MAYO CLINIC

PATIENT EDUCATION

Lynch syndrome: An inherited condition

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PATIENT EDUCATION CENTER

Lynch syndrome: An inherited condition

Lynch syndrome is an inherited condition. It can be passed from parent to child. This syndrome increases your risk of colorectal cancer. It increases your risk of cancer of the endometrium, which is the lining of the uterus. It also may increase your risk of several other cancers. See Figure 1.

You can inherit several syndromes that may increase your risk of colorectal cancer or endometrial cancer. Lynch syndrome is the most common. In the U.S., 3 to 5 of every 100 colorectal or endometrial cancers develop in someone with Lynch syndrome.

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

People with Lynch syndrome have a high risk of more than one colorectal cancer. These cancers develop more often on the right side of the colon.

People who have Lynch syndrome have some increased risk of other cancers. They include:

- Stomach.
- Small intestine.
- Urinary tract or bladder.
- Skin.
- Liver and biliary tract.
- Pancreas.
- Brain.
- Prostate.
- Ovarian.

The risk of these cancers is much lower than the risk of colorectal cancer or endometrial cancer.

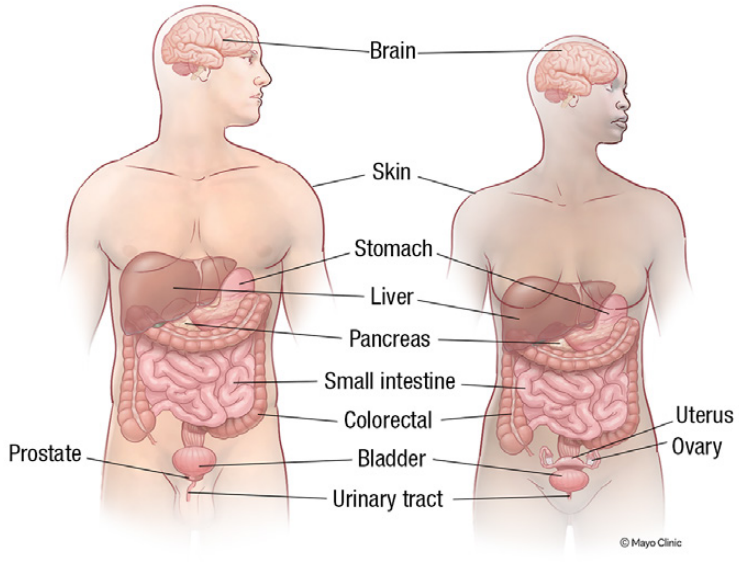

Figure 1. Cancers caused by Lynch syndrome

Cancer screenings for people with Lynch syndrome

People with Lynch syndrome need regularly scheduled cancer screenings. Finding cancer early significantly increases the chances of a cure. For example, the five-year survival rate is over 90% when colorectal cancer is found early.

This condition runs in families. Once one person is diagnosed, other family members can test to see whether they have the syndrome. Early testing helps 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 genetic specialist. This person helps you decide whether genetic testing is right for you. See "Diagnosing Lynch syndrome."

If you have any questions or concerns about what you read in this resource, be sure to ask a member of your healthcare team. Your care team is here to help you.

Causes of Lynch syndrome

DNA carries genetic information in every cell. Each strand of DNA contains many individual **genes.** The DNA strands inside a cell are tightly coiled into **chromosomes**. See Figure 2.

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.

Sometimes the process goes wrong, and a mistake is made when the DNA is copied. Four genes can fix errors in DNA. These genes are *MLH1, 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. Inherited changes in one of these five genes causes Lynch syndrome.

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 it called a **pathogenic variant** or **likely pathogenic variant.**

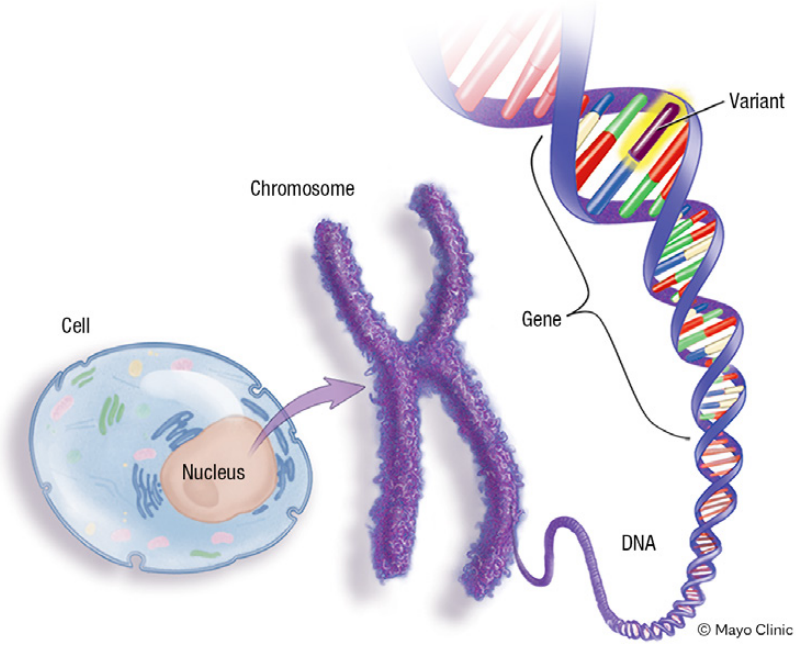

Figure 2. Example of genetic material

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, you have a 50% chance to inherit the gene. See Figure 3.

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, damage can happen to that single healthy copy. That gene then 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 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 has a diagnosis of Lynch syndrome.

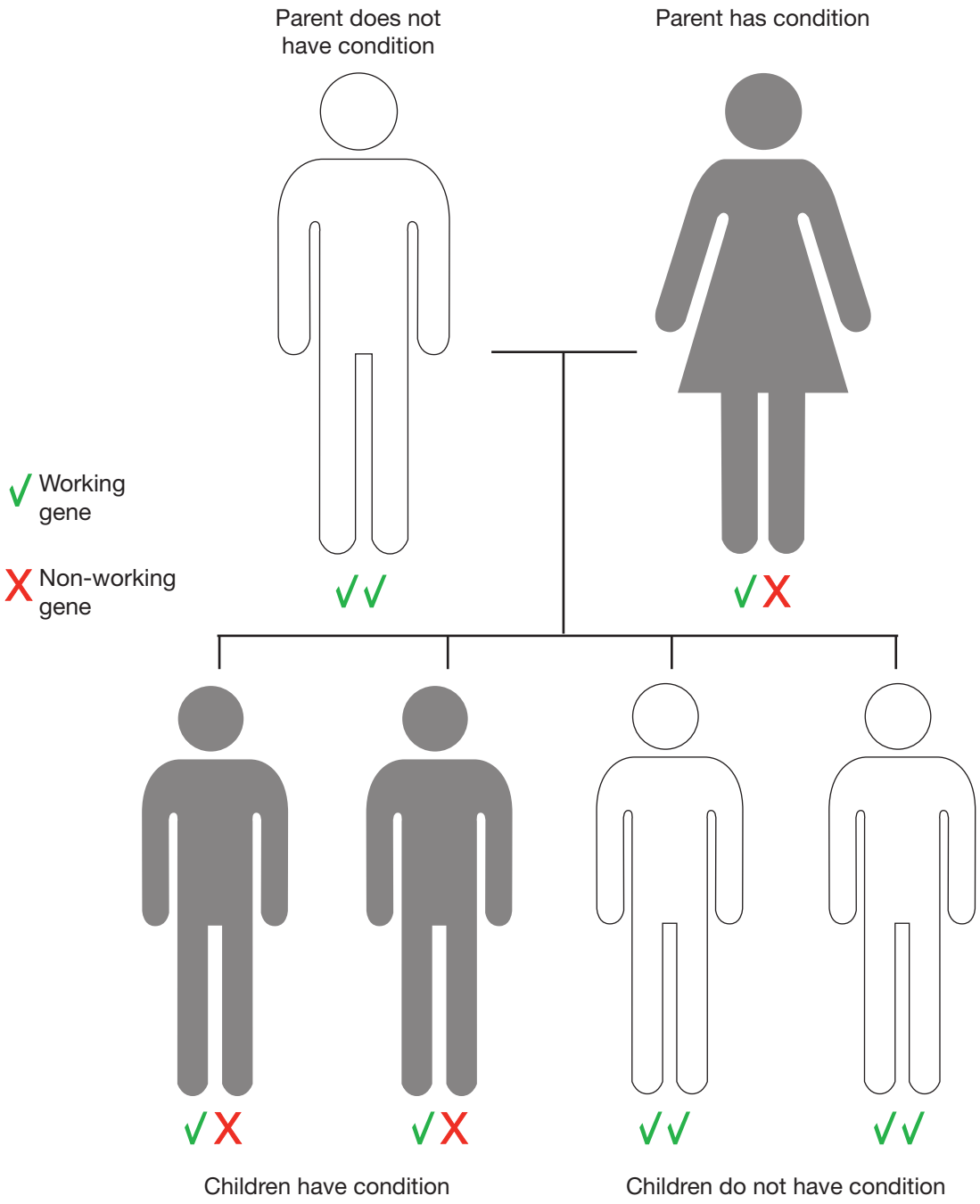

Figure 3. If one parent has the condition and the other does not, there is a 50% chance of having a child who also has the condition. This is a risk with each pregnancy.

Diagnosing Lynch Syndrome

Many people find out they have Lynch syndrome after they have a diagnosis of colorectal 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. 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. This person can help you decide whether genetic testing is right for you.

Family history

Your healthcare team asks 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 close to you in the blood line, such as 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 and ovarian. They include pancreatic, urinary tract or bladder. They include the brain, usually glioblastoma. They include the skin, such as sebaceous carcinoma, adenoma carcinoma and keratoacanthoma. And they include the small intestine.

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. If you were adopted, you may not know your family 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 tells 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. These proteins are made by proofreading genes that may have changed. 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 IHC or MSI test results mean you have mistakes in the genes that are connected to Lynch syndrome. But the results cannot tell you whether you have Lynch syndrome.

Emerging treatment strategies

In some cases, the immune system can be activated with medicines to treat cancers in people with Lynch syndrome.

One of these treatments is called immunotherapy. Immunotherapies are treatments that help stimulate the body's own immune system to destroy cancer cells. Cancers that are found in those with Lynch syndrome often respond well to these treatments.

Other treatments being studied are cancer vaccines. These seek to both prevent and treat cancers that are associated with Lynch syndrome.

It is important to seek treatment with an oncologist who has experience in treating people with Lynch syndrome.

Genetic testing

Genetic testing looks for changes in your genes that show you have Lynch syndrome. To do the test, you give a sample of blood or saliva.

You may have:

A positive genetic test result. A positive result means that the test found a gene change that causes Lynch syndrome. A gene change does not mean you have cancer or will get cancer. But 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 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 still may have an increase in your risk of cancer.

A gene change or variant of uncertain 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 explains what this result means to you.

Is genetic testing right for me?

The decision to go forward with genetic testing is not a simple decision. The 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 learn what genetic testing can and cannot tell you.

Treating Lynch syndrome

While there is no cure for Lynch syndrome, there is good news. Regular health screenings and other measures to lessen risk greatly lessen the chance of dying of cancer for people with Lynch syndrome.

One of the benefits of a diagnosis of Lynch syndrome is that your healthcare team can set up 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 healthcare decisions that are right for them. Family members should get genetic testing to see whether they also have 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 diagnosis of Lynch syndrome, your first-degree relatives are at the highest risk of the disease. These are your close blood relatives, such as your parents, siblings and children. While there are no rules for how to share your diagnosis with family members, doing so allows them to make informed healthcare decisions.

Genetic testing can confirm whether family members have a gene change that causes Lynch syndrome. This information may help them protect themselves and their families.

Talk to your healthcare team 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, members of your care team work with you to treat your cancer. They also develop a care plan to prevent more cancer. It includes a schedule for tests to detect cancer early.

If you are told you have Lynch syndrome but you don't have cancer, your care team works with you to develop a care plan to prevent cancer. It includes a schedule for tests to detect cancer early.

Work with your care team

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.

You can do a lot 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 or drink alcohol, quit. You can lessen your risk to develop cancer.

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

People with Lynch syndrome share that they sometimes feel overwhelmed by the challenge of living with a high cancer risk. They also report 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 the gene involved and things such as 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 test looks at the colon and rectum. It is the most important thing you can do to lessen your colon cancer risk. Follow what your care team tells you. A colonoscopy may be done more often if polyps or cancer is found.
- **Schedule an upper endoscopy every 2 to 4 years.** This test looks at the lining of the throat and into the upper digestive tract. The timing for this test may change if your healthcare team finds any areas that may need closer monitoring.
- **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 team right away. Talk with your care team about whether surgery to remove the uterus and ovaries may be right for you.
- **Schedule a yearly urine test** to look for blood in the urine.

Other guidelines include:

- Have a yearly skin check and a full physical exam. This includes a neurological exam by your primary healthcare professional or other specialists.
- Talk with your healthcare team about screening for Helicobacter pylori. Called H. pylori, this is a bacterium that can cause gastritis and increase the risk of stomach cancer.
- Talk about other tests that may include abdominal scans and blood work.
- 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.

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.

Habit changes to stay healthy with Lynch syndrome

The best way to live well and live longer is to practice healthy habits. People who stay at a healthy weight and avoid red meat and processed foods tend to have lower rates of colon cancer. Those who avoid tobacco and excessive alcohol also have lower rates of colon cancer.

Add resistant starches to your diet

One diet change you can make to maintain your gut health is to eat foods that have resistant starches. The fiber these foods contain does not break down in the stomach or small intestine. The food makes it to the large intestine where it ferments. There it feeds bacteria and breaks down to create compounds that are important for your gut health.

Foods that are good sources of resistant starch include:

- Cooked or cold-soaked oats, also called overnight oats.
- Chickpeas and lentils.
- Sourdough, pumpernickel and rye bread.
- Cooked or cooked and cooled cannellini, adzuki, black, pinto, kidney and lima beans.
- Cooked millet.
- Sushi rice and brown rice.
- Yams.
- Green or unripe bananas.
- Raw plantain.
- Corn and corn tortillas.
- Cooked then reheated potatoes and pasta.

Talk to your care team about diet changes you can make to lessen your risk of certain cancers and improve your health.

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 for Lynch syndrome

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:

- Learn about your cancer and Lynch syndrome to help you make decisions about your care. Knowing more can help 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 may bring a lot of change to your life. Many 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 healthcare team is here to help you.

For more information

If you have any questions about the information in this resource or about Lynch syndrome, talk to a member of your healthcare team.

To watch a video about Lynch syndrome, open the camera on your smartphone or tablet. Aim it at this QR code. Then touch the link that appears.

You may also watch the video at this link:
https://www.mayoclinic.org/pe?mc=MC2484-02

Notes

Notes

Barbara Woodward Lips

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Mrs. Lips, a resident of San Antonio, Texas, was a loyal patient of Mayo Clinic for more than 40 years. She was a self-made business leader who significantly expanded her family's activities in oil, gas and ranching, even as she assembled a museum-quality collection of antiques and fine art. She was best known by Mayo staff for her patient advocacy and support. Upon her death in 1995, Mrs. Lips paid the ultimate compliment by leaving her entire estate to Mayo Clinic.

Mrs. Lips had a profound appreciation for the care she received at Mayo Clinic. By naming the Barbara Woodward Lips Patient Education Center, Mayo Clinic honors her generosity, her love of learning, her belief in patient empowerment, and her dedication to high-quality care.

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