

# KNOWN DES HEALTH EFFECTS

## Overview

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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](http://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](http://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

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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

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### 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

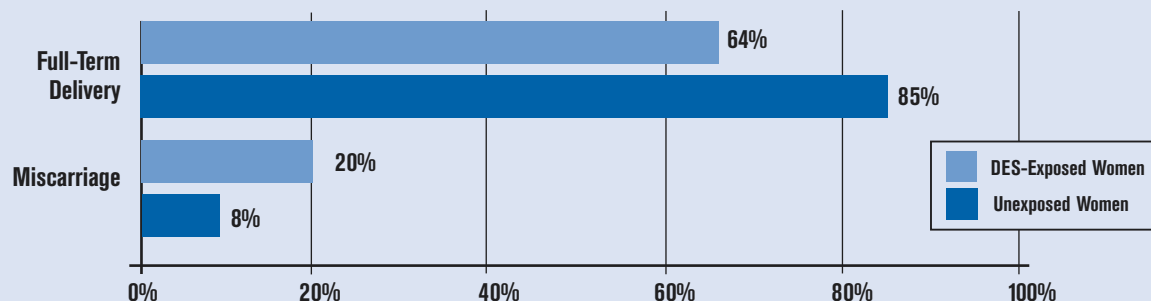
Most DES Daughters will be able to conceive and carry a healthy baby to term. However, DES Daughters are at an increased risk of reproductive problems, including complications during pregnancy and infertility.

- **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

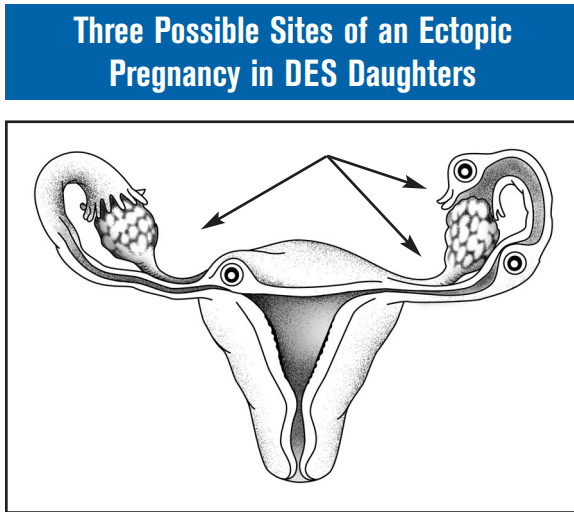
If you are a DES Daughter, it is critical that you tell your health care provider when you begin planning your pregnancy. Many of the risk factors associated with DES exposure during pregnancy are preventable or treatable if you take action. Any pregnancy of a DES Daughter should be treated as “high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

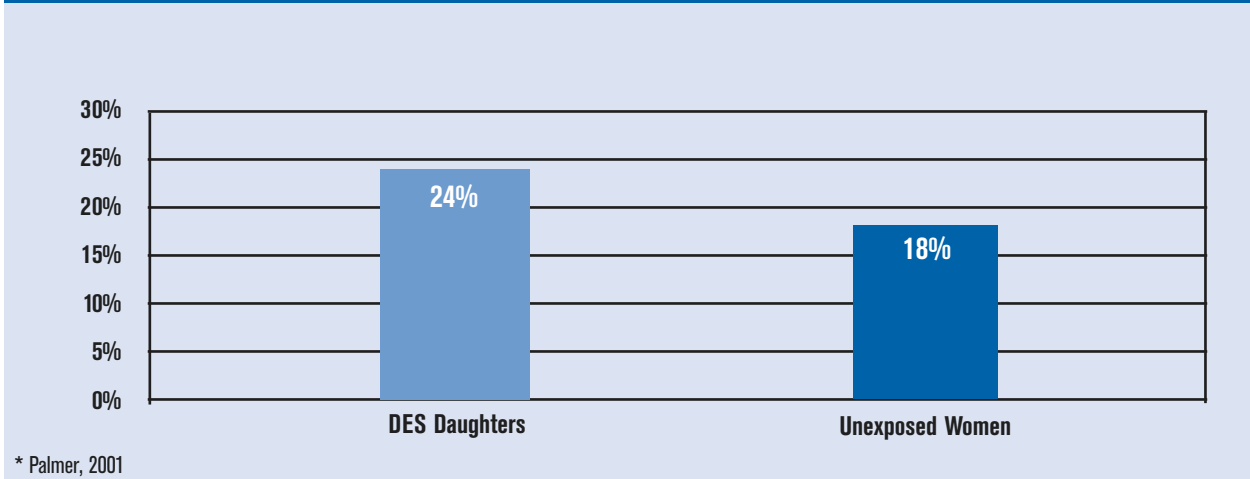
- Other Pregnancy Complications.** DES Daughters are also at an increased risk for other complications during pregnancy, including ectopic (tubal) pregnancy, and miscarriage. Estimates of a DES Daughter's risk for an ectopic pregnancy range from 3–5 times higher than the risk for a woman not exposed 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).



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

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### 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

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### 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?

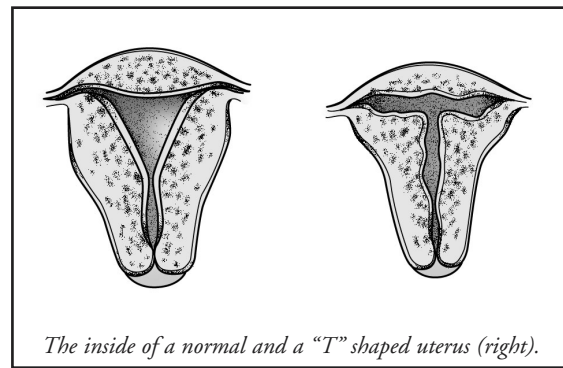
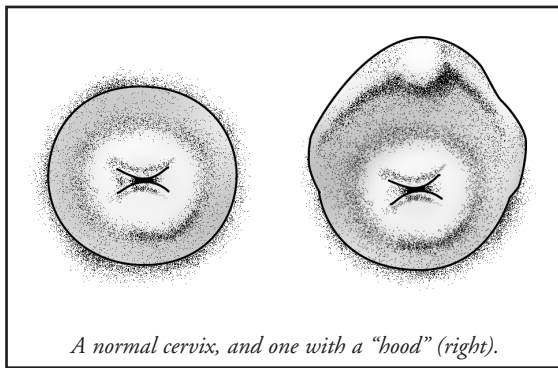
Your risk of experiencing infertility or pregnancy complications depends on what reproductive tract structural difference you have. An “abnormal” structure is not necessarily a faulty one; it could just mean that an organ is shaped differently or has an additional feature that is not usually present (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



### 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](#).