Lynch Syndrome

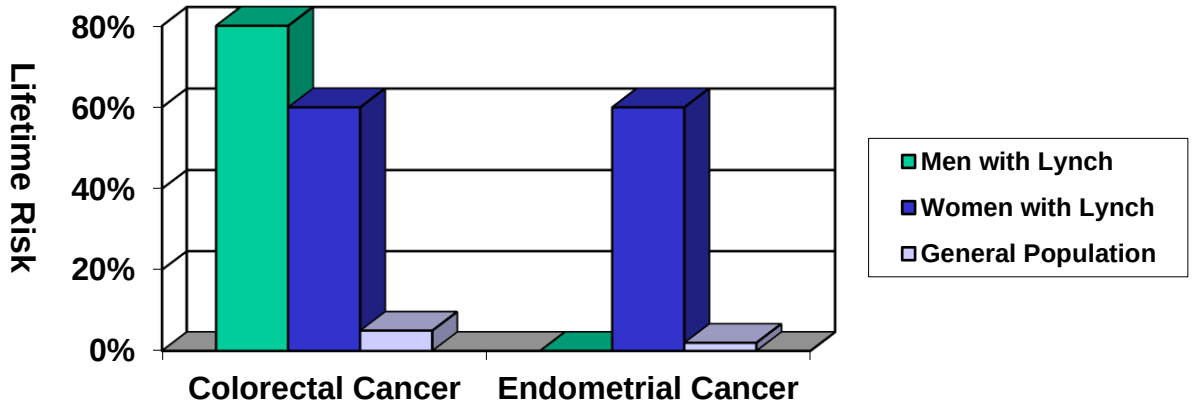
Hereditary Nonpolyposis Colorectal Cancer Syndrome

Lynch syndrome, also called hereditary nonpolyposis colorectal cancer syndrome (HNPCC for short), is an inherited tendency to develop colorectal, endometrial (uterine) and other cancers. Inherited conditions are passed to a person through their mother or father. Although most cancers are not inherited, about 5% of people who have colorectal or endometrial cancer have Lynch syndrome.

What are the cancer risks for people with Lynch syndrome?

- A higher than usual risk of developing colorectal cancer (20-80% lifetime risk). These cancers tend to occur before the age of 50. See Figure 1.
- An increased risk of developing a second primary colorectal cancer.
- Women have a 15-60% lifetime risk of developing endometrial cancer.

Lynch Syndrome Cancer Risks Compared to the General Population



Other cancers that occur less commonly in Lynch syndrome include: ovarian, stomach, urinary tract, hepatobiliary tract (part of the liver and bile ducts), small intestine, pancreas, skin (sebaceous gland tumors) and brain.

People with Lynch syndrome who have sebaceous gland skin tumors are often referred to as having the Muir-Torre variant of Lynch syndrome. The sebaceous tumors include: sebaceous adenomas, sebaceous carcinomas, epitheliomas and keratoacanthomas.

Cancer risk can be reduced by following cancer screening and prevention guidelines.

How can I find out if I have Lynch syndrome?

The following features are common in families with Lynch syndrome:

- Three or more closely related family members have colorectal, endometrial or other Lynch-associated cancer.
- Two or more generations have cancer.
- A family member is diagnosed before the age of 50 with colorectal or endometrial cancer.

These features are often referred to as the Amsterdam criteria. However, not all families that meet the Amsterdam criteria have Lynch syndrome. In addition, families that have Lynch syndrome may not meet all of the Amsterdam criteria. If you are concerned about Lynch syndrome in your family, contact Clinical Cancer Genetics at 713-745-7391 to schedule a consultation.

What causes Lynch syndrome?

Lynch syndrome is caused by an inherited gene change (mutation). Genes are the set of instructions that tell all of the cells in our bodies what to do. A gene mutation is a mistake in a gene's DNA that causes the gene to stop working. In the case of Lynch syndrome, a gene has stopped working that normally helps to prevent colon and endometrial cancer. Therefore, colon and endometrial cancers are more likely to develop, and are also more likely to occur at a younger age than usual.

Lynch syndrome is caused by mutations in five genes: *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM*. Specific risks for the Lynch syndrome-associated cancer depend on which gene is causing Lynch syndrome within a family.

What are the chances of inheriting Lynch syndrome?

Each person has two copies of each of the Lynch syndrome genes. One copy is inherited from the mother, and one copy is inherited from the father. One inherited gene mutation in either copy will cause Lynch syndrome. There is a 50% (1 in 2) chance that a person with Lynch syndrome will pass the mutation to each of their children. Lynch syndrome does not skip generations. Both male and females are equally likely to be affected.

Why is it important to diagnose Lynch syndrome?

People who have Lynch syndrome are at much higher risk to develop colorectal, endometrial, and other cancers than people in the general population. For someone who has cancer, the diagnosis of Lynch syndrome may indicate a higher risk of developing a new cancer in the future. However, following the early detection and prevention guidelines for Lynch syndrome can reduce these cancer risks.

Because Lynch syndrome is inherited, the diagnosis also affects family members. If the specific mutation causing Lynch syndrome in the family is found through genetic testing, then other family members can be tested.

How is Lynch syndrome diagnosed?

Family History

Screening for Lynch syndrome includes a medical and family history review and construction of a multi-generation family tree. A genetic counselor usually conducts this screening process and assesses the family's risk. Further tests will be considered if the medical and family history review suggests the possibility of Lynch syndrome.

Testing

Special tests can be performed on a colon tumor or other tumor. These screening tests are called microsatellite instability (MSI) assay and immunohistochemical (IHC) analysis. The tests look for characteristics in tumors that may be caused by Lynch syndrome. They can identify which gene may be responsible for Lynch syndrome in the family. Genetic testing is recommended if the pathology results suggest the possibility of Lynch syndrome.

Genetic testing looks for mutations in the Lynch syndrome genes. Testing is usually performed on a blood sample. If a mutation is found, then the Lynch syndrome diagnosis is confirmed. In addition, genetic testing may then be offered to other members of the family who wish to learn whether or not they have Lynch syndrome.

How is Lynch syndrome managed?

It is important to manage Lynch syndrome by following cancer prevention and early detection guidelines. Management plans include cancer screening exams that are tailored to each patient and their family. Cancer screening exams are medical tests performed to ensure that any existing cancers are identified at their earliest, most treatable stages. General management guidelines for Lynch syndrome are described below.

Colorectal Cancer

A screening colonoscopy at regular intervals is very important. Beginning at age 20-25 years (or 10 years younger than the earliest age of colon cancer diagnosis in the family), a colonoscopy is recommended every 1-2 years. If present, precancerous polyps are removed during the colonoscopy so they will **not** develop into cancer.

For persons having colon cancer surgery, the surgeon may suggest removing the entire colon rather than part of the colon. This helps reduce the risk of developing a second primary colorectal cancer.

Symptoms

People who have Lynch syndrome should contact their doctor if they have any of the following symptoms:

- Rectal bleeding
- Blood in the stool or toilet after a bowel movement
- Prolonged diarrhea or constipation
- A change in the size or shape of your stool
- Abdominal pain in your lower stomach
- A feeling of discomfort or urge to have a bowel movement when there is no need

Gynecologic Cancers (endometrial cancer and ovarian cancer)

Gynecologic cancer screening at regular intervals is important. Women with Lynch syndrome have a risk of endometrial cancer equal to or greater than the risk for colorectal cancer. Beginning at age 30-35 years an annual pelvic exam, endometrial biopsy and vaginal ultrasound is recommended. Particularly in women who have not gone through menopause, gynecologic cancers are hard to detect by symptoms alone.

Surgical removal of the uterus, ovaries and fallopian tubes is a preventive measure to decrease the risk of developing endometrial and ovarian cancer. Your doctor would recommend the timing of this surgery based on your genetic mutation as well as personal and family history.

Although pap smears can screen for cervix cancer, and are recommended for all women, they **do not detect** endometrial or ovarian cancer.

Symptoms

Endometrial cancer: Any abnormal vaginal bleeding (bleeding between periods, heavy periods or prolonged periods) or any post-menopausal vaginal bleeding should be reported. It is often suggested to have an in-office endometrial biopsy or dilatation and curettage (D&C) procedure.

Ovarian cancer: There are no specific early warning signs for ovarian cancer. However, report to your doctor any signs of bloating, an increase or swelling in the abdominal area or change in bowel and bladder habits.

Other cancers

Upper endoscopy, also known as an EGD, may be considered every 2-3 years to check for polyps or cancers in the stomach and small intestine. This may be performed at the same time as a colonoscopy, although there is no proven benefit to this screening test.

Your doctor may suggest having an annual urinalysis with cytology as a screening test for urinary tract cancers, although there is no proven benefit to this screening test.

Depending on family history and other factors, screening for other Lynch-associated cancers may be considered.

Resources

MD Anderson Cancer Center
Clinical Cancer Genetics Program
https://www.mdanderson.org/research/departments-labs-institutes/programs-centers/clinical-cancer-genetics.html
The Clinical Cancer Genetics Program at MD Anderson Cancer Center is dedicated to providing hereditary cancer risk assessment and consultation services. Click on the link “Hereditary Cancer Syndromes” to learn more about Lynch syndrome.

Collaborative Group of the Americas on Inherited Colorectal Cancer (CGA)
http://www.cgaicc.com/
The CGA focuses on families with rare forms of colorectal cancer, including Lynch syndrome.

National Cancer Institute (NCI)
Genetics of Colorectal Cancer
https://www.cancer.gov/types/colorectal/hp/colorectal-genetics-pdq
800-4-CANCER (800-422-6237)

Cancer.Net
http://www.cancer.net/
Oncologist-approved cancer information from the American Society of Clinical Oncology. Click on the "Types of Cancer" tab to find information on colorectal cancer and Lynch syndrome.