

Patient Education

Lynch Syndrome

Lynch syndrome, which is sometimes referred to as hereditary nonpolyposis colorectal cancer syndrome (HNPCC), is a condition that causes an increased risk of developing certain types of cancer. These cancers can include colorectal, endometrial (uterine), ovarian, stomach and others. While most cancers are not caused by an inherited syndrome, approximately 3% to 5% of people who have colorectal or endometrial cancer have Lynch syndrome.

What Causes Lynch Syndrome?

Lynch syndrome is caused by a mutation in a gene. Genes are the set of instructions that tell all of the cells in our bodies how to work properly. Genes determine physical characteristics such as hair and eye color, nose shape and blood type. Some genes protect us from developing cancer.

A mutation is a change in a gene that causes it to stop working. If someone has a mutation in a gene that normally protects against cancer, that person does not have as much protection as the average person and is more likely to develop cancer. Since genes are passed down from a parent, a child may inherit a mutation.

There are five genes that can cause Lynch syndrome. These genes are called *MLH1*, *MSH2*, *MSH6*, *PMS2* and *EPCAM*. When these genes are working properly, they protect us from developing colorectal and endometrial cancer, as well as a few other types. If someone is born with a mutation in any of these genes, he or she has Lynch syndrome and is at an increased risk of developing certain types of cancer. Most people with Lynch syndrome have a mutation in either *MLH1* or *MSH2*.

What Are the Cancer Risks for People with Lynch Syndrome?

The lifetime chance of developing colon cancer is between 40% to 80%. In addition, people with Lynch syndrome are more likely to develop colon cancer at a younger age than individuals who do not have Lynch syndrome.

Women with Lynch syndrome have a 25% to 60% chance of developing endometrial cancer in their lifetime. Women with Lynch syndrome also have a greater than average chance of developing ovarian cancer.

Individuals with Lynch syndrome have a greater than average chance of developing stomach, urinary tract, hepatobiliary tract (bile duct and liver), small intestine, brain, skin and pancreatic cancer.

How is Lynch Syndrome Passed in a Family?

Every person has two copies of the genes that can cause Lynch syndrome. We receive one copy from our mother and one copy from our father. If someone inherits a copy that has a mutation (meaning it is not working properly), he or she has Lynch syndrome.

When we have children, we pass on one copy of each of our genes. If someone passes on the copy of their Lynch syndrome gene that has a mutation, that child will have Lynch syndrome as well. Each time a person with Lynch syndrome has a child, there is a 50% chance that the child will inherit the gene mutation and will have Lynch syndrome. However, if a person does not inherit the Lynch syndrome gene mutation that was detected in his/her family member(s), that person is most likely at average risk to develop cancers that are associated with Lynch syndrome.

Why Is It Important to Diagnose Lynch Syndrome in a Family?

People who have Lynch syndrome are at higher risk of developing colorectal, endometrial and other cancers than people in the general population. For someone who has already been diagnosed with a Lynch-associated cancer, a Lynch syndrome diagnosis indicates a higher risk of developing another cancer in the future.

Because Lynch syndrome is inherited, the diagnosis also affects family members. If genetic testing identifies the specific mutation causing Lynch syndrome, then family members can be tested for that gene mutation.

It is very important for people with Lynch syndrome to consider specialized screening and prevention strategies. Once someone is diagnosed with Lynch syndrome, that person's health care providers can make medical recommendations. These recommendations typically include screening exams to detect cancers as early as possible and/or surgeries that lower the chance of developing cancer in the future. Recommendations can be tailored to each patient and his or her family members.

How Is Lynch Syndrome Diagnosed?

A medical and family history review is used to screen for the possibility of Lynch syndrome. This includes the construction of a family tree with multiple generations. A genetic counselor usually conducts this screening process to assess the family's risk for Lynch syndrome.

The following features are common in families with Lynch syndrome:

- Three or more closely related family members with colorectal, endometrial or other Lynch-associated cancers.
- The Lynch-associated cancers are present in at least two generations in the family.
- One of these cancers was diagnosed in someone before the age of 50.

These features are referred to as the Amsterdam criteria. They are guidelines used to determine whether or not Lynch syndrome is likely to be present in a family. However, not all families that meet Amsterdam criteria have Lynch syndrome. Conversely, those that do not meet Amsterdam criteria may still have Lynch syndrome.

Tumors that are caused by Lynch syndrome may have specific features that are not seen as often tumors of other causes. Tests can be performed on colon, endometrial and some other types of tumors to determine if they are more likely than average to be associated with Lynch syndrome. These screening tests are called microsatellite instability (MSI) assay and immunohistochemical (IHC) analysis. If these tests identify features that are suggestive of Lynch syndrome, genetic testing is usually recommended.

Genetic testing looks for mutations in the Lynch syndrome genes. Genetic testing is done by collecting a blood or saliva sample. The sample is sent to a laboratory to look for a mutation in the Lynch syndrome genes. In general, with genetic testing, there are three possible types of results:

- Positive for a mutation. If a mutation is found, then the diagnosis of Lynch syndrome is confirmed. Next, other family members may have a genetic test to learn whether or not they carry the same mutation and have Lynch syndrome.
- Negative for a mutation. The cancer in the family may not be caused by Lynch syndrome. However, it is still possible the cancer in the family is being caused by a gene mutation. In some cases, current genetic testing technology cannot identify all mutations that cause Lynch syndrome. In other cases, there may be a different gene that is causing the colon, endometrial or other cancers in the family. It is also possible that there is a gene not yet discovered by scientists that is causing cancer in the family.
- Variant of unknown significance. A variant is a change that may or may not prevent the gene from working properly. Some variants are genetic changes that have no effect on cancer risk, while a small proportion increases the risk. Until more information regarding the variant is collected by researchers, it remains unknown whether a genetic variant increases cancer risks. Due to the limited information about this type of result, a variant 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 an evaluation and discussion of your options. If genetic testing is warranted and you choose to proceed, a blood or saliva sample will be taken during your visit to start the genetic testing process. Please note that health insurance companies may cover most, if not all, of the cost of genetic testing on a case-by-case basis.

Resources

Visit the Lynch Syndrome Screening Network at lynchscreening.net.

For oncologist-approved cancer information from the American Society of Clinical Oncology, search “Lynch syndrome” in the search tool on the home page of Cancer.Net at www.cancer.net.

The National Cancer Institute at www.cancer.gov 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.

American Cancer Society (ACS) at www.cancer.org 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.

Genetic Alliance, Inc. at www.geneticalliance.org 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.