Printed October 26, 2014 from http://www.cancer.net/cancer-types/lynch-syndrome

Lynch Syndrome [1]

What is Lynch syndrome?

Lynch syndrome, also known as hereditary non-polyposis colorectal cancer (HNPCC), is a type of inherited cancer of the digestive tract. People who have Lynch syndrome have a significantly increased risk of developing colorectal cancer and an increased risk of developing other types of cancers such as endometrial (uterine), [2] stomach [3], breast [4], ovarian [5], small bowel (intestinal) [6], pancreatic [7], prostate [8], urinary tract [9], liver [10], kidney [11], and bile duct [12] cancers. Lynch syndrome may be a possible diagnosis when there are multiple cases of colorectal cancer on the same side of the family. There is also an increased risk of a person with Lynch syndrome to develop multiple cancers during his or her lifetime.

In addition, cancer is more likely to be diagnosed at a young age. The average age for colorectal cancer to be diagnosed in someone with Lynch syndrome is 45, as compared with the average age of 72 for a new diagnosis of colorectal cancer in the general population. In Lynch syndrome, colorectal cancer is somewhat more likely to develop on the right side of the colon.

The classic diagnostic criteria for Lynch syndrome are called the Amsterdam Criteria. Over time, the Amsterdam Criteria have been modified to include the variety of cancers that are seen in Lynch syndrome families. The Modified Amsterdam Criteria, also known as the Amsterdam II Criteria, are listed below:

- Three or more relatives with a Lynch syndrome-related cancer;* one relative must be a first-degree relative (parent, brother, sister, or child) of the other two
- At least two generations with cancer (such as a parent and child)
- One or more cases of cancer diagnosed younger than age 50
- Familial adenomatous polyposis [13] (FAP) is ruled out as the cause

*(colorectal cancer, endometrial cancer, small bowel, ureter, or renal pelvis cancer; some people would also consider including ovarian cancer)

The definition of Lynch syndrome is still evolving. A family may still have Lynch syndrome even if the Amsterdam Criteria does not fully match the family history. Therefore, meeting with a health professional who specializes in genetics, such as a genetic counselor or medical geneticist (a doctor with training in genetic diseases and conditions), is recommended for people who have a

family history that suggests Lynch syndrome.

There are two variant forms of Lynch syndrome called Muir-Torre syndrome [14] and Turcot syndrome [15].

What causes Lynch syndrome?

Lynch syndrome is a genetic condition. This means that the cancer risk can be passed from generation to generation in a family. Several genes have been identified that are linked to Lynch syndrome. They include *MLH1*, *MSH2*, *MSH6*, *PMS2,* and *EPCAM*. A mutation (alteration) in any of these genes gives a person an increased lifetime risk of developing colorectal cancer [16] and other related cancers. Women also have an increased risk of developing endometrial [2] and ovarian cancers [5].

Most mutations that cause Lynch syndrome are found in the *MLH1* or *MSH*2 genes. Not all families that appear to have Lynch syndrome will have mutations in *MLH1*, *MSH2*, *MSH6*, *PMS2,* or *EPCAM*. Research is ongoing to identify other genes associated with Lynch syndrome. Some people will develop changes in these genes that are not inherited, but are related to the aging process and other causes that are not well understood. If a tumor is found to have alterations in these genes, the person?s blood will also be tested for that abnormal gene. If the blood and tumor both have the changed gene, the condition is inherited rather than acquired, meaning other family members could be affected; testing is available (see below).

How is Lynch syndrome inherited?

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. Lynch syndrome follows an autosomal dominant inheritance pattern, in which a mutation needs to happen in only one copy of the gene for the person to have an increased risk of getting that disease. This means that a parent with a gene mutation may pass along a copy of their normal gene or a copy of the gene with the mutation. Therefore, a child who has a parent with a mutation has a 50% chance of inheriting that mutation. A brother, sister, or parent of a person who has a mutation also has a 50% chance of having the same mutation.

How common is Lynch syndrome?

Most colorectal cancer [16] is sporadic (occurs by chance with no known cause). Approximately 3% to 5% of all cases of colorectal cancer are thought to be due to Lynch syndrome.

How is Lynch syndrome diagnosed?

Lynch syndrome is likely if a family history meets the Modified Amsterdam Criteria listed above. Lynch syndrome can be confirmed through a blood test. The test can determine if someone has a mutation in one of the genes associated with Lynch syndrome. Currently testing is available for the *MLH1*, *MSH2*, *MSH6,* and *EPCAM* genes. The *PMS2* gene is tested for in some clinical trials [17] (research studies) as well as cancer centers that specialize in Lynch syndrome. However, not all families with Lynch syndrome will have a mutation in one of these genes.

For patients who have a family history that suggests Lynch syndrome, screening tests can be

performed on tumor (cancer) tissue to help determine if Lynch syndrome is likely. The two screening tests suggested are microsatellite instability testing (MSI) and immunohistochemistry testing (IHC). The results of these tests can indicate whether more specific genetic testing should be considered.

Since most colorectal cancer [16] is sporadic, genetic testing is only recommended for people who have a family history that suggests Lynch syndrome. Testing for mutations in the Lynch syndrome genes may not be beneficial for the average person.

What are the estimated cancer risks associated with Lynch syndrome?

General cancer risks for people with Lynch syndrome

- Colorectal cancer [16] 80%
- Stomach cancer [3] 11% to 19%
- Hepatobiliary tract [12] cancer (liver/bile duct [12]) 2% to 7%
- Urinary tract [9] cancer 4% to 5%
- Small bowel [6] cancer (intestines) 1% to 4%
- Brain [18] or central nervous system [19] tumor 1% to 3%

Cancer risks for women with Lynch syndrome

- Endometrial cancer [2] 20% to 60%
- Ovarian cancer [5] 9% to 12%

As noted above, Lynch syndrome has been linked to higher risk of other types of cancer as well, including pancreatic, prostate, kidney, and breast cancers [20].

What are the screening options for Lynch syndrome?

It is important to discuss with your doctor the following screening options, as each individual is different:

General screening guidelines

- Colonoscopy [21] every one to two years, beginning between the ages of 20 to 25 (or five years younger than the earliest age at diagnosis in the family, whichever is sooner)
- Periodic upper endoscopy [22] screening (this procedure uses a thin, flexible tube with a light inserted into the body to examine a specific region) for stomach [3] or intestinal cancer [23] (especially if a family member has had one of these cancers)
- Yearly urine cytology to screen for urinary tract cancer [9]

Screening for women

- Yearly pelvic examination, Pap test [24], transvaginal ultrasound [25] (a test where a small ultrasound probe is inserted for a pelvic examination in order to obtain better imaging of the uterus), endometrial biopsy [26] (an examination on a sample of tissue from the inner lining of the uterus done as part of a pelvic examination), and CA-125 blood test (a test to detect a protein found to be elevated in the blood of some women with ovarian cancer), beginning

between the ages of 25 to 30

Screening options may change over time as new technologies are developed and more is learned about Lynch syndrome. It is important to talk with your doctor about appropriate screening tests.

Learn more about what to expect with common tests and procedures [27].

Questions to ask the doctor

If you are concerned about your risk of colorectal cancer [16] or other types of cancer, talk with your doctor. Consider asking the following questions of your doctor:

- What is my risk of developing colorectal cancer [16] or other types of cancer?
- What can I do to reduce my risk of cancer?
- What are my options for cancer screening?

If you are concerned about your family history and think your family may have Lynch syndrome, consider asking the following questions:

- Does my family history increase my risk of colorectal cancer [16] or other types of cancer?
- Have MSI or IHC tests been done on my tumor tissue?
- Should I meet with a genetic counselor?
- Should I consider genetic testing [28]?

Additional resources

Guide to Colorectal Cancer [16]

Guide to Uterine Cancer [2]

Guide to Stomach Cancer [3]

Guide to Ovarian Cancer [5]

Guide to Liver Cancer [10]

Guide to Bile Duct [12]

Guide to Small Bowel Cancer [6]

Guide to Brain Tumor [18]

Guide to Breast Cancer [4]

Guide to Prostate [8]

Guide to Pancreatic Cancer [7]

Guide to Kidney Cancer [11]

What to Expect When You Meet With a Genetic Counselor [29]

Lynch Syndrome International
http://www.lynchcancers.com/ [30]

Colon Cancer Alliance
www.ccalliance.org [31]

C3: Colorectal Cancer Coalition
www.fightcolorectalcancer.org [32]

To find a genetic counselor in your area, ask your doctor or visit the following websites:

National Society of Genetic Counselors
www.nsgc.org [33]

National Cancer Institute: Cancer Genetics Services Directory
www.cancer.gov/cancertopics/genetics/directory [34]

Links:
[1] http://www.cancer.net/cancer-types/lynch-syndrome
[2] http://www.cancer.net/node/19308
[3] http://www.cancer.net/node/19645
[4] http://www.cancer.net/node/18618
[5] http://www.cancer.net/node/19481
[6] http://www.cancer.net/node/19632
[7] http://www.cancer.net/node/19495
[8] http://www.cancer.net/node/19562
[9] http://www.cancer.net/node/18520
[10] http://www.cancer.net/node/19134
[11] http://www.cancer.net/node/18969
[12] http://www.cancer.net/node/18505
[13] http://www.cancer.net/node/18852
[14] http://www.cancer.net/node/19364
[15] http://www.cancer.net/node/19307
[16] http://www.cancer.net/node/18701
[17] http://www.cancer.net/patient/Diagnosis+and+Treatment/Treating+Cancer/Clinical+Trials
[18] http://www.cancer.net/node/18562
[19] http://www.cancer.net/node/18660
[20] http://www.cancer.net/node/24431
[21] http://www.cancer.net/node/24481
[22] http://www.cancer.net/node/24731
[23] http://www.cancer.net/node/18870
[24] http://www.cancer.net/node/24638
[25] http://www.cancer.net/node/24714
[26] http://www.cancer.net/node/24406
[27] http://www.cancer.net/node/24959
[28] http://www.cancer.net/node/24895

[29] http://www.cancer.net/node/24907
[30] http://www.lynchcancers.com/
[31] http://www.ccalliance.org
[32] http://www.fightcolorectalcancer.org/
[33] http://www.nsgc.org
[34] http://www.cancer.gov/cancertopics/genetics/directory