

Lynch Syndrome

Lynch syndrome is a condition that causes an increased risk of developing certain types of cancer, such as colorectal, endometrial (uterine), ovarian, stomach, and others. Approximately three to five percent of people who have colorectal or endometrial cancer have Lynch syndrome.

What Causes Lynch Syndrome?

Genes are the set of instructions that tell all of the cells in our bodies how to work properly. A mutation is a change in a gene that causes it to stop working. In the case of Lynch syndrome, a gene that normally helps to prevent certain types of cancer has stopped working. Lynch syndrome is caused by a mutation in one of five genes: MLH1, MSH2, MSH6, PMS2, and EPCAM. Someone who is born with a mutation in any of these genes has Lynch syndrome and has an increased chance of developing certain types of cancer.

What Are The Cancer Risks For People With Lynch Syndrome?

Lynch syndrome is associated with increased lifetime cancer risks, including:

Type of Cancer	General Population Risk	MLH1 Mutation Carrier Risk	MSH2 and EPCAM Mutation Carrier Risk	MSH6 Mutation Carrier Risk	PMS2 Mutation Carrier Risk
Colon	4.5%	46-49%	43-52%	15-44%	12-20%
Endometrial	2.7%	43-57%	21-57%	17-46%	0-15%
Ovarian	1.3%	5-20%	10-38%	1-11%	Risk not well established
Gastric/stomach	<1%	5-7%	0.2-16%	0-5%	
Small bowel	<1%	0.4-11%	1-10%	0-3%	
Bladder, kidney, and urinary tract	<1%	0.2-5%	2-18%	0.7-7%	
Prostate	11.6%	0-17%	30-32%	0-5%	
Brain/CNS, biliary tract, pancreas, sebaceous gland tumors, other	<1%	2- 6%	Risk not well established	Risk not well established	

*Gupta S, et al. NCCN Clinical Practice Guidelines in Oncology® Genetic/Familial High-Risk Assessment: Colorectal. V 1.2021.

How Is Lynch Syndrome Passed On In A Family?

Every person has two copies of each of the genes that can cause Lynch syndrome. We receive one copy from our mother and one copy from our father. Someone who inherits a copy that has a mutation (meaning it is not working properly) has Lynch syndrome. There is a 50 percent chance that a person with Lynch syndrome will pass it to each of their children. However, if a person does not inherit the Lynch syndrome gene mutation present in their family member(s), that person is usually at general population risk to develop colon, endometrial, and other Lynch syndrome cancers.

Why Is It Important To Diagnose Lynch Syndrome In A Family?

For someone who has already been diagnosed with a Lynch syndrome-associated cancer, a Lynch syndrome diagnosis indicates a higher risk of developing another cancer in the future and may impact treatment.

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 same genetic mutation.

It is very important for people with Lynch syndrome to consider specialized cancer screening. Cancer screening may help identify cancers at their earlier, more treatable stages. There may also be medical options that can lower the risk of developing cancer. Usually, a team of specialists will tailor a cancer screening and risk reduction plan to each patient and their family members.

How Is Lynch Syndrome Diagnosed?

A genetics evaluation includes a review of a person's medical and family history. 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 Lynch syndrome. A genetic counselor usually conducts this evaluation.

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, and some families that do not meet Amsterdam criteria may still have Lynch syndrome.

Testing

Tumors that are caused by Lynch syndrome may have specific features that are not seen as often in tumors that are not caused by Lynch syndrome. 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 that will analyze the genes in the sample 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 that 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 the patient did not have testing for, that is causing the colon, endometrial, or other cancers in the family. It is also possible that there is a gene that has not yet been discovered by scientists, that is causing cancer in the family.
- **Variant of unknown significance.** A variant is a genetic 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 of variants are gene changes that increase cancer 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 at Cooper for genetic evaluation and discussion of your genetic testing options. If genetic testing is warranted and you choose to proceed, a blood or possibly saliva sample will be taken during your visit to the Cancer Genetics Program to start the genetic testing process. Please note that health insurance companies may cover most, if not all, of the cost of genetic testing.

Where Can I Find More Information?

Lynch Syndrome Screening Network at www.lynchsyndrome.net.

Colon Cancer Alliance for Research and Education for Lynch Syndrome (CCARE Lynch Syndrome) at www.fightlynch.org.

Lynch Syndrome International: A global organization providing support, creating public awareness, and educating the public and healthcare providers. Visit www.lynchsyndrome.com.

Alive N' Kickn: A Lynch syndrome advocacy organization. Visit www.alivenkickn.org.

Cancer.Net: Oncologist-approved cancer information from the American Society of Clinical Oncology. Visit www.cancer.net/cancer-types/colorectal-cancer.

The National Cancer Institute: 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. Visit www.cancer.gov.

The American Cancer Society (ACS): 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. Visit www.cancer.org.

Genetic Alliance, Inc.: An organization that 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. Visit www.geneticalliance.org.