NIH NATIONAL CANCER INSTITUTE

Oral Contraceptives and Cancer Risk

What types of oral contraceptives are available in the United States today?

Two types of oral contraceptives (birth control pills) are currently available in the United States. The most commonly prescribed type of oral contraceptive contains man-made versions of the natural female hormones estrogen and progesterone. This type of birth control pill is often called a "combined oral contraceptive." The second type is called the minipill. It contains only progestin, which is the man-made version of progesterone that is used in oral contraceptives.

How could oral contraceptives influence cancer risk?

Naturally occurring estrogen and progesterone have been found to influence the development and growth of some cancers. Because birth control pills contain female hormones, researchers have been interested in determining whether there is any link between these widely used contraceptives and cancer risk.

The results of population studies to examine associations between oral contraceptive use and cancer risk have not always been consistent. Overall, however, the risks of endometrial and ovarian cancer appear to be reduced with the use of oral contraceptives, whereas the risks of breast, cervical, and liver cancer appear to be increased (1). A summary of research results for each type of cancer is given below.

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 and reproductive history factors that increase the risk of breast cancer include factors that may allow breast tissue to be exposed to high levels of hormones for longer periods of time, such as the following:

- Beginning menstruation at an early age
- Experiencing menopause at a late age
- Later age at first pregnancy
- Not having children at all

A 1996 analysis of epidemiologic data from more than 50 studies worldwide 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 higher risk of developing breast cancer than women who had never used the pill (2). The risk was highest for women who started using oral contraceptives as teenagers. However, 10 or more

years after women stopped using oral contraceptives, their risk of developing breast cancer had 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(s) used, or duration of use. In addition, breast cancers diagnosed in women who had stopped using oral contraceptives for 10 or more years were less advanced than breast cancers diagnosed in women who had never used oral contraceptives.

A recent analysis of data from the Nurses' Health Study, which has been following more than 116,000 female nurses who were 24 to 43 years old when they enrolled in the study in 1989 (3), found that the participants who used oral contraceptives had a slight increase in breast cancer risk. However, nearly all of the increased risk was seen among women who took a specific type of oral contraceptive, a "triphasic" pill, in which the dose of hormones is changed in three stages over the course of a woman's monthly cycle.

Because the association with the triphasic formulation was unexpected, more research will be needed to confirm the findings from the Nurses' Health Study.

How do oral contraceptives affect ovarian cancer risk?

Oral contraceptive use has consistently been found to be associated with a reduced risk of ovarian cancer. In a 1992 analysis of 20 studies, researchers found that the longer a woman used oral contraceptives the more her risk of ovarian cancer decreased. The risk decreased by 10 to 12 percent after 1 year of use and by approximately 50 percent after 5 years of use (4).

Researchers have studied how the amount or type of hormones in oral contraceptives affects ovarian cancer risk. One study, the Cancer and Steroid Hormone (CASH) study, found that the reduction in ovarian cancer risk was the same regardless of the type or amount of estrogen or progestin in the pill (5). A more recent analysis of data from the CASH study, however, indicated that oral contraceptive formulations with high levels of progestin were associated with a lower risk of ovarian cancer than formulations with low progestin levels (6). In another study, the Steroid Hormones and Reproductions (SHARE) Study, researchers investigated new, lower-dose progestins that have varying androgenic (testosterone-like) effects. They found no difference in ovarian cancer risk between androgenic and nonandrogenic pills (7).

Oral contraceptive use by women at increased risk of ovarian cancer due to a genetic mutation in the *BRCA1* or *BRCA2* gene has been studied. One study showed a reduction in risk among *BRCA1*- or *BRCA2*-mutation carriers who took oral contraceptives, whereas another study showed no effect (8, 9). A third study, published in 2009, found that women with *BRCA1* mutations who took oral contraceptives had about half the risk of ovarian cancer as those who did not (10).

How do oral contraceptives affect endometrial cancer risk?

Women who use oral contraceptives have been shown to have a reduced risk of endometrial cancer. This protective effect increases with the length of time oral contraceptives are used and continues for many years after a woman stops using oral contraceptives (11).

How do oral contraceptives affect cervical cancer risk?

Long-term use of oral contraceptives (5 or more years) is associated with an increased risk of cervical cancer (12). An analysis of 24 epidemiologic studies found that the longer a woman used oral contraceptives, the higher her risk of cervical cancer. However, among women who stopped taking oral contraceptives, the risk tended to decline over time, regardless of how long they had used oral contraceptives before stopping (13).

In a 2002 report by the International Agency for Research on Cancer, which is part of the World Health Organization, data from eight studies were combined to assess the association between oral contraceptive use and cervical cancer risk among women infected with the human papillomavirus (HPV). Researchers found a nearly threefold increase in risk among women who had used oral contraceptives for 5 to 9 years compared with women who had never used oral contraceptives. Among women who had used oral contraceptives for 10 years or longer, the risk of cervical cancer was four times higher (14).

Virtually all cervical cancers are caused by persistent infection with high-risk, or oncogenic, types of HPV, and the association of cervical cancer with oral contraceptive use is likely to be indirect. The hormones in oral contraceptives may change the susceptibility of cervical cells to HPV infection, affect their ability to clear the infection, or make it easier for HPV infection to cause changes that progress to cervical cancer. Questions about how oral contraceptives may increase the risk of cervical cancer will be addressed through ongoing research (15).

How do oral contraceptives affect liver cancer risk?

Oral contraceptive use is associated with an increase in the risk of benign liver tumors, such as hepatocellular adenomas (16). Benign tumors can form as lumps in different areas of the liver, and they have a high risk of bleeding or rupturing. However, these tumors rarely become malignant (17).

Whether oral contraceptive use increases the risk of malignant liver tumors, also known as hepatocellular carcinomas, is less clear. Some studies have found that women who take oral contraceptives for more than 5 years have an increased risk of hepatocellular carcinoma, but others have not.

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