOVERNMENT ORGANIZATIONS

Overview

Researchers continue to learn about DES. Therefore, staying informed about DES is important for protecting your health. CDC and several partner organizations can help you stay informed about DES and related health issues through Web sites, mailing lists, and newsletters. This section of CDC's DES Update contains a list of the names and contact information for organizations that provide useful DES-related resources.

PARTNER AND GOVERNMENT ORGANIZATIONS

CDC's DES Update

CDC's DES Update
Phone: (toll-free) 1-888-232-6789
Web site: www.cdc.gov/DES

CDC's DES Update was developed as a resource for the public and for health care providers to provide them with the latest, most comprehensive, and accurate information about diethylstilbestrol (DES).

Resources for patients and consumers include

- a binder of DES fact sheets;
- DES Self-Assessment: A Guide to Understanding Your Risk for DES Exposure;
- DES Health Information Record; and
- DES Web site.

Resources for health care providers include

- DES Grand Rounds presentations;
- DES case studies;
- DES review essays;
- CME and CEU self-study modules; and
- DES Web site.

DES Advocacy Organizations

DES Action USA
610 16th Street, Suite 301
Oakland, CA 94612
Phone: (toll-free) 1-800-DES-9288 or 510-465-4011
Fax: 510-465-4815
E-mail: desaction@earthlink.net
Web site: www.desaction.org

DES Action USA is a national, non-profit consumer organization dedicated to informing the public about DES and helping DES-exposed people. This organization offers a quarterly newsletter and many publications on various aspects of DES exposure and links DES-exposed people, DES researchers, and the medical community.

DES Sons Network
Michael Freilick
104 Sleepy Hollow Place
Cherry Hill, NJ 08003
E-mail: msfreilick@hotmail.com

DES Sons Network is a national network providing information and support for DES Sons and counseling for men with testicular cancer. It is affiliated with DES Action USA.

DES Cancer Network
P.O. Box 220465
Chantilly, VA 20153-0465
Phone: (toll-free) 1-800-DES-NET-4
E-mail: desnetwrk@aol.com
Web site: www.descancer.org

DES Cancer Network is an international advocacy organization that addresses the special needs of women exposed to DES who have had clear cell adenocarcinoma (CCA) of the vagina and cervix. This network provides a support system that gives members access to one another and to information about CCA.

The DES Third Generation Network
P.O. Box 21
Mahwah, NJ 07430
E-mail: des3gen@aol.com

The DES Third Generation Network is an advocacy network designed to collect and share information about the health of children born to DES Daughters and DES Sons.

DES Sons' International Network
c/o Scott Kerlin, Ph.D.
1611 Clawthorpe Avenue
Victoria, British Columbia, Canada V8T 2R9
Phone: 250-595-6173
E-mail: scott@kerlins.net

or

Wayne Beyer, M.D.
8 East Irving Street
Chevy Chase, MD 20815-4221
E-mail: wbb3@cornell.edu
Web site:
http://groups.yahoo.com/group/des-sons

DES Sons' International Network is a private online professional health information and support network for DES Sons and for others with an interest in research related to DES exposure.

Other Government Resources

Centers for Disease Control and Prevention (CDC)

National Breast and Cervical Cancer Early Detection Program
Phone: (toll-free) 1-888-842-6355
Web site:
www.cdc.gov/cancer/nbccedp/index.htm

The National Breast and Cervical Cancer Early Detection Program provides information regarding obtaining free or low-cost mammograms or Pap tests; the program also provides information about risks for and early detection of breast and cervical cancers.

CDC's Reproductive Health Information Source
Assisted Reproductive Technology Success Rates, National Summary and Fertility Clinic Reports
Web site: www.cdc.gov/nccdphp/drh/

This Web site contains the annual reports of the success rates of assisted reproductive technology, as well as information on reproductive health issues.

National Institutes of Health

National Cancer Institute's Cancer Information Service (CIS)
Phone: (toll-free) 1-800-4-CANCER
(1-800-422-6237)
TTY Line: 1-800-332-8615
Web site: www.cancer.gov or
http://cis.nci.nih.gov/fact/3_4.htm

CIS is a service providing accurate, up-to-date information on cancer and related issues (including DES) to patients and their families, health professionals, and the general public.

National Institute on Aging (NIA)
31 Center Drive
Room 5C27
Bethesda, MD 20892
Phone: 301-496-1752
Web site: www.nia.nih.gov

NIA conducts research about aging and provides health information to the public on issues related to this topic, including menopause, hormone replacement therapy, and osteoporosis.

National Institute of Environmental Health Sciences (NIEHS)
P.O. Box 12233
Research Triangle Park, NC 27709
Phone: 919-541-3345
Web site: www.niehs.nih.gov

NIEHS defines how environmental exposures, genetic susceptibility, and age interact to affect a person's health. The Web site contains information on DES studies among animals and research findings.

National Heart, Lung, and Blood Institute (NHLBI)
"Facts about HRT and Heart Disease: The PEPI Trial"
31 Center Drive
MSC 2480, Room 4A10
Bethesda, MD 20892
Phone: 301-496-4236
E-mail: NHLBIinfo@rover.nhlbi.nih.gov
Web site: www.nhlbi.nih.gov

You can order a copy of this publication about hormone replacement therapy (HRT) and heart disease, by phone, through the Web site, or by e-mail.

Centers for Medicaid and Medicare Services (CMS)
"Your Medicare Benefits"

"Women with Medicare – Visiting Your Doctor for a Pap Test, Pelvic Exam, and Clinical Breast Exam"

"Medicare Preventive Services to Keep You Healthy"

Phone: 410-786-3000
Web site: www.medicare.gov

This Web site includes publications that explain Medicare's coverage of routine health screenings, as well as additional tests or procedures.

DES GLOSSARY

Source: The National Cancer Institute (www.cancer.gov/dictionary)

Adenocarcinoma A cancer that begins in cells that line certain internal organs and that have glandular (secretory) properties.

Adenosis Any disease of a gland or abnormal development of a gland. See also "vaginal adenosis."

Androgens A family of hormones that promote the development and maintenance of male sex characteristics.

Autoimmune Disease A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. Examples include multiple sclerosis, rheumatoid arthritis, lupus, and diabetes mellitus.

Benign Not cancerous; does not invade nearby tissue or spread to other parts of the body.

Benign Prostatic Hyperplasia (BPH) A benign (non-cancerous) condition in which an overgrowth of prostate tissue pushes against the urethra and the bladder, blocking the flow of urine. Also called benign prostatic hypertrophy.

Biopsy The removal of cells or tissues for examination under a microscope. When only a sample of tissue is removed, the procedure is called an incisional biopsy or core biopsy. When an entire lump or suspicious area is removed, the procedure is called an excisional biopsy. When a sample of tissue or fluid is removed with a needle, the procedure is called a needle biopsy or fine-needle aspiration. When a cone-shaped piece of tissue from the cervix and cervical canal is removed in a surgical procedure, it is called a cone biopsy or conization. Cone biopsy may be used to diagnose or treat a cervical condition.

British Randomized Trial A group assembled to study DES-related health effects. Participants included women exposed to DES during pregnancy and men and women exposed before birth (in the womb). The DES-exposed group included 379 mothers, 144 daughters, and 177 sons. A control group of unexposed people included 371 mothers, 170 daughters, and 163 sons.

British Research Medical Council (BRMC) Study Participants include pregnant diabetic women enrolled in clinical trial and DES Daughters and DES Sons identified through follow-up study. Total number of participants is 151 (79 DES-exposed and 72 unexposed).

Cancer A term for diseases in which abnormal cells divide without control. Cancer cells can invade nearby tissues and can spread through the bloodstream and lymphatic system to other parts of the body.

Cancer Information Service (CIS) CIS, part of the National Cancer Institute, is the federal government's principal resource for public information about cancer. CIS interprets and explains research findings in a clear and understandable manner and provides personalized responses to specific questions about cancer. Access CIS by calling 1-800-4-CANCER (1-800-422-6237) or by visiting the Web site at http://cis.nci.nih.gov.

Carcinoma Cancer that begins in the skin or in tissues that line or cover internal organs.

Carcinoma In Situ Cancer that involves only the cells in which it began and has not spread to nearby tissues.

Carcinosarcoma A malignant (cancerous) tumor that is a mixture of carcinoma (cancer of epithelial tissue, which is skin and tissue that lines or covers the internal organs) and sarcoma (cancer of connective tissue, such as bone, cartilage, and fat).

Cervical Relating to the neck, or the neck of any organ or structure. The cervix is the lower, narrow end (or neck) of the uterus.

Cervical Cancer Refers to cancer of the uterine cervix. Routine screening for cervical cancer with Papanicolaou (Pap) testing is recommended for all women who are or have been sexually active and who have a cervix.

Cervical Intraepithelial Neoplasia (CIN) A general term for the growth of abnormal cells on the surface of the cervix.

Cervix The lower, narrow end of the uterus that forms a canal between the uterus and vagina.

Clear Cell Adenocarcinoma (CCA)

Clear Cell Carcinoma A rare type of tumor of the female genital tract in which the inside of the cells look clear when viewed under a microscope.

Adenocarcinoma A cancer that begins in cells that line certain internal organs and that have glandular (secretory) properties.

Clinical Breast Examination An examination by a medical professional during which the breasts are palpated (or lightly felt) with the hand and fingers to determine the condition underneath. Breast appearance is checked for dimpling, rashes, and nipple discharge.

Cohort A group of people sharing common characteristics or experiences, often followed by a research study over long periods of time. By compiling and summarizing data from a cohort, scientists can observe whether disease conditions develop at higher rates in a cohort group than they would expect in the general population. The DES Combined Cohort Study (DCCS) is an example of research using a cohort.

Colposcopy Examination of the vagina and cervix using a lighted magnifying instrument called a colposcope.

Complete Hysterectomy A surgical procedure to remove the entire uterus, including the cervix. Also called total hysterectomy.

Connecticut Mothers Study A group assembled as participants in DES-related research. The participants included women who delivered babies during 1946–1965, at medical offices in Fairfield and New Haven Counties, Connecticut. The participants included 1,706 DES-exposed mothers, and 1,405 unexposed mothers. The participants are now included in the DES Combined Cohort Studies.

Corticosteroids Steroid-type hormones that have antitumor activity in lymphomas and lymphoid leukemias. In addition, corticosteroids may be used for hormone replacement and for the management of some of the complications of cancer and its treatment.

Cortisone A natural steroid hormone produced in the adrenal gland. It can also be made in the laboratory. Cortisone reduces swelling and can suppress immune responses.

Cryptorchidism A condition in which one or both testicles fail to move from the abdomen, where they develop before birth, into the scrotum. Also called undescended testicles.

Dieckmann Cohort A group assembled in 1974 to study DES-related health risks. Participants included approximately 800 women exposed to DES while pregnant and 800 unexposed mothers; approximately 400 women exposed to DES before birth (in the womb) and 400 women in a control group; and approximately 400 men exposed to DES before birth and 400 unexposed men. The 1974 group represented the second Dieckmann cohort. The first included mothers who were participants in a study at the University of Chicago in the early 1950s. Results based on the initial study indicated that DES was not effective in preventing miscarriages.

Diethylstilbestrol (DES) A synthetic estrogen that was developed in 1938 to supplement a woman's natural estrogen production. DES was prescribed by doctors for women who experienced miscarriages or premature deliveries. DES was originally considered effective and safe for both the pregnant woman and the developing baby. In the United States, an estimated 5–10 million persons were exposed to DES during 1938–1971. Since 1971, DES has been linked to an increased risk of clear cell adeno carcinoma of the vagina and cervix, infertility, and pregnancy complications in women exposed to DES before birth (in the womb), known as DES Daughters. In addition, women who were prescribed DES while pregnant are at a modestly increased risk for breast cancer. Men exposed to DES before birth (in the womb), known as DES Sons, are at an increased risk for non-cancerous epididymal cysts.

Diethystilbestrol Adenosis Project (DESAD) The DESAD began in 1974 at Baylor College of Medicine, Gundersen Clinic, Massachusetts General Hospital, the Mayo Clinic, and the University of Southern California. The DESAD, the largest DES cohort, included 4,014 DES Daughters (women exposed to DES before birth) and 1,033 unexposed women. Exposed women had documented evidence of DES exposure through review of prenatal records or through physician referral. The DESAD was assembled to conduct studies to determine if DES Daughters were at an increased risk of health problems related to their DES exposure.

DES Combined Cohort Studies (DCCS) The DCCS combines previously established DES study group participants (cohorts). The combined groups include approximately 5,000 women exposed to DES during pregnancy and 4,000 unexposed mothers; 5,000 exposed and 2,500 unexposed daughters; and 2,000 exposed and 2,000 unexposed sons. The goal of the DCCS is to determine whether the risk for cancer among DES-exposed persons is increased as a result of exposure to DES. Other health outcomes (such as infertility and pregnancy outcomes) also are being investigated through the DCCS.

DES Mothers Study The DES Mothers Study began in 1980. The participant group (cohort) included approximately 3,000 women exposed to DES while pregnant and 3,000 unexposed women. These participants had delivered babies during 1940–1960 at Boston Lying-In Hospital, the Mayo Clinic, Dartmouth Medical School, and a private practice in Portland, Maine. Exposure status was determined through review of medical records. The cohort was created as a means to determine if women exposed to DES during pregnancy were at increased risk for cancer.

Dose-dependent Refers to the effects of treatment with a drug. If the effects change when the dose of the drug is changed, the effects are said to be dose-dependent.

Dysplasia Cells that look abnormal under a microscope but are not cancer.

Ectopic Pregnancy A pregnancy outside the uterus, typically in a fallopian tube.

Embryo Early stage in the development of a plant or an animal. In vertebrate animals (those that have a backbone or spinal column), this stage lasts from shortly after fertilization until all major body parts appear. In humans, this stage lasts from about 2 weeks after fertilization until the end of the eighth week of pregnancy.

Endocrine Therapy Treatment that adds, blocks, or removes hormones. For certain conditions (such as diabetes or menopause) hormones are given to adjust low hormone levels. To slow or stop the growth of certain cancers (such as prostate and breast cancer) hormones may be given to block the body's natural hormones. Sometimes surgery is needed to remove the source of hormones. Also called hormone therapy, hormonal therapy, and hormone treatment.

Endocrinologist A doctor who specializes in diagnosing and treating hormone disorders.

Endometriosis A noncancerous (benign) condition that occurs when tissue that looks like endometrial (uterine) tissue grows in abnormal places in the abdomen.

Endometrium The layer of tissue that lines the uterus (womb).

Epididymal Cyst A benign (non-cancerous) sac or capsule on the testes.

Epididymis A cord-like structure along the back border of each testis. Sperm matures and is stored in the coiled duct that runs through this structure.

Epithelial Refers to the cells that line the internal and external surfaces of the body.

Epithelium A thin layer of tissue that covers organs, glands, and other structures within the body.

Estradiol The most potent naturally occurring estrogen in humans.

Estrogen Replacement Therapy (ERT) Estrogen given to postmenopausal women or to women who have had their ovaries surgically removed. Hormones are given to replace the estrogen no longer produced by the ovaries.

Estrogens A family of hormones that promote the development and maintenance of female sex characteristics. Estrogen is a generic term for estrus-producing compounds (female sex hormones) including estradiol, estriol, and estrone.

Etiology The cause or origin of disease.

Excisional Biopsy A surgical procedure in which an entire lump or suspicious area of tissue is removed for diagnosis. The tissue is then examined under a microscope.

Fallopian Tubes Part of the female reproductive tract; the long slender tubes through which eggs pass from the ovaries to the uterus.

Fetus A developing unborn offspring in the uterus (womb). This stage of pregnancy begins 8 weeks after conception and lasts until birth.

Fibroid A non-cancerous (benign) smooth-muscle tumor, usually in the uterus (womb) or digestive (gastrointestinal) tract. Also called leiomyoma.

Fine-needle Aspiration The removal of tissue or fluid with a needle for examination under a microscope. Also called needle biopsy.

Focal In terms of cancer, limited to a specific area.

Follow-up Monitoring an person's health over time after treatment. This includes keeping track of the health of people who participate in a clinical study or clinical trial for a period of time, both during and after the study ends.

Food and Drug Administration (FDA) FDA, part of the United States Department of Health and Human Services, is the federal government's principal agency to promote and protect the public health by helping safe and effective products reach the market in a timely way and by monitoring products for continued safety after they are in use. In 1971, the FDA issued a Drug Bulletin advising physicians to stop prescribing DES to pregnant women because it was linked to a rare vaginal cancer in female offspring. The bulletin is titled FDA Drug Bulletin: Diethylstilbestrol Contraindicated in Pregnancy. Washington, DC: U.S. Department of Health, Education and Welfare (DHEW), 1971. You can access the FDA's Web site at www.fda.gov.

Gene The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein.

Gland An organ that produces and releases one or more substances for use in the body. Some glands produce fluids that affect tissues or organs. Others glands produce hormones.

Glucocorticoid A substance that belongs to the family of compounds called corticosteroids (steroids). Glucocorticoids affect metabolism (chemical and physical changes in living cells). In addition glucocorticoids and have anti-inflammatory and immunosuppressive effects. They may be naturally produced (hormones) or synthetic (drugs).

Gonads The part of the reproductive system that produces and releases eggs in females (ovaries) and sperm in males (testicles/testes).

Grade When referring to a tumor, the grade indicates the level of abnormality found in the cancer cells when viewed through a microscope and how quickly the tumor is likely to grow and spread. Grading systems vary for each type of cancer.

Gynecologic Having to do with the female reproductive tract (including the cervix, endometrium, fallopian tubes, ovaries, uterus, and vagina).

Gynecologic Cancer Cancer of the female reproductive tract, including the cervix, endometrium, fallopian tubes, ovaries, uterus, and vagina.

Gynecologic Oncologist A doctor who specializes in treating cancers of the female reproductive organs.

Gynecologist A doctor who specializes in health conditions and problems related to the female reproductive organs.

Half-life The time required for half the amount of a substance (such as a drug or radioactive substance) in a living system (body tissue) or ecosystem to be eliminated or disintegrated by natural processes (decay or biological elimination).

High-grade Squamous Intraepithelial Lesion (HSIL) A pre-cancerous condition in which the cells of the uterine cervix are moderately or severely abnormal. Not all HSILs become cancerous, even if left untreated.

Hysterosalpingogram An X-ray that can check for differences and physical alterations in the female upper genital tract.

Hormonal Therapy Treatment that adds, blocks, or removes hormones. For certain conditions (such as diabetes or menopause), hormones are given to adjust low hormone levels. To slow or stop the growth of certain cancers (such as prostate and breast cancer), hormones may be given to block the body's natural hormones. Sometimes surgery is needed to remove the source of hormones. Also called hormone therapy, hormone treatment, hormone replacement therapy, or endocrine therapy.

Hormone Chemicals produced by glands in the body and circulated in the bloodstream. Hormones control the actions of certain cells or organs.

Hormone Replacement Therapy (HRT) Hormones (estrogen, progesterone, or both) given to postmenopausal women or women who have had their ovaries surgically removed to replace the estrogen no longer produced by the ovaries.

Hyperplasia An abnormal increase in the number of cells in an organ or tissue.

Hypospadias A developmental abnormality in males in which the urethra (opening of the penis) is misplaced on the underside of the penis.

Hysterectomy An operation in which the uterus is removed.

Immune System The complex group of organs and cells that defends the body against infection and disease.

Incidence The number of new cases of a disease diagnosed each year.

Incisional Biopsy A surgical procedure in which a portion of a lump or suspicious area of tissue is removed for diagnosis. The tissue is then examined under a microscope.

Infertility The inability to produce children.

Inflammatory Breast Cancer A type of breast cancer in which the breast looks red and swollen and feels warm. The skin of the breast may also show the pitted appearance called peau d'orange (like the skin of an orange). The redness and warmth occur because the cancer cells block the lymph vessels in the skin.

In Situ Cancer Early cancer that has not spread to neighboring tissue.

Institutional Review Board (IRB) A group that may include scientists, physicians, clergy, and consumers at agencies and other facilities that participates in clinical trials. IRBs are designed to protect research participants. They review and must approve the action plan for every clinical trial. They check to see that the trial is well designed, does not involve undue risks, and includes safeguards for research participants.

Invasive Cervical Cancer Cancer that has spread from the surface of the cervix to tissue deeper in the cervix or to other parts of the body.

Laboratory Study Research done in a laboratory. These studies may use test tubes or animals to find out if a drug, procedure, or treatment is likely to be useful. Laboratory studies take place before testing is done in humans.

Laboratory Test A medical procedure that involves testing a sample of blood, urine, or other substance from the body. These tests can help determine a diagnosis, plan treatment, check to see if treatment is working, or monitor a disease over time.

Lesion An area of abnormal tissue change.

Leuprolide A drug that belongs to a family of drugs called gonadotropin-releasing hormone analogues. It is used to block hormone production in the ovaries or testicles.

Lupus A chronic inflammatory connective tissue disease marked by skin rashes, joint pain and swelling, inflammation of the kidneys, inflammation of the fibrous tissue surrounding the heart, and other problems. Not all affected persons have all of these problems. Also called systemic lupus erythematosus.

Lutenizing Hormone-Releasing Hormone (LH-RH) A hormone that stimulates the production of sex hormones in men and women.

Lutenizing Hormone-Releasing Hormone (LH-RH) Agonist A drug that inhibits the secretion of sex hormones. In men, LH-RH agonist causes testosterone levels to fall. In women, LH-RH agonist causes the levels of estrogen and other sex hormones to fall.

Lymph Gland A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph glands are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic (lymph) fluid.

Malignant Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body.

Mammogram An X-ray of the breast.

Mayo Clinic Sons Study The Sons Study included approximately 800 men exposed to DES before birth (in the womb) and 600 unexposed men. This cohort was identified by review of medical records of women who gave birth at Mayo Clinic hospitals.

Menopause The time of life when a woman's menstrual periods stop permanently. Also called change of life.

Menstrual Cycle The monthly cycle of a woman's hormonal changes from the beginning of one menstrual period to the beginning of the next.

Menstruation Periodic discharge of blood and tissue from the uterus (womb). Until menopause, menstruation occurs approximately every 28 days when a woman is not pregnant.

Microphallus A smaller than normal penis.

Miscarriage When a fetus leaves the uterus before the fifth month of pregnancy.

Myometrium The muscular outer layer of the uterus.

National Cancer Institute (NCI) Part of the National Institutes of Health of the United States Department of Health and Human Services. NCI is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs regarding the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at www.cancer.gov.

National Institutes of Health (NIH) Part of the United States Department of Health and Human Services. NIH is the federal government's principal agency for biomedical research. NIH conducts research in its own laboratories; supports the research of non-federal scientists in universities, medical schools, hospitals, and research institutions throughout the country and abroad; helps in the training of research investigators; and fosters communication of medical information. Access the NIH Web site at www.nih.gov.

Neuroendocrine Having to do with the interactions between the nervous system and the endocrine system. Certain cells release hormones into the blood in response to stimulation of the nervous system.

Nonmalignant Not cancerous.

Observation Closely monitoring a patient's condition without treatment until symptoms appear or change. Also called watchful waiting.

Oncogene A gene that normally directs cell growth. If altered, an oncogene can promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by an environmental exposure to carcinogens.

Oncologist A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment. For example, a radiation oncologist specializes in treating cancer with radiation.

Oophorectomy A surgical procedure to remove one or both ovaries.

Orchiectomy A surgical procedure to remove one or both testicles.

Osteoporosis A condition that is characterized by a decrease in bone mass and density and causes bones to become fragile.

Ovarian Suppression A surgical procedure, radiation therapy, or a drug treatment to stop the functioning of the ovaries. Also called ovarian ablation.

Ovaries The pair of female reproductive glands in which the eggs (ova) are formed. The ovaries are located in the pelvis, one on each side of the uterus (womb).

Ovulation The release of an egg from an ovary during the menstrual cycle.

Pap Smear The collection of cells from the cervix for examination under a microscope. Pap smears are used to detect changes that may be cancer or may lead to cancer (pre-cancerous) and can detect non-cancerous conditions (such as infection or inflammation). Also called a Pap test.

Patient Advocate A person who helps a patient work with others who have an effect on the patient's health, including doctors, insurance companies, employers, case managers, and lawyers. A patient advocate helps resolve issues about health care, medical bills, and job discrimination related to a patient's medical condition. Patient advocacy groups try to raise public awareness about important health issues (such as the need for support services, education, and research). Such groups work to bring about change that will help patients and their families.

Pelvic Having to do with the pelvis (the lower part of the abdomen located between the hip bones).

Perimenopausal The time in a woman's life when menstrual periods become irregular. Refers to the time near menopause.

Pilot Study The initial study examining a new method or treatment.

Placenta The organ that nourishes the developing fetus in the uterus.

Postmenopausal The time in a woman's life after menopause.

Pre-cancerous A term used to describe a condition that might or is likely to become cancer. Also called premalignant.

Premenopausal The time in a woman's life before menopause.

Prescription A doctor's order for medicine or another treatment.

Primary Care Physician A doctor who manages a person's health care over time. A primary care physician can provide a wide range of care (including prevention and treatment) can discuss treatment choices, and can refer a patient to a specialist.

Progesterone A female hormone.

Progesterone Receptor Negative (PR-) Breast cancer cells that do not have a protein (receptor molecule) to which progesterone will attach. Breast cancer cells that are PR- do not need the hormone progesterone to grow and usually do not respond to hormonal therapy.

Progesterone Receptor Positive (PR+) Breast cancer cells that have a protein (receptor molecule) to which progesterone will attach. Breast cancer cells that are PR+ need the hormone progesterone to grow and will usually respond to hormonal therapy.

Prospective A research study or clinical trial in which participants are identified and then followed over time.

Prostate A gland in the male reproductive system just below the bladder. The prostate surrounds part of the urethra, the canal that empties the bladder, and produces a fluid that forms part of semen.

Prostate-Specific Antigen (PSA) A substance produced by the prostate that may be found in an increased amount in the blood of men who have prostate cancer, benign prostatic hyperplasia, or infection or inflammation of the prostate.

p-value A term used in statistics. A p-value expresses statistical significance in scientific studies. P-values are calculated using a statistical formula that includes the number of people and health effects being studied. It is designed to answer the question, "Could a group of this many people, who all experienced a common exposure, have had this health problem in common by chance alone?" It is standard practice to consider a finding statistically significant if there is less than a 5% probability (p=.05 or less) that the findings resulted from chance. Conversely, if there is greater than a 5% probability (p=.06 or greater) that a finding was due to chance, the finding is not statistically significant.

Raloxifene A drug that belongs to the family of drugs called selective estrogen receptor modulators (SERMs) and is used in the prevention of osteoporosis in postmenopausal women. Raloxifene is also being studied as a cancer-prevention drug.

Receptor A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell.

Registry for Research on Hormonal Transplacental Carcinogenesis The Registry was established at Massachusetts General Hospital in 1971 to track incidence of clear cell adenocarcinoma (CCA) of the vagina or cervix. Originally numbering 21 cases, by 2002 approximately 750 cases were recorded at the registry. Most of the information on treatment outcome and recurrence rates of CCA has come from the study of patients in the Registry. The registry is now located at the University of Chicago (Department of Obstetrics and Gynecology, The University of Chicago, 5841 South Maryland Avenue, Mail Code 2050, Chicago, IL, 60637. Phone: 773-702-6671. Fax: 773-702-5161).

Reproductive Cells Egg and sperm cells. Each mature reproductive cell carries a single set of 23 chromosomes.

Reproductive System In women, this system includes the ovaries, fallopian tubes, uterus (womb), cervix, and vagina (birth canal). The reproductive system in men includes the prostate, testes, and penis.

Retrospective Study A study that looks backward in time, usually using medical records and interviews with patients who already have or had a disease.

Risk Factor Anything that increases a person's chance of developing a disease, including a substance, agent, genetic alteration, trait, habit, or condition.

Salpingo-Oophorectomy A surgical procedure to remove the fallopian tubes and ovaries.

Sarcoma A cancer of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.

Scrotum In males, the external sac that contains the testicles.

Selective Estrogen Receptor Modulator (SERM) A drug that acts like estrogen on some tissues but blocks the effect of estrogen on other tissues. Tamoxifen and raloxifene are SERMs.

Semen The fluid that is released through the penis during orgasm. Semen is made up of sperm from the testicles and fluid from the prostate and other sex glands.

Seminal Fluid The fluid from the prostate and other sex glands that helps transport sperm out of the man's body during orgasm. Seminal fluid contains sugar as an energy source for sperm.

Seminal Vesicles Glands that help produce semen.

Side Effects Problems that occur when treatment affects healthy cells. For example, common side effects of cancer treatment are fatigue, nausea, vomiting, decreased blood cell counts, hair loss, and mouth sores.

Speculum An instrument used to widen an opening of the body to make it easier to look inside.

Squamous Cell Carcinoma Cancer that begins in squamous cells, which are thin, flat cells resembling fish scales. Squamous cells are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the passages of the respiratory and digestive tracts. Also called epidermoid carcinoma.

Squamous Cells Flat cells that look like fish scales under a microscope. These cells cover internal and external surfaces of the body.

Squamous Intraepithelial Lesion (SIL) A general term for the abnormal growth of squamous cells on the surface of the cervix. The changes in the cells are described as low grade or high grade, depending on how much of the cervix is affected and how abnormal the cells appear.

Statistically Significant A statistical concept used to determine causal links or associations in scientific studies. Statistical significance is expressed in scientific studies by a probability value (p-value). P-values are calculated using a statistical formula that includes the number of people and health effects being studied and is designed to answer the question, "Could a group of this many people, who all experienced a common exposure, have had this health problem in common by chance alone?" It is standard practice to consider a finding statistically significant if there is less than a 5% probability (p=.05 or less) that the findings resulted from chance. Conversely, if there is greater than a 5% probability (p=.06 or greater) that a finding was due to chance, the finding is not statistically significant.

T-shaped Uterus A structural malformation in which the uterus resembles the letter "T" rather than the letter "U."

Tamoxifen An anticancer drug that belongs to the family of drugs called antiestrogens. Tamoxifen blocks the effects of the hormone estrogen in the body. It is used to prevent or delay the return of breast cancer or to control its spread.

Testosterone A hormone that promotes the development and maintenance of male sex characteristics.

Third Generation The offspring (children) of DES Daughters or Sons. Also called DES Grandchildren.

Total Hysterectomy Surgery to remove the entire uterus, including the cervix. Also called complete hysterectomy.

Tubal Ligation An operation to tie the fallopian tubes closed. This procedure prevents pregnancy by blocking the passage of eggs (ova) from the ovaries to the uterus (womb).

Undescended Testicles A condition in which one or both testicles fail to move from the abdomen, where they develop before birth, into the scrotum. Also called cryptorchidism.

Urologist A physician who specializes in diseases of the urinary organs in females and the urinary and sex organs in males.

Uterus The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the womb.

Vagina The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal.

Vaginal Adenosis Cellular changes on the surface of the vagina. Adenosis is a type of tissue on the surface of the vagina that is usually not found on the vagina. Vaginal adenosis is benign (non-cancerous). Over time, vaginal adenosis is usually replaced by normal tissue. Monitoring adenosis is recommended, but no treatment is necessary.

Vulva The external female genital organs, including the clitoris, vaginal lips, and the opening to the vagina.

Womb The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the uterus.

DES BIBLIOGRAPHY

Overview

Much has been written about the health risks of DES exposure and other topics related to DES. To help you find more information about a specific topic or study, a list of published research and other sources of DES is included below. The list is organized by main topic. This section of CDC's DES Update includes a bibliography organized by the following topics.

- History
- Women Prescribed DES While Pregnant
- Women Exposed to DES Before Birth (In the Womb), Known as DES Daughters
  - Structural/Functional Differences
  - Fertility
  - Clear Cell Adenocarcinoma (CCA)
  - Other Cancer
- Men Exposed to DES Before Birth (In the Womb), Known as DES Sons
- Third Generation (Offspring of DES Daughters and Sons)
- Immunology
- Psychology
- Reviews
- General

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DES *Self-Assessment*

A Guide to Understanding Your Risk for DES Exposure

1938–1971: DES prescribed for pregnant women
1971–2002: Research identifies long-term DES health risks
2003: CDC's DES UPDATE begins...

CDC
SAFER • HEALTHIER • PEOPLE™

What is DES?

Diethylstilbestrol (DES) is a synthetic estrogen that was developed to supplement a woman's natural estrogen production. First prescribed by physicians in 1938 for women who experienced miscarriages or premature deliveries, DES was originally considered effective and safe for both the pregnant woman and the developing baby. In the United States, an estimated 5–10 million persons were exposed to DES during 1938–1971, including women who were prescribed DES while pregnant and the female and male children born of these pregnancies. In 1971, the Food and Drug Administration (FDA) issued a Drug Bulletin advising physicians to stop prescribing DES to pregnant women because it was linked to a rare vaginal cancer in female offspring.

Is There a Medical Test for DES Exposure?

No known medical test (such as blood, urine or skin analysis) has been developed that can detect DES exposure. However, the DES Self-Assessment Guide is designed to help you assess whether you might have been exposed to DES.

Who Should Use the DES Self-Assessment Guide?

- **Women** pregnant between 1938 and 1971
- **Women** born between 1938 and 1971
- **Men** born between 1938 and 1971

Note: Women who were BOTH born AND pregnant during 1938–1971 should respond to the statements for both women who were pregnant and women who were born during 1938–1971.

This self-assessment is part of the Centers for Disease Control and Prevention's DES Update – information for you, your family, and your health care provider.

Available at no charge by calling toll-free 1-888-232-6789 or visiting www.cdc.gov/DES.

Known Health Risks of DES Exposure

More than 30 years of research have confirmed that health risks are associated with DES exposure. However, not all exposed persons will experience DES-related health problems.

Research published 1971–2002 linked DES exposure with increased health risks:

WOMEN PRESCRIBED DES WHILE PREGNANT. These women are at a modestly increased risk for

- Breast cancer

WOMEN EXPOSED TO DES BEFORE BIRTH (in the womb), known as DES Daughters, are at an increased risk for

- Clear cell adenocarcinoma (CCA) of the vagina and cervix
- Reproductive tract structural differences
- Pregnancy complications
- Infertility

MEN EXPOSED TO DES BEFORE BIRTH (in the womb), known as DES Sons, are at an increased risk for

- Non-cancerous epididymal cysts

What Does the Term "Increased Health Risk" Mean?

Increased risk means that the women and men who were exposed to DES are more likely to have certain health problems than people who were not exposed.

The Self-Assessment will guide you through 4 Steps. **Please turn the page for Step 1.**

DES *Self-Assessment Step 1*

How Do I Use the Self-Assessment?

The Self-Assessment has 4 Steps. Start with Step 1 on this page.

- Read each numbered statement.
- Mark your personal responses: **Yes/Not Sure (NS), No/Not Applicable (NA)**
- Follow directions in the section, **"What do my responses mean?"** at the bottom of each page.

1. When I was pregnant,* I had regular medical care. . . . . ○ **Yes/NS** ○ **No/NA**

2. When my mother was pregnant with me,* she had regular medical care. . . . . ○ **Yes/NS** ○ **No/NA**

3. I was prescribed DES when I was pregnant.* . . . . . ○ **Yes/NS** ○ **No/NA**

4. When my mother was pregnant with me,* she was prescribed DES. . . . . ○ **Yes/NS** ○ **No/NA**

**during 1938–1971*

How Was DES Given to Pregnant Women?

Women who obtained DES were required to have a physician's prescription filled by a pharmacist, although some physicians gave DES directly to their patients. Therefore, women who were not under a physician's care during their pregnancy most likely did not receive the drug.

Note: DES is sometimes confused with the drug Thalidomide that caused birth defects. Thalidomide was never approved for prescription in the United States. DES was called by different labels. Some of the most common were stilbestrol and DESPlex.

WHAT DO MY RESPONSES MEAN?

If you marked Yes/Not Sure to any of the statements 1–4, continue to STEP 2.

If you marked No/Not Applicable to all statements 1–4, it is unlikely that you were exposed to DES. However, it is still important for you to receive regular health checkups and consult with your health care provider about any potential health problems.

DES *Self-Assessment Step 2*

All women and men who responded Yes/Not Sure to any of the statements 1–4 should continue to respond to statements 5–8.

5. My mother had at least one miscarriage* before I was born. ..... ○ **Yes/NS** ○ **No/NA**

6. My mother's doctor prescribed medication to treat or help prevent pregnancy problems while she was pregnant with me.* ..... ○ **Yes/NS** ○ **No/NA**

7. I had at least one miscarriage.* ..... ○ **Yes/NS** ○ **No/NA**

8. My doctor prescribed medication while I was pregnant* to treat or help prevent pregnancy problems. ..... ○ **Yes/NS** ○ **No/NA**

**during 1938–1971*

How Did Physicians Decide to Prescribe DES?

Most women who were prescribed DES had a history of miscarriage and/or giving birth prematurely before the pregnancy when they were prescribed DES. DES was prescribed in different forms (most commonly as a pill); but it also was given by injection or as a vaginal suppository.

WHAT DO MY RESPONSES MEAN?

If you marked Yes/Not Sure to any of the statements 5–8, continue to STEP 3.

If you marked No/Not Applicable to all statements 5–8, it is unlikely that you were exposed to DES. However, it is still important for you to receive regular health checkups and consult with your health care provider about any potential health problems.

DES *Self-Assessment Step 3*

If you are a woman, respond to statements 9–14;
if you are a man, skip these statements and respond to statements 15–17.

Women PREGNANT between 1938 and 1971

9. I have been diagnosed with breast cancer. . . . . ○ **Yes/NS** ○ **No/NA**

10. My daughter has been diagnosed with one or more of the following conditions: clear cell cancer of the vagina or cervix, infertility, ectopic (tubal) pregnancy, miscarriage. . . . . ○ **Yes/NS** ○ **No/NA**

11. My son has had non-cancerous growths on the outside of the testicles or other genital abnormalities. . . . . ○ **Yes/NS** ○ **No/NA**

Women BORN between 1938 and 1971

12. I have experienced problems becoming pregnant. . . . . ○ **Yes/NS** ○ **No/NA**

13. I have had an ectopic (tubal) pregnancy and/or a miscarriage. . . . . ○ **Yes/NS** ○ **No/NA**

14. My physician has said that some of my reproductive organs are irregular in shape or structure (for example, a T-shaped uterus). ○ **Yes/NS** ○ **No/NA**

Men BORN between 1938 and 1971

15. I was born with undescended testicles. . . . . ○ **Yes/NS** ○ **No/NA**

16. I have had non-cancerous growths on the outside of the testicles (epididymal cysts). . . . . ○ **Yes/NS** ○ **No/NA**

17. I have had other genital abnormalities. . . . . ○ **Yes/NS** ○ **No/NA**

If I Have a Health Condition Listed Above, Does That Mean I Have Been Exposed to DES?

Not necessarily. People exposed to DES are at an increased risk for developing these conditions, but all of these problems also can occur in persons not exposed to DES.

WHAT DO MY RESPONSES MEAN?

If you marked Yes/Not Sure to any of the statements 9–17, continue to STEP 4.

If you marked No/Not Applicable for all statements 9–17, you have not experienced the known health problems linked to DES exposure. It is still important for you to receive regular health checkups and consult with your health care provider about any potential health problems.

DES *Self-Assessment Step 4*

What Should I Do Next?

Remember that the DES SELF-ASSESSMENT is a guide. Its main purpose is to provide information on the conditions and health risks of DES exposure. The DES SELF-ASSESSMENT cannot determine whether or not you were exposed to DES.

If you have responded Yes/Not Sure to one or more of the 17 numbered statements in Steps 1–3, you have some characteristics or conditions linked to DES exposure and should be aware of the possibility of DES exposure as part of your health history.

- Review the information in each statement where you responded Yes/Not Sure.
- Use the information in those statements to start a discussion about DES with your health care provider, your family, and friends.
- Consult CDC's DES Update available by calling toll-free 1-888-232-6789 or visiting www.cdc.gov/DES. You can also refer to "Additional DES Resources" listed on the back cover.

Suggested Steps for Women Pregnant or Born During 1938–1971 and Men Born during These Years

WOMEN PREGNANT BETWEEN 1938 AND 1971

- Contact your health care provider if you discover breast lumps.
- Be sure to get your recommended mammograms and have regular checkups.
- Discuss DES with your family, especially any child you were pregnant with when you might have been prescribed DES.

WOMEN BORN BETWEEN 1938 AND 1971

- Schedule regular gynecological exams, including a Pap test, pelvic exam, clinical breast exam, and recommended mammogram.

MEN BORN BETWEEN 1938 AND 1971

- Contact your health care provider if you feel lumps in your testicles.

Additional DES *Resources*

Use the contact information for these organizations and agencies to find out more about DES-related health risks and to locate free or low-cost health screenings.

Centers for Disease Control and Prevention
4770 Buford Highway NE, Mailstop F-29
Atlanta, GA 30033
Toll-free: 1-888-232-6789
Web site: www.cdc.gov/DES

CDC's Reproductive Health Information Source
Women's reproductive health;
Men's reproductive health;
Research and scientific reports
Web site: www.cdc.gov/nccdphp/drh/

CDC National Breast and Cervical Cancer Early Detection Program
A service providing information about where you can get a free or low-cost mammogram or Pap test.
Toll-free: 1-888-842-6355
Web site: www.cdc.gov/cancer/nbccedp/index.htm

Center for Medicare and Medicaid Services –
The following publications are available.
"Your Medicare Benefits"
"Women with Medicare – Visiting Your Doctor for a Pap Test, Pelvic Exam, and Clinical Breast Exam"
"Medicare Preventative Services to Keep You Healthy"
Toll-free: 1-800-MEDICARE (1-800-633-4227)
Web site: www.medicare.gov

DES Action USA
610 16th Street, Suite 301
Oakland, CA 94612
Toll-free: 1-800-DES-9288 (1-800-337-9288)
Phone: 510-465-4011
Fax: 510-465-4815
Web site: www.desaction.org
E-mail: desaction@earthlink.net

DES Sons Network
104 Sleepy Hollow Place
Cherry Hill, NJ 08003
E-mail: msfreilick@hotmail.com

DES Cancer Network
P.O. Box 220465
Chantilly, VA 20153-0465
Toll-free: 1-800-DESNET4 (1-800-337-6384)
Phone: 202-628-6330
Fax: 202-628-6217
Web site: www.descancer.org
E-mail: desnetwrk@aol.com

National Cancer Institute's Cancer Information Service
A service providing information on all types of cancer.
Toll-free: 1-800-4-CANCER (1-800-422-6237)
TTY Line: 1-800-332-8615
Web site: www.cancer.gov

Where Can I Get Additional Copies of the DES Self-Assessment?

You can request printed copies by calling CDC's toll-free number 1-888-232-6789. The Self-Assessment is also available online at CDC's DES Update Web site at www.cdc.gov/DES.