

## Hereditary Uterine Cancer

Most people develop uterine cancer by chance or as a result of risk factors that occur over the course of a lifetime. However, up to 10% (percent) of people who are diagnosed with uterine cancer develop it due to a hereditary uterine cancer syndrome.

A hereditary uterine cancer syndrome is an inherited increased risk to develop uterine cancer and possibly other cancers. Inherited conditions are passed to an individual through their blood relatives. People who have a hereditary uterine cancer gene mutation have a higher than average risk of developing uterine and possibly other cancers.

### What Causes Hereditary Uterine Cancer?

Hereditary uterine cancer syndromes are caused by an inherited change, called a mutation, in a gene. Genes are the set of instructions that tell all of the cells in our bodies what to do. Genes determine physical characteristics, such as our hair and eye color, the shape of our nose and our blood type.

A mutation is a change in a gene that causes it to stop working. In the case of hereditary uterine cancer, a gene that normally helps to prevent uterine and possibly some other cancers has stopped working. Therefore, these types of cancer are more likely to develop and are also more likely to occur at a younger age than usual.

The majority of hereditary uterine cancer is due to Lynch syndrome, which is caused by a mutation in one of five genes: *MLH1*, *MSH2*, *MSH6*, *PMS2* and *EPCAM*. A person who has a mutation in one of these genes has increased lifetime risks for colon, uterine, ovarian, stomach, skin and other cancers. Cowden syndrome is also associated with hereditary uterine cancer. Cowden syndrome, caused primarily by mutations in the *PTEN* gene, causes increased lifetime risks for breast, uterine, certain types of thyroid, colon, renal and other cancers. There are also a number of other genes, including *STK11* and *TP53*, that increase lifetime uterine and other cancer risks.

### How Is Hereditary Uterine Cancer Passed On Through a Family?

Each person inherits two copies of most genes. We receive one copy from our mother and one from our father. Inheriting a mutation in just one copy of a hereditary uterine cancer syndrome gene is enough to increase the risk for uterine and possibly also other types of cancer. There is a 50 percent chance that a person with a hereditary uterine cancer syndrome gene mutation will pass it to each of his or her children. However, if a person does not inherit the hereditary uterine cancer syndrome gene mutation present in his or her family member(s), there is an average risk of developing uterine cancer.

### Why Is It Important to Diagnose Hereditary Uterine Cancer in a Family?

People who have a hereditary uterine cancer syndrome have a greater than average chance to develop uterine and possibly other types of cancers. For someone who already has been diagnosed with uterine cancer, the diagnosis of a hereditary uterine cancer syndrome may indicate a greater chance of developing another cancer.

Because a hereditary uterine cancer syndrome is inherited, the diagnosis also affects family members. If genetic testing identifies a mutation in a gene that causes a hereditary uterine cancer syndrome, family members can be tested for that same gene mutation.

It is very important for people with a hereditary uterine cancer syndrome to consider specialized cancer screening exams. Cancer screening exams are medical tests performed to help identify cancers at their earliest, most treatable stages. They may also consider medical options that can lower their risk of developing cancer. Usually a team of specialists will tailor a cancer screening and risk reduction plan to each patient and his or her family members.

### **How Is Hereditary Uterine Cancer Diagnosed?**

A genetics evaluation, including review of a person's medical and family history, is completed. A multi-generation family tree, called a pedigree, is often drawn during the evaluation. This information is used to determine the likelihood that the person has a hereditary uterine cancer syndrome. A genetic counselor usually conducts this evaluation.

Some signs in a family history that suggest hereditary uterine cancer may include:

- Several close blood relatives with uterine, ovarian, colon or other related cancers on the same side of the family.
- Relatively early ages at the time of cancer diagnoses (< 50 years old).
- More than one primary cancer in one person (such as uterine and colon cancer or uterine and breast cancer).
- Uterine cancer that does not produce certain proteins or that has a feature called "microsatellite instability".

If you or your family members have any of the above features, you may consider the option of genetic counseling and testing. We encourage you to discuss this with your physicians.

### **Genetic Testing**

A person's blood or saliva sample can be tested to search for a genetic mutation that causes hereditary uterine cancer. This testing may be limited to the Lynch syndrome genes or may also include other genes that cause hereditary uterine cancer. In general, there are three types of results:

- Positive for a mutation. If a mutation is found, then the diagnosis of a hereditary uterine cancer syndrome is confirmed. Next, other family members may have a genetic test to learn whether or not they carry the same mutation and have the same hereditary uterine cancer syndrome.
- Negative for a mutation. If no mutation is found the cancer in the family may not be hereditary. However, a negative genetic test result does not eliminate the possibility of a hereditary uterine cancer syndrome in the family. This is because current genetic testing technology is not able to identify all mutations that cause hereditary uterine cancer. It is possible that uterine cancer in the family is caused by a gene that was not included in the test.
- Variant of unknown significance. A variant is a gene change that does not provide clear information regarding cancer risks. More research is needed to determine whether a genetic variant increases cancer risks. Thus, a variant result should not be used to make medical decisions.

If you are concerned about the possibility of a hereditary cancer syndrome in your family, you are encouraged to discuss your personal and/or family history with your health care provider. Your physician may refer you to the Cancer Genetics Program of the MD Anderson Cancer Center at Cooper for a genetic evaluation and discussion of your testing options. If genetic testing is recommended and you choose to proceed, a blood or saliva sample will be taken during your visit. Please note that health insurance companies may cover most, if not all, of the cost of genetic testing on a case-by-case basis.

**Where Can I Find More Information?**

Gilda's Club South Jersey (GCSJ) is a cancer support community in southern New Jersey offering a free, comprehensive program of psychosocial support including educational lectures, workshops, social activities and support groups to men, women, teens and children impacted by cancer.  
[www.gildasclubsouthjersey.org](http://www.gildasclubsouthjersey.org)

Lynch Syndrome Screening Network  
[www.lynchscreening.net](http://www.lynchscreening.net)

Cancer Net offers oncologist-approved cancer information from the American Society of Clinical Oncology.  
[www.cancer.net/cancer-types/uterine-cancer](http://www.cancer.net/cancer-types/uterine-cancer)

National Cancer Institute website has valuable cancer related health information on more than 200 cancer types, clinical trials, cancer statistics, prevention, screening, risk factors, genetics and support resources. Information is available in Spanish.  
[www.cancer.gov](http://www.cancer.gov)

American Cancer Society (ACS) is a voluntary national health organization that supports research, provides information about cancer and offers many programs and services to patients and their families. Information is available in Spanish.  
[www.cancer.org](http://www.cancer.org)

Genetic Alliance, Inc., supports individuals with genetic conditions and their families, educates the public and advocates for consumer-informed public policies. This site provides information on genetic policy, research and a helpline for people with genetic questions.  
[www.geneticalliance.org](http://www.geneticalliance.org)