Patient Education

MD Anderson Cancer Center Cooper
Making Cancer History®

Hereditary Colorectal Cancer Syndromes

Most people develop colorectal cancer by chance or as a result of risk factors that occur over the course of a lifetime. However, approximately three to five percent of people who are diagnosed with colorectal cancer develop it due to a hereditary colorectal cancer syndrome.

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

What Causes Hereditary Colorectal Cancer?
Hereditary colorectal 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 features such as hair and eye color, the shape of our nose and blood type. A mutation is a change in a gene that causes the gene to stop working. Hereditary colorectal cancer syndromes occur when a gene that normally helps to prevent colorectal cancer stops working. People with a hereditary colorectal cancer syndrome are more likely to develop certain cancers, especially colorectal cancer. In addition, people with a hereditary colorectal cancer syndrome are more likely to develop cancer at a younger age than usual.

The most common hereditary colorectal cancer syndrome is called Lynch syndrome. Lynch syndrome is sometimes referred to as hereditary non-polyposis colorectal cancer syndrome (HNPCC). Lynch syndrome is caused by a mutation in any one of the following genes: *MLH1, MSH2, MSH6, PMS2* or *EPCAM*. When someone has a mutation in one of these genes he/she has an increased chance of developing colorectal, uterine, ovarian, stomach and some other types of cancer.

There are many other genes that can cause hereditary colorectal cancer. Some of these genes, like the Lynch syndrome genes, greatly increase colorectal cancer risk. Some of these genes also cause a large number of colon polyps to develop. These colon polyps can become cancerous. The two most common syndromes that cause hereditary colon polyposis are called familial adenomatous polyposis (FAP) syndrome and *MUTYH*-associated polyposis (MAP) syndrome. These syndromes are caused by mutations in the *APC* and *MUTYH* genes and can cause hundreds or thousands of colon polyps, as well as colon cancer and other cancers. There are several other genes that can increase colorectal cancer risk. Many of them are listed below.

Hereditary Colorectal Cancer Genes		
Lynch Syndrome	**High Risk Polyposis Syndromes**	**Others**
MLH1, MSH2, MSH6, PMS2, EPCAM	*APC, MUTYH*	*BMPR1A, CDH1, PTEN, SMAD4, STK11, TP53, ATM, CHEK2, AXIN2, POLE, POLD1, GREM1*

How is a Hereditary Colorectal Cancer Syndrome Passed on Through a Family?
Each person inherits two copies of most genes. We receive one copy from our mother and one copy from our father. In most cases, inheriting a mutation in just one copy of a hereditary colorectal cancer gene is enough to increase the risk of developing colorectal cancer and possibly other types of cancer. Each time a person with a hereditary colorectal cancer gene mutation has a child there is a 50 percent chance that the child will inherit the gene mutation. If a person inherits the gene mutation, he/she will also have an increased risk of developing colorectal and possibly other types of cancer. However, if a person does not inherit the gene mutation that was identified in his or her family member(s), that person usually has an average chance of developing colorectal cancer.

There are some exceptions to the type of inheritance described above. For example, the hereditary polyposis syndrome MAP is only inherited if a person receives two mutated copies of the *MUTYH* gene. In other words, a person must inherit a mutated copy of the *MUTYH* gene from both of his/her parents in order to have a diagnosis of MAP.

Why is it Important to Diagnose a Hereditary Colorectal Cancer Syndrome in a Family?
People who have a hereditary colorectal cancer syndrome have a higher than average chance of developing colorectal cancer. They may also have a higher than average chance of developing other types of cancer. For someone who already has been diagnosed with colorectal cancer, genetic testing may provide information about the chance of developing another cancer. Because hereditary colorectal cancer syndromes are inherited, the diagnosis also affects family members. If genetic testing identifies a mutation in a gene that causes a hereditary colorectal cancer syndrome, family members can be tested for that same gene mutation.

It is very important for people with a hereditary colorectal cancer syndrome to consider specialized cancer screenings. Cancer screenings 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 a Hereditary Colorectal Cancer Syndrome Diagnosed?
A genetics evaluation includes a review of a person's medical and family history. This information is used to determine the likelihood that the person has a hereditary colorectal cancer syndrome. A genetic counselor usually conducts this evaluation.

Some signs that suggest hereditary colorectal cancer may run in a family include:

- Multiple close relatives with colon, uterine and other Lynch syndrome related cancers.
- Colorectal cancer that does not produce certain proteins or that has a feature called "microsatellite instability".
- Colorectal cancer diagnosed at a young age (<50 years old).
- More than one occurrence of colorectal cancer in a single person.
- Multiple colon polyps.

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 can be tested for a genetic mutation that causes a hereditary colorectal cancer syndrome. This testing may be limited to the Lynch syndrome genes, colon polyposis genes and/or other genes that cause hereditary colorectal cancer. In general, there are three types of results:

- Positive for a mutation. If a mutation is found, then the diagnosis of a hereditary colorectal 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 colorectal 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 colorectal cancer syndrome in the family. This is because current genetic testing technology is not able to identify all mutations that cause hereditary colorectal cancer. It is also possible that the colorectal cancer in the family is being 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 genetic evaluation and discussion of your genetic testing options. If genetic testing is warranted 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?

Lynch Syndrome Screening Network at lynchscreening.net.

Hereditary Colon Cancer Foundation is a resource site for patients and providers regarding a variety of hereditary colorectal cancer syndromes. Visit www.hcctakesguts.org.

Cancer.Net at www.cancer.net/cancer-types/colorectal-cancer.

National Cancer Institute 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. Visit 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. Visit www.cancer.org.

Genetic Alliance, Inc. organization 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.

Cancer.Net provides oncologist-approved cancer information from the American Society of Clinical Oncology. Visit www.cancer.net.