Uterine/Endometrial Cancers

Approximately 2.7% of women will be diagnosed with uterine cancer (cancer of the womb) during their lifetimes. There are many different causes and risk factors for developing uterine cancer, including genetics, environment, and chance. As with most cancers, a specific cause for the great majority of uterine cancers cannot be identified. Rather it is likely that there are multiple factors which play a part in the development of the cancer.

Some things that are known to increase the risk for uterine cancer are:

Demographics

- Age: the risk for uterine cancer (and most other cancers) increases as we get older. Most women with uterine cancer are diagnosed after menopause.
- Race: Uterine cancer is slightly more common in white women compared with other races.

Lifestyle/Environmental Factors

- Obesity: Obesity is a well known risk factor for uterine cancer. Studies have also shown that a high-fat diet can increase the risk of several cancers, including uterine cancer
- Sedentary lifestyle: Women who exercise more have a lower risk of uterine cancer

Hormonal Factors

- Estrogen-only hormone replacement therapy (HRT): Estrogen-based HRT taken after menopause can increase a woman's risk of uterine cancer. To lower this risk, a second hormone called progesterone is usually taken at the same time as estrogen replacement. This is called combination hormonal therapy, and it has not been shown to increase risk of uterine cancer.
- Number of menstrual cycles: Women who start their periods at a young age (prior to age 12) and/or enter menopause at a late age (after age 55) have a higher risk of uterine cancer
- Pregnancy: Women who have never been pregnant have a higher risk of uterine cancer

Personal Medical Factors

- Diabetes: Women with diabetes are 4 times as likely to develop uterine cancer
- Tamoxifen: Pre-menopausal women who take tamoxifen to treat or prevent breast cancer have an increased risk of uterine cancer
- Polycystic Ovarian Cancer Syndrome (PCOS): The hormonal imbalances associated with PCOS can result in an increased risk of uterine cancer
- Endometrial atypical hyperplasia: increased atypical growth of the endometrium (lining of the uterus) can turn into uterine cancer. Mild or simple hyperplasia is rarely associated with uterine cancer.
- Prior pelvic radiation: Radiation treatment for a prior cancer can damage nearby cells are increased risk for a new cancer

Family History

- Having a close relative who has been diagnosed with uterine cancer increases a woman's risk to develop the same type of cancer. This is likely due to a combination of shared environmental and genetic factors
- Some families have a very strong predisposition to uterine cancer called Lynch syndrome. Another name for Lynch syndrome is Hereditary Non-Polyposis Colorectal Cancer syndrome (HNPCC), which also increases the risk of colorectal cancer.

A small number of all uterine cancers are due to a genetic reason such as Lynch syndrome. However, families that show multiple relatives with uterine or colon cancer, early onset (under age 50) of uterine cancer, or being diagnosed with a new primary cancer multiple times may want to consider genetic counseling and possibly genetic testing for Lynch syndrome.

There are other less common hereditary predispositions to uterine cancer associated with other genes such as PTEN (Hamartoma Tumor syndrome/Cowden syndrome), TP53 (Li Fraumeni syndrome), STK11, and POLD1 (polymerase proofreading-associated polyposis syndrome).

Cancer Screening and Prevention

If you have risk factors for endometrial cancer, it is important to discuss this with your

gynecologist so that they can discuss warning signs and screening options. Healthcare providers may offer regular exams or ultrasounds of the pelvis to look for any concerning changes in the uterus/womb. Sometimes biopsies are used to see if these changes are cancerous even at an early stage. Finally, women at high risk of uterine cancer may be eligible to have their uterus removed through surgery to prevent a cancer (called a prophylactic hysterectomy).

Ovarian Cancer

Approximately 1 in 78 women (about 1.2%) will be diagnosed with ovarian cancer during their lifetimes. There are many different causes and risk factors for developing ovarian cancer, including genetics, environment, and chance. As with most cancers, a specific cause for the great majority of ovarian cancers cannot be identified. Rather it is likely that there are multiple factors which play a part in the development of the cancer.

There are three different types of cells within the ovary. Germ cells produce eggs, stromal cells produce the female hormones estrogen and progesterone, and epithelial cells cover the surface of the ovary. There are many types of ovarian tumors in all three types of cells which can be benign or malignant (cancerous), however the majority of malignant ovarian cancers (90%) begin in the epithelial cells (called *carcinomas*).

Some of the factors that are known to increase the risk for this more common epithelial ovarian cancer are:

Demographics

- Age: The risk for ovarian cancer (and most other cancers) increases as we get older and most are diagnosed in women who have entered menopause
- Race: Ovarian cancer is more common in white women

Hormonal Factors

- Estrogen-only hormone replacement therapy (HRT): Estrogen-based HRT taken after menopause can increase a woman’s risk of ovarian cancer when taken for a long period of time (at least 5-10 years). It is unclear if women who take HRT of estrogen combined with a second hormone called progesterone at the same time are also at increased risk of ovarian cancer.

- Pregnancy: Women who have their first full-term pregnancy after age 35 or have never been pregnant have a higher risk of ovarian cancer

Unclear risk factors

- Androgen hormones: Exposure to male hormones like testosterone appear to be linked to certain types of ovarian cancer however more studies are needed
- Talcum powder: There have been conflicting studies about whether there is a link between talcum powder and a higher risk of ovarian cancer. In those studies that show an increased risk of ovarian cancer, the overall increase is thought to be relatively small.

Family History

- Having a close relative who has been diagnosed with ovarian cancer increases a woman's risk to develop the same type of cancer. This is likely due to a combination of shared environmental and genetic factors.
- Some families have a very strong predisposition to ovarian cancer due to a genetic factor. In fact, up to 25% of all ovarian cancers are attributed to a hereditary cause and because of this high prevalence, all women diagnosed with epithelial ovarian cancer are recommended to undergo genetic testing. There are multiple well known genetic syndromes that increase the risk of ovarian cancer:
- Hereditary Breast and Ovarian Cancer syndrome (HBOC) due to mutations in the BRCA1 and BRCA2 genes
- Lynch syndrome (also known as Hereditary Non-Polyposis Colorectal Cancer), which increases the risk for uterine, ovarian, and colorectal cancer, among others.
- Peutz Jeghers syndrome
- RAD51C-related Ovarian Cancer
- RAD51D-related Ovarian Cancer
- BRIP1-related Ovarian Cancer

Cancer Screening and Prevention

If you have risk factors for ovarian cancer, it is important to discuss this with your

gynecologist so that they can discuss warning signs and screening options. Healthcare providers may offer regular exams or ultrasounds of the pelvis to look for any concerning changes in the uterus/womb. Blood tests to look for a marker of ovarian cancer (called CA-125) can also be used, but as of now the combination of pelvic ultrasounds and blood tests has not been shown to be an effective method of diagnosing ovarian cancer at an early stage.

Women at high risk of ovarian cancer may be eligible to have their ovaries and fallopian tubes removed through surgery to prevent a cancer (called a prophylactic bilateral salpingo-oophorectomy). Many ovarian cancers are thought to originate in the nearby fallopian tubes, so it is recommended to remove the tubes along with the ovaries.

Click here to learn more about scheduling a genetic counseling appointment for questions about hereditary cancer predisposition.

Additional Resources

*Positive Results Facebook Group
Genetic Support Foundation hosts a Facebook group for Hereditary Cancer Support and Resources. Get trusted information and join a community of support.
*Cascade Screening Connector
Genetic Support Foundation has partnered with the Washington State Department of Health to provide cascade screening to help people identify and contact family members who may have an increased chance of developing cancer.
*FORCE (Facing Our Risk of Cancer Empowered)
The FORCE mission is to improve the lives of individuals and families facing hereditary cancer. Resources include peer navigation and expert-reviewed information.
*AliveAndKicknAliveAndKickn is a nonprofit working to improve the lives of individuals and families affected by Lynch Syndrome and associated cancers through research, education, and screening.
*Health Experiences USAThis national research project brings patient voices into the healthcare experience and features video clips of people facing hereditary cancer. Individuals from a variety of backgrounds share both positive and negative experiences about living with hereditary cancer.