

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 (Trichopoulos, 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](#).