NIH NATIONAL CANCER INSTITUTE

Reproductive History and Cancer Risk

Is there a relationship between pregnancy and breast cancer risk?

Studies have shown that a woman's risk of developing breast cancer is related to her exposure to hormones that are produced by her ovaries (endogenous estrogen and progesterone). Reproductive factors that increase the duration and/or levels of exposure to ovarian hormones, which stimulate cell growth, have been associated with an increase in breast cancer risk. These factors include early onset of menstruation, late onset of menopause, and factors that may allow breast tissue to be exposed to high levels of hormones for longer periods of time, such as later age at first pregnancy and never having given birth.

Conversely, pregnancy and breastfeeding, which both reduce a woman's lifetime number of menstrual cycles, and thus her cumulative exposure to endogenous hormones (1), are associated with a decrease in breast cancer risk. In addition, pregnancy and breastfeeding have direct effects on breast cells, causing them to differentiate, or mature, so they can produce milk. Some researchers hypothesize that these differentiated cells are more resistant to becoming transformed into cancer cells than cells that have not undergone differentiation (2, 3).

Are any pregnancy-related factors associated with a lower risk of breast cancer?

Some pregnancy-related factors have been associated with a reduced risk of developing breast cancer later in life. These factors include:

- **Early age at first full-term pregnancy.** Women who have their first full-term pregnancy at an early age have a decreased risk of developing breast cancer later in life. For example, in women who have a first full-term pregnancy before age 20, the risk of developing breast cancer is about half that of women whose first full-term pregnancy occurs after the age of 30 (4). This risk reduction is limited to hormone receptor–positive breast cancer; age at first full-term pregnancy does not appear to affect the risk of hormone receptor-negative breast cancer (5, 6).
- **Increasing number of births.** The risk of breast cancer declines with the number of children borne. Women who have given birth to five or more children have half the breast cancer risk of women who have not given birth (7). Some evidence indicates that the reduced risk associated with a higher number of births may be limited to hormone receptor-positive breast cancer.
- **History of preeclampsia.** Women who have had preeclampsia may have a decreased risk of developing breast cancer (8–11). Preeclampsia is a complication of pregnancy in which a woman develops high blood pressure and excess amounts of protein in her urine. Scientists are studying whether certain hormones and proteins associated with preeclampsia may affect breast cancer risk

(8, 12, 13).

• Longer duration of breastfeeding. Breastfeeding for an extended period (at least a year) is associated with decreased risks of both hormone receptor–positive and hormone receptor–negative breast cancers (6, 14).

Are any pregnancy-related factors associated with an increase in breast cancer risk?

Some factors related to pregnancy may increase the risk of breast cancer. These factors include:

- Older age at birth of first child. The older a woman is when she has her first full-term pregnancy, the higher her risk of breast cancer. Women who are older than 30 when they give birth to their first child have a higher risk of breast cancer than women who have never given birth (15).
- **Recent childbirth.** Women who have recently given birth have a short-term increase in breast cancer risk that declines after about 10 years. The reason for this temporary increase is not known, but some researchers believe that it may be due to the effect of high levels of hormones on the development of cancers or to the rapid growth of breast cells during pregnancy (16).
- **Taking diethylstilbestrol (DES) during pregnancy.** DES is a synthetic form of estrogen that was used between the early 1940s and 1971 to prevent miscarriages and other pregnancy problems. Women who took DES during pregnancy may have a slightly higher risk of developing breast cancer than women who did not take DES during pregnancy (17). Some studies have shown that daughters of women who took DES during pregnancy may also have a slightly higher risk of developing breast cancer after age 40 than women who were not exposed to DES while in the womb (18), but the evidence is inconsistent (19).

Is abortion linked to breast cancer risk?

A few retrospective (case-control) studies reported in the mid-1990s suggested that induced abortion (the deliberate ending of a pregnancy) was associated with an increased risk of breast cancer. However, these studies had important design limitations that could have affected the results. A key limitation was their reliance on self-reporting of medical history information by the study participants, which can introduce bias. Prospective studies, which are more rigorous in design and unaffected by such bias, have consistently shown no association between induced abortion and breast cancer risk (20–25). Moreover, in 2009, the Committee on Gynecologic Practice of the American College of Obstetricians and Gynecologists concluded that "more rigorous recent studies demonstrate no causal relationship between induced abortion and a subsequent increase in breast cancer risk" (26). Major findings from these studies include:

- Women who have had an induced abortion have the same risk of breast cancer as other women.
- Women who have had a spontaneous abortion (miscarriage) have the same risk of breast cancer as other women.
- Cancers other than breast cancer also appear to be unrelated to a history of induced or spontaneous abortion.

Does pregnancy affect the risk of other cancers?

Research has shown the following with regard to pregnancy and the risk of other cancers:

- Women who have had a full-term pregnancy have reduced risks of ovarian (27, 28) and endometrial (29) cancers. Furthermore, the risks of these cancers decline with each additional full-term pregnancy.
- Pregnancy also plays a role in an extremely rare type of tumor called a gestational trophoblastic tumor. In this type of tumor, which starts in the uterus, cancer cells grow in the tissues that are formed following conception.
- There is some evidence that pregnancy-related factors may affect the risk of other cancer types, but these relationships have not been as well studied as those for breast and gynecologic cancers. The associations require further study to clarify the exact relationships.

As in the development of breast cancer, exposures to hormones are thought to explain the role of pregnancy in the development of ovarian, endometrial, and other cancers. Changes in the levels of hormones during pregnancy may contribute to the variation in risk of these tumors after pregnancy (30).

Does fertility treatment affect the risk of breast or other cancers?

Women who have difficulty becoming pregnant or carrying a pregnancy to term may receive fertility treatment. Such treatment can include surgery (to repair diseased, damaged, or blocked fallopian tubes or to remove uterine fibroids, patches of endometriosis, or adhesions); medications to stimulate ovulation; and assisted reproductive technology.

Ovarian stimulation and some assisted reproductive technologies involve treatments that temporarily change the levels of estrogen and progesterone in a woman's body. For example, women undergoing in vitro fertilization (IVF) receive multiple rounds of hormone treatment to first suppress ovulation until the developing eggs are ready, then stimulate development of multiple eggs, and finally promote maturation of the eggs. The use of hormones in some fertility treatments has raised concerns about possible increased risks of cancer, particularly cancers that are linked to elevated levels of these hormones.

Many studies have examined possible associations between use of fertility drugs or IVF and the risks of breast, ovarian, and endometrial cancers. The results of such studies can be hard to interpret because infertility itself is linked to increased risks of these cancers (that is, compared with fertile women, infertile women are at higher risk of these cancers even if they do not use fertility drugs). Also, these cancers are relatively rare and tend to develop years after treatment for infertility, which can make it difficult to link their occurrence to past use of fertility drugs.

- **Breast cancer:** The bulk of the evidence is consistent with no increased risk of breast cancer associated with the use of fertility drugs or IVF (31–34).
- **Ovarian cancer:** There is some uncertainty about whether treatment for infertility is a risk factor for ovarian cancer. A 2013 systematic review of 25 studies that included more than 180,000 women found, overall, no strong evidence of an increased risk of invasive ovarian cancer for women treated with

fertility drugs (35). In one study, women who underwent IVF had an increase in risk of ovarian borderline malignant tumors (36).

• **Endometrial cancer:** Overall, the use of fertility drugs or IVF does not appear to increase the risk of endometrial cancer (34).

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Related Resources

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