Hereditary Nonpolyposis Colorectal Cancer or Lynch Syndrome

Hereditary nonpolyposis colorectal cancer syndrome, also called HNPCC-Lynch syndrome is an inherited tendency to develop colorectal, endometrial (uterine), and other cancers. Inherited conditions are passed to an individual through their blood relatives. Although most cancers are not inherited, about 5 percent (%) of people who have colorectal or endometrial cancer have HNPCC-Lynch syndrome.

What are the cancer risks for people with HNPCC-Lynch Syndrome?

- A higher than usual risk of developing colorectal cancer (60-80% lifetime risk). These cancers tend to occur before the age of 50. (See Figure 1)
- Women with HNPCC-Lynch syndrome have a 40-60% lifetime risk of developing endometrial cancer.
- An increased risk of developing a second primary colorectal cancer.

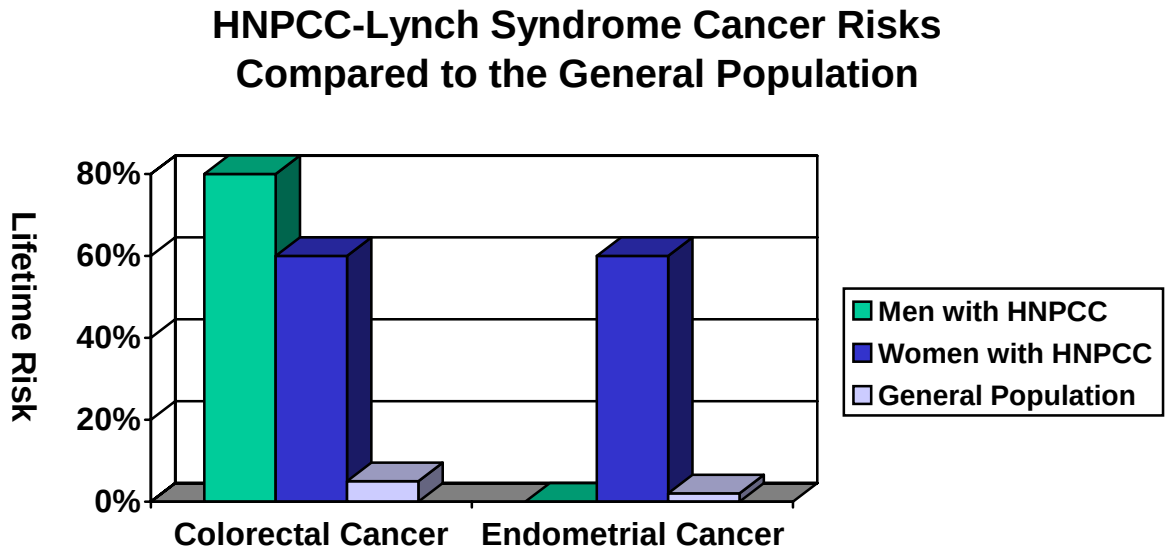

Figure 1

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

People with HNPCC-Lynch syndrome can reduce their cancer risks by following cancer

screening and prevention guidelines.

How can I find out if I have HNPCC-Lynch syndrome?

The following features are common in families with HNPCC-Lynch syndrome:

- Three or more closely related family members have colorectal, endometrial, or other HNPCC-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 HNPCC-Lynch syndrome. In addition, families that have HNPCC-Lynch syndrome may not meet all of the Amsterdam criteria. If you are concerned about HNPCC-Lynch syndrome in your family, contact Clinical Cancer Genetics at 713-745-7391 to schedule a consultation.

What causes HNPCC-Lynch syndrome?

HNPCC-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 HNPCC-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.

The majority of HNPCC-Lynch syndrome is due to a mutation in either the MLH1 or MSH2 gene. Mutations in the MSH6 gene, the PMS2 gene, and possibly other genes can also cause HNPCC-Lynch syndrome.

What are the chances of inheriting HNPCC-Lynch syndrome?

Each person has two copies of each of the HNPCC-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 HNPCC-Lynch syndrome. There is a 50% chance that a person with HNPCC-Lynch syndrome will pass the mutation to each of their children.

Why is it important to diagnose HNPCC-Lynch syndrome?

People who have HNPCC-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 HNPCC-Lynch syndrome may indicate a higher risk of developing a new cancer in the future. However, following the early detection and prevention guidelines that have been established for HNPCC-Lynch syndrome can reduce these cancer risks.

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

How is HNPCC-Lynch syndrome diagnosed?

Family History

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

Testing

Specific pathology tests can be performed on a colon tumor or other tumor. These tests look for characteristics in tumors that may be caused by HNPCC-Lynch syndrome and can identify which gene may be responsible for HNPCC-Lynch syndrome in the family. Genetic testing is recommended if the pathology results suggest a possibility of HNPCC-Lynch syndrome.

Genetic testing looks for mutations in the HNPCC-Lynch syndrome genes. It is usually performed on a blood sample. If a mutation is found, then the HNPCC-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 HNPCC-Lynch syndrome.

How is HNPCC-Lynch syndrome managed?

It is important to manage HNPCC-Lynch syndrome by following cancer prevention and early detection guidelines. Management plans include specific cancer screening exams and are tailored to each patient and their family by a team of specialists. 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 HNPCC-Lynch syndrome include:

Colorectal Cancer

A screening colonoscopy at regular intervals is very important. Beginning at age 20-25, a colonoscopy with chromoendoscopy (dye spray) is recommended every one to two years. If present, precancerous polyps are removed during the colonoscopy **before** they develop into cancer.

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

Symptoms of colorectal cancer:

People who have HNPCC-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 very important. Women with HNPCC-Lynch syndrome have a risk of endometrial cancer equal to or greater than the risk for colorectal cancer. Beginning at age 25-35 an annual pelvic exam, endometrial biopsy, CA-125 testing, 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 (also referred to as a hysterectomy with bilateral salpingo-oophorectomy) is recommended for women in their mid to late forties who have completed childbearing. This protective surgery will decrease the risk of developing endometrial and ovarian cancer.

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

Symptoms of HNPCC-associated gynecologic cancers

Endometrial cancer: Any abnormal vaginal bleeding (bleeding between periods, heavy periods, or prolonged periods) or any post-menopausal vaginal bleeding should be reported, and an office endometrial biopsy or dilatation and curettage (D & C) should be performed.

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

Other cancers

Depending on family history and other factors, a genetic counselor will assess the need to screen for other HNPCC-associated cancers.

Where can I find information about HNPCC-Lynch syndrome?

The University of Texas M. D. Anderson Cancer Center
Hereditary Gynecologic Cancer Home Page
http://www.mdanderson.org/diseases/hereditarygyn/
For more information and to learn about current research studies at M. D. Anderson, click on

About HNPCC, or call M. D. Anderson's Clinical Cancer Genetics Program, 713-745-7391.

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 HNPCC-Lynch Syndrome.

National Cancer Institute (NCI)
Genetics of Colorectal Cancer
http://www.cancer.gov/cancertopics/pdq/genetics/colorectal/healthprofessional
1-800- 4-CANCER (1-800-422-6237)
Click on the link on the left hand side of the page to access more information on HNPCC-Lynch Syndrome.