Oral Contraceptives and Cancer Risk: Questions and Answers

Key Points

- Some cancers depend on naturally occurring sex hormones for their development and growth. Researchers are interested in learning whether the hormones in oral contraceptives affect cancer risk in women (see Question 1).
- Some studies have shown an increased risk of breast cancer in women taking oral contraceptives, while other studies have shown no change in risk (see Question 2).
- Oral contraceptive use has been shown in multiple studies to decrease the risk of ovarian and endometrial cancer (see Question 3).
- Oral contraceptives have been shown to increase the risk of cervical cancer; however, human papillomavirus is the major risk factor for this disease (see Question 4).
- The risk of liver cancer is increased in women who take oral contraceptives and are otherwise considered low risk for the disease (see Question 5).

Introduction

Oral contraceptives (OCs) first became available to American women in the early 1960s. The convenience, effectiveness, and reversibility of action of birth control pills (popularly known as "the pill") have made them the most popular form of birth control in the United States. However, concerns have been raised about the role that the hormones in OCs might play in a number of cancers, and how hormone-based OCs contribute to their development. Sufficient time has elapsed since the introduction of OCs to allow investigators to study large numbers of women who took birth control pills for many years.

This fact sheet addresses only what is known about OC use and the risk of developing cancer. It does not deal with other serious side effects of OC use, such as the increased risk of cardiovascular disease for certain groups of women. Recently, alternative methods of delivering hormones for contraception have been developed, including a topical patch, vaginal ring, and intrauterine delivery system, but these products are too new to have been tested in clinical trials (research studies) for long-term safety and other effects (1). They also are not covered in this fact sheet.

1. What types of oral contraceptives are available in the United States? Why do researchers believe that oral contraceptives may influence cancer risk?

Currently, two types of OCs are available in the United States. The most commonly prescribed OC contains two man-made versions of natural female hormones (estrogen and progesterone) that are similar to the hormones the ovaries normally produce. This type of pill is often called a "combined oral contraceptive." The second type of OC available in the United States is called the minipill. It contains only a type of progesterone.

Estrogen stimulates the growth and development of the uterus at puberty, causes the endometrium (the inner lining of the uterus) to thicken during the first half of the menstrual cycle, and influences breast tissue throughout life, but particularly from puberty to menopause.

Progesterone, which is produced during the last half of the menstrual cycle, prepares the endometrium to receive the egg. If the egg is fertilized, progesterone secretion continues, preventing release of additional eggs from the ovaries. For this reason, progesterone is called the "pregnancy-supporting" hormone, and scientists believe that it has valuable contraceptive effects. The man-made progesterone used in OCs is called progestogen or progestin.

Because medical research suggests that some cancers depend on naturally occurring sex hormones for their development and growth, scientists have been investigating a possible link between OC use and cancer risk. Researchers have focused a great deal of attention on OC users over the past 40 years. This scrutiny has produced a wealth of data on OC use and the development of certain cancers, although results of these studies have not always been consistent. The risk of endometrial and ovarian cancers is reduced with the use of OCs, while the risk of breast and cervical cancers is increased (1). A summary of research results for each type of cancer is given in Questions 2–5.

2. How do oral contraceptives affect breast cancer risk?

A woman's risk of developing breast cancer depends on several factors, some of which are related to her natural hormones. Hormonal factors that increase the risk of breast cancer include conditions that may allow high levels of hormones to persist for long periods of time, such as beginning menstruation at an early age (before age 12), experiencing menopause at a late age (after age 55), having a first child after age 30, and not having children at all.

A 1996 analysis of worldwide epidemiologic data conducted by the Collaborative Group on Hormonal Factors in Breast Cancer found that women who were current or recent users of birth control pills had a slightly elevated risk of developing breast cancer. The risk was highest for women who started using OCs as teenagers. However, 10 or more years after women stopped using OCs, their risk of developing breast cancer returned to the same level as if they had never used birth control pills, regardless of family history of breast cancer, reproductive history, geographic area of residence, ethnic background,

differences in study design, dose and type of hormone, or duration of use. In addition, breast cancers diagnosed in women after 10 or more years of not using OCs were less advanced than breast cancers diagnosed in women who had never used OCs. To conduct this analysis, the researchers examined the results of 54 studies. The analysis involved 53,297 women with breast cancer and 100,239 women without breast cancer. More than 200 researchers participated in this combined analysis of their original studies, which represented about 90 percent of the epidemiological studies throughout the world that had investigated the possible relationship between OCs and breast cancer (2).

The findings of the Women's Contraceptive and Reproductive Experiences (Women's CARE) study were in contrast to those described above. The Women's CARE study examined the use of OCs as a risk factor for breast cancer in women ages 35 to 64. Researchers interviewed 4,575 women who were diagnosed with breast cancer between 1994 and 1998, and 4,682 women who did not have breast cancer. Investigators collected detailed information about the participants' use of OCs, reproductive history, health, and family history. The results, which were published in 2002, indicated that current or former use of OCs did not significantly increase the risk of breast cancer. The findings were similar for white and black women. Factors such as longer periods of use, higher doses of estrogen, initiation of OC use before age 20, and OC use by women with a family history of breast cancer were not associated with an increased risk of the disease (3).

In a National Cancer Institute (NCI)-sponsored study published in 2003, researchers examined risk factors for breast cancer among women ages 20 to 34 compared with women ages 35 to 54. Women diagnosed with breast cancer were asked whether they had used OCs for more than 6 months before diagnosis and, if so, whether the most recent use had been within 5 years, 5 to 10 years, or more than 10 years. The results indicated that the risk was highest for women who used OCs within 5 years prior to diagnosis, particularly in the younger group (4).

3. How do oral contraceptives affect ovarian and endometrial cancer risk?

Studies have consistently shown that using OCs reduces the risk of ovarian cancer. In a 1992 analysis of 20 studies of OC use and ovarian cancer, researchers from Harvard Medical School found that the risk of ovarian cancer decreased with increasing duration of OC use. Results showed a 10 to 12 percent decrease in risk after 1 year of use, and approximately a 50 percent decrease after 5 years of use (5).

Researchers have studied how the amount or type of hormones in OCs affects ovarian cancer risk reduction. One of the studies used in the Harvard analysis, the Cancer and Steroid Hormone Study (CASH), found that the reduction in ovarian cancer risk was the same regardless of the type or amount of estrogen or progestin in the pill (6). A more recent analysis of data from the CASH study, however, indicated that OC formulations with high levels of progestin reduced ovarian cancer risk more than preparations with low progestin levels (7). In another recent study, the Steroid Hormones and Reproductions (SHARE) study, researchers investigated new, lower-dose progestins that have varying

androgenic properties (testosterone-like effects). They found no difference in ovarian cancer risk between androgenic and nonandrogenic pills (8).

OC use in women at increased risk of ovarian cancer due to BRCA1 and BRCA2 genetic mutations has been studied. One study showed a reduction in risk, but a more recent study showed no effect (9, 10).

The use of OCs has been shown to significantly reduce the risk of endometrial cancer. This protective effect increases with the length of time OCs are used, and continues for many years after a woman stops using OCs (11).

4. How do oral contraceptives affect cervical cancer risk?

Evidence shows that long-term use of OCs (5 or more years) may be associated with an increased risk of cancer of the cervix (the narrow, lower portion of the uterus) (12). Although OC use may increase the risk of cervical cancer, human papillomavirus (HPV) is recognized as the major cause of this disease. Approximately 14 types of HPV have been identified as having the potential to cause cancer, and HPVs have been found in 99 percent of cervical cancer biopsy specimens worldwide (12). More information about HPV and cancer is available in *Human Papillomaviruses and Cancer: Questions and Answers* at http://www.cancer.gov/cancertopics/factsheet/risk/HPV on the Internet.

A 2003 analysis by the International Agency for Research on Cancer (IARC) found an increased risk of cervical cancer with longer use of OCs. Researchers analyzed data from 28 studies that included 12,531 women with cervical cancer. The data suggested that the risk of cervical cancer may decrease after OC use stops (13). In another IARC report, data from eight studies were combined to assess the effect of OC use on cervical cancer risk in HPV-positive women. Researchers found a fourfold increase in risk among women who had used OCs for longer than 5 years. Risk was also increased among women who began using OCs before age 20 and women who had used OCs within the past 5 years (14). The IARC is planning a study to reanalyze all data related to OC use and cervical cancer risk (12).

5. How do oral contraceptives affect liver cancer risk?

Several studies have found that OCs increase the risk of liver cancer in populations usually considered low risk, such as white women in the United States and Europe who do not have liver disease. In these studies, women who used OCs for longer periods of time were found to be at increased risk for liver cancer. However, OCs did not increase the risk of liver cancer in Asian and African women, who are considered high risk for this disease. Researchers believe this is because other risk factors, such as hepatitis infection, outweigh the effect of OCs (15).

6. What screening tests are available for the cancers described?

Studies have found that regular breast cancer screening with mammograms reduces the number of deaths from breast cancer for women ages 40 to 69. Women who are at increased risk for breast cancer should seek medical advice about when to begin having mammograms and how often to be screened. A high-quality mammogram, with a clinical breast exam (an exam done by a professional health care provider), is the most effective way to detect breast cancer early.

Abnormal changes in the cervix can often be detected by a Pap test and treated before cancer develops. Women who have begun to have sexual intercourse or are age 21 should check with their doctor about having a Pap test. Researchers are working on developing screening tests for ovarian and endometrial cancer.

Women who are concerned about their risk for cancer are encouraged to talk with their health care provider. More information is also available from the Cancer Information Service (see below).

Selected References

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Related Resources

Publications (available at http://www.cancer.gov/publications)

- National Cancer Institute Fact Sheet 3.20, *Human Papillomaviruses and Cancer: Questions and Answers*
- *What You Need To Know About™ Breast Cancer*
- *What You Need To Know About™ Cancer of the Cervix*

National Cancer Institute (NCI) Resources

Cancer Information Service (toll-free)

Telephone: 1–800–4–CANCER (1–800–422–6237)
TTY: 1–800–332–8615

Online

NCI's Web site: http://www.cancer.gov
LiveHelp, NCI's live online assistance:
https://cissecure.nci.nih.gov/livehelp/welcome.asp

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