PATIENT EDUCATION

Lynch Syndrome
What Is Lynch Syndrome?

Lynch syndrome is a condition you can inherit. It can be passed from parent to child. This syndrome increases your risk of colon cancer, endometrial cancer and several other cancers. The endometrium is the lining of the uterus. See Figure 1.

You can inherit several syndromes that can increase your risk of colon cancer or endometrial cancer. But Lynch syndrome is the most common. It causes 3 to 5 out of every 100 colon cancers or endometrial cancers in the U.S.

Families with Lynch syndrome usually have more cases of colon cancer and endometrial cancer than expected. Lynch syndrome also typically causes these cancers to occur at an earlier age than expected.

People with Lynch syndrome have a high risk of getting more than one cancer in the colon. With Lynch syndrome, colon cancers develop mostly on the right side of the colon.

People who have Lynch syndrome have some increased risk of other cancers. These include the following cancers:

- Stomach
- Small intestine
- Urinary tract or bladder
- Skin
- Liver and biliary tract
- Pancreas
- Brain
- Prostate
- Ovarian
Fortunately, the risk of these cancers is much less than the risk of colon cancer or endometrial cancer.

People with Lynch syndrome should have cancer screenings for much of their adult lives. Finding cancer early can significantly increase the chances of a cure. For example, the five-year survival rate is 90% when colon cancer is found early. That is why it is important to identify people with Lynch syndrome.

This condition runs in families. Once one person is diagnosed, other family members can test to see whether they have Lynch syndrome. Early testing can help prevent cancers.

If you or a family member has been told you have Lynch syndrome, ask to be referred to a genetic counselor or other genetics specialist who can help you decide whether genetic testing is right for you. See “How Is Lynch Syndrome Diagnosed?”

If you have any questions or concerns about this information, be sure to ask your care team. Your care team is here to help you.
What Causes Lynch Syndrome?

Four genes can fix errors in DNA. DNA are the codes that carry genetic information. These genes are MLHL, MSH2, MSH6, and PMS2. You might hear these genes called “proofreading” genes. It is their job to check for and fix errors as DNA divides. A fifth gene, EPCAM, can influence MSH2 function. Lynch syndrome is caused by inherited changes in one of these five genes.

The DNA inside a cell is packaged into many individual genes. All the cells in the human body divide on a regular basis. Sometimes this can be as often as every few days. Every time a cell divides, a complete copy of the cell’s DNA must be made.

But sometimes the process goes wrong, and a mistake is made when the DNA is copied. If the proofreading genes miss the mistake, a change occurs in the DNA. You may hear this change called a mutation. You also may hear this called a pathogenic or likely pathogenic variant.
If you have Lynch syndrome, that means you were born with a change in one of the proofreading genes. You inherited that change. Everyone has two copies of each of the genes linked to Lynch syndrome. You get one copy from each parent.

If one of your parents has the gene that causes Lynch syndrome, there is a 50% chance that you will inherit the gene. See Figure 2.

Not everyone with Lynch syndrome gets cancer. But the risk is higher if you inherit a change in a Lynch syndrome gene. While you still have the healthy copy of the gene from your other parent, that single healthy copy can get damaged. That gene may change and stop working as it should. This results in a higher risk of cancer earlier in life.

What if both parents have a gene that causes Lynch syndrome?

If both parents have a gene that causes Lynch syndrome, a child may inherit a changed gene from each parent. This can cause a variety of cancers to develop very early in a child’s life.

If you have Lynch syndrome and want to have a child, talk to your care team about genetic testing for partners.

Ask about fertility counseling if you or your partner have a diagnosis of Lynch syndrome.
Figure 2. If one parent has the condition and the other does not, there is a 50% chance of having a child who also has the condition. This is a risk with each pregnancy.
How Is Lynch Syndrome Diagnosed?

Families with Lynch syndrome have more instances of colon cancer or endometrial cancer than expected. And these cancers happen at an earlier age than in the general population.

Many people find out they have Lynch syndrome after they have a diagnosis of colon cancer or endometrial cancer. It is now common to test the tumor tissue of people who have been diagnosed with certain types of cancers for Lynch syndrome.

Others learn they have Lynch syndrome because a close family member has been diagnosed with Lynch syndrome. Then they decide to have genetic testing. If a member of your family has been diagnosed with Lynch syndrome, ask to be referred to a genetic counselor. A genetic counselor can help you decide whether genetic testing is right for you.
Family history

Your health care provider will ask you about cancer in your family. If one side of your family has a pattern of cancer that includes the following, you may have Lynch syndrome.

- At least 3 first- or second-degree family members have had a cancer linked to Lynch syndrome. **A first-degree relative** is a parent, sibling or child. **A second-degree relative** is an aunt, uncle, grandparent, niece, nephew or half-sibling. **Cancers related to Lynch syndrome** include colorectal, endometrial, gastric, ovarian, pancreatic, urothelial (urinary tract or bladder), brain (usually glioblastoma), small intestine, and skin (sebaceous adenoma/carcinoma, keratoacanthoma).

- At least 2 first-or second-degree family members have had a cancer linked to Lynch syndrome and at least 1 was diagnosed before age 50.

- At least 1 first-degree relative with a colorectal or endometrial cancer AND a second cancer that is related to Lynch syndrome.

- At least 1 first-degree relative with a colorectal or endometrial cancer diagnosed before age 50.

It can be hard to diagnose Lynch syndrome based on family cancer history alone. Small families and families without a shared health history may not have enough information to make a diagnosis. And if you were adopted, you may not know your health history.

If you have a family pattern of cancer that puts you at risk of Lynch syndrome, other tests and procedures are needed to make a diagnosis.
Testing tumors

Lynch syndrome can be hard to diagnose based just on family history. Because of this, it is now common to test tumor tissue that comes from certain cancers.

Testing can tell whether genes related to Lynch syndrome may have caused your cancer. Tumor tests include the following:

- **Immunohistochemistry testing, also called IHC testing.** Samples of tumor tissue are stained. The stain shows which proofreading proteins are present or absent. Missing proteins may tell doctors if a gene related to Lynch syndrome caused the cancer.

- **Microsatellite instability testing, also called MSI testing.** Microsatellites are sequences of DNA. This test looks for proofreading errors in DNA that are potentially caused by Lynch syndrome.

Positive ICH or MSI test results mean you have malfunctions in the genes that are connected to Lynch syndrome. But the results cannot tell you whether you have Lynch syndrome. Only specific genetic testing can tell whether you have Lynch syndrome.
**Genetic testing**

Genetic testing looks for changes in your genes that indicate that you have Lynch syndrome.

A sample of blood or saliva is tested to see whether you have gene changes that cause Lynch syndrome.

Genetic testing may show:

- **A positive genetic test result.** A positive result means that the test found a gene change that causes Lynch syndrome. But a gene change does not mean you have cancer or will get cancer. It does mean that during your life, you have an increase in your risk of certain cancers.

- **A negative genetic test result.** A negative result means that a gene change that causes Lynch syndrome was not found. It means that you likely do not have Lynch syndrome. But if you have a strong family history of cancer, you may still have an increase in your risk of cancer.

- **A gene change of unknown significance, often referred to as a VUS.** Genetic tests don’t always give you a yes or no answer about your cancer risk. Sometimes genetic testing reveals a gene change that has no known significance. In this case, Lynch syndrome cannot be ruled out. Your genetic counselor can explain what this result means to you.

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**Is genetic testing right for me?**

The decision to go forward with genetic testing is not a simple decision. Genetic tests do not always give you a yes or no answer about your cancer risk.

Ask to meet with a genetic counselor or genetics specialist. Your genetic counselor can discuss the benefits and risks of genetic testing with you. You can learn what genetic testing can and cannot tell you.
Lynch syndrome and hereditary nonpolyposis colorectal cancer

Sometimes you may hear or see the terms Lynch syndrome and hereditary nonpolyposis colorectal cancer, shortened to HNPCC, used in place of each other. But the definitions are different.

HNPCC is a group of diseases that have a family history that looks like Lynch syndrome.

Lynch syndrome is the most common cause of HNPCC. It can only be diagnosed with genetic testing.

Other diseases that cause HNPCC include:

- Lynch-like syndrome. In this case, genetic testing for Lynch syndrome is negative. But immunohistochemistry testing (IHC) or microsatellite instability testing (MSI) is positive.

- Familial colorectal cancer type X. Here tumor testing by IHC or MSI is negative. And genetic testing for Lynch syndrome is negative. These families typically do not have cancers outside the colon and rectum.
How Is Lynch Syndrome Treated?

While there is no cure for Lynch syndrome, there is good news. Regular health screenings and other measures to reduce risk can greatly lessen the chance of dying from cancer for people with Lynch syndrome. **One of the benefits of a diagnosis of Lynch syndrome is that your health care provider can set up cancer early detection and prevention guidelines that fit you and your family.** Your care team makes changes to your care and preventive testing schedule as needed.

If you have a diagnosis of Lynch syndrome, share it with your family members. That allows them to make health care decisions that are right for them. Family members should get genetic testing to see whether they also carry a gene change that causes Lynch syndrome.

Researchers continue to find out more about Lynch syndrome.
Family testing: Talk to family members

Lynch syndrome passes down through families. When you share your diagnosis of Lynch syndrome with family members who also may be at risk, you can save lives. Cancer prevention and early detection measures for Lynch syndrome can greatly lessen the risk of dying of cancer.

If you have a Lynch syndrome diagnosis, your first-degree relatives are at the highest risk of the disease. These are your biological parents, siblings and children. While there is no manual for how to share your diagnosis with family members, doing so allows them to make informed health care decisions. Genetic testing can confirm whether they carry a gene change that causes Lynch syndrome. This information may help them protect themselves and their families.

Talk to your health care provider or your genetic counselor if you need advice about how to talk to family members about Lynch syndrome.

Personalized cancer prevention measures

If you are told you have cancer at the same time you find out you have Lynch syndrome, your care team will work with you to treat your cancer. They also will develop a care plan to prevent more cancer. This includes a schedule for tests to detect cancer early.

If you were told you have Lynch syndrome but you don’t have cancer, your care team will work with you to develop a care plan to prevent cancer. This includes a schedule for tests to detect cancer early.
Shared decision-making

People living with Lynch syndrome have an increased risk of more than one cancer. Because of this, several specialists may be involved in your care.

There is a lot you can do to lessen your cancer risk. You can make healthy choices every day. You can move more and eat a diet proven to lessen cancer risk. If you smoke, stop.

You also may want to learn all you can about how Lynch syndrome affects your cancer risk. And you can take an active role in managing your condition. Talk to your care team about all the ways you can reduce cancer risk.

People with Lynch syndrome have shared that they sometimes feel overwhelmed by the challenge of living with a high cancer risk. But some also have reported feeling empowered once they follow their care plans and commit to healthy living.

Work closely with your care team. Take an active part in your care plan. Understand the ways you can live with less cancer risk.
Early detection tests

Your care plan depends on things like your age, sex and overall health. These are some general guidelines for screening tests to detect cancer early.

- **Schedule a colonoscopy every 1 to 2 years. This is the most important thing you can do to reduce your cancer risk.** Follow what your care team tells you. A colonoscopy may be done more often if polyps or cancer are found.

- Schedule early detection tests for endometrial and ovarian cancers as told by your care team. This may include an ultrasound and a biopsy of the uterus. **If you have any vaginal bleeding between menstrual periods or after menopause, tell your care provider right away.** Talk to your care team about whether surgery to remove the uterus and ovaries may be right for you.

- Talk to your health care provider about early detection tests for prostate cancer.

- Schedule a yearly urine test to look for blood in the urine.

- Other tests may include upper endoscopy or abdominal scans. These tests depend on the gene change you may have and on your family history.

- Follow the American Cancer Society guidelines for all other cancer screening.
Talk with your care team about your care plan. Find out the early detection tests you should have. Guidelines continue to be updated as researchers learn more about Lynch syndrome, and the tests also may change. For this reason, it is important to see your care team as scheduled. Talk about other things you can do to have less cancer risk. Be sure you get all your questions answered.

**Aspirin**

Research suggests that aspirin may lessen the risk of colon polyps and cancer for people with Lynch syndrome. Talk to your care team about whether you might benefit from taking aspirin. Ask about the risks involved with long-term use of aspirin.
Coping and Support

After you find out you have cancer or a condition that comes with a high risk of cancer, you may have many questions and concerns.

People who live with Lynch syndrome say they find benefit from a support group, such as Lynch Syndrome International. Ask your care team about support groups in your area.

You also may find it helpful to:

- **Find out enough about your cancer and Lynch syndrome to make decisions about your care.** Learn about Lynch syndrome so that you feel comfortable enough to make treatment choices.

- **Keep up a strong support system.** Strong relationships may help you as you follow your care plan and make important decisions about your care. Talk with close friends and family members about how you feel. Connect with other people who live with Lynch syndrome.

- **Wherever you are in your Lynch syndrome journey, know that you are not alone.** Cancer or the increased risk of cancer brings a lot of change to your life. Most people face some degree of depression, anxiety or distress when they face a serious health issue. Be sure to talk to your care team about your questions and concerns. Your care team is here to help you.
BARBARA WOODWARD LIPS PATIENT EDUCATION CENTER

Mrs. Lips, a resident of San Antonio, Texas, was a loyal Mayo Clinic patient of more than 40 years and a self-made business leader who significantly expanded her family’s activities in oil, gas and ranching. Upon her death in 1995, Mrs. Lips paid the ultimate compliment by leaving her entire estate to Mayo Clinic. By naming the Barbara Woodward Lips Patient Education Center, Mayo honors her generosity, her love of learning, her belief in patient empowerment and her dedication to high-quality care.

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