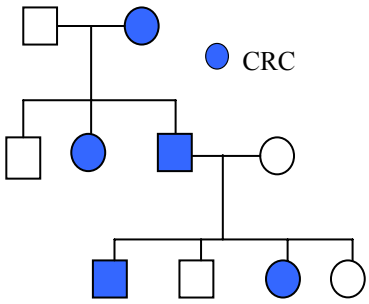
Hereditary Non-polyposis Colorectal Cancer (HNPCC)

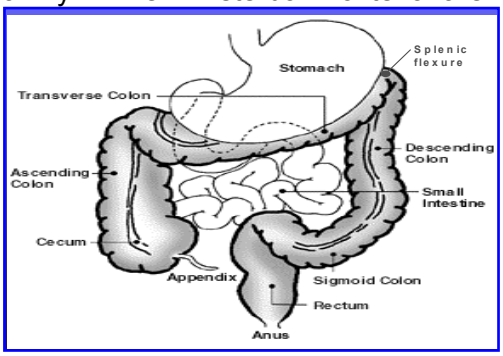
What is Hereditary Non-polyposis Colorectal Cancer?

HNPCC is a condition in which the tendency to develop colon or rectal cancer is inherited.



HNPCC is a condition that poses an increased risk for developing colon or rectal cancer. Approximately 3-5% of colorectal cancer (CRC) is associated with HNPCC. HNPCC is a dominant condition, meaning that people with HNPCC have a 50% chance of passing the HNPCC gene mutation (change) to each of their children.

The Amsterdam criteria are a set of characteristics which can provide the clinical diagnosis of HNPCC in a family. The Amsterdam criteria are described as three or more closely related family members affected with colon cancer, colon cancer in two or more generations, and at least one individual diagnosed with colorectal cancer before the age of 50 years. In addition, families with HNPCC may include a history of other associated cancers including endometrial, ovarian, stomach, urinary tract, bile duct, and small bowel cancer. With HNPCC, the lifetime risk for colorectal cancer is approximately 80% and the lifetime risk of endometrial cancer is 40%. The lifetime risk associated with the other cancers is 10% or less.



Genes associated with HNPCC

Mutations or large deletions in 5 different genes (MLH1, MSH2, MSH6, PMS2, and PMS1) have been found to cause HNPCC.

MLH1 and MSH2 genes: It is believed that 90% of detectable HNPCC mutations will be found in either the MLH1 or MSH2 genes. Usually, they are point mutations, meaning that a single DNA base (letter) is altered. However, it is now believed that 20-30% of changes in the MSH2 gene, in particular, are due to large deletions of genetic material that were not detectable using previous testing methods. Therefore, if a family meets the Amsterdam criteria, full sequencing of the MLH1 and MSH2 genes is the initial step in testing. If no mutation is found in one of these two genes, testing can be performed to look for large deletions in the MSH2 and MLH1 genes or full sequencing of the MSH6 gene can be performed.

MSH6 gene: Less than 10% of detectable mutations are found in the MSH6 gene and this low detection rate is the reason genetic testing is not performed on this gene initially. Individuals with HNPCC due to a mutation in the MSH6 gene usually have tumors that show a low level of instability, termed microsatellite instability low (MSI-Low). Tumors from individuals thought to have HNPCC can be tested for microsatellite instability and if the result is MSI-Low, genetic testing for the MSH6 gene is considered the next step in the testing process.

PMS2 and PMS1 genes: HNPCC caused by mutations in these two genes is very rare with only a few cases reported. Genetic testing for these two genes is not clinically available.

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Look for these Clues

Family history is an important risk factor for hereditary colorectal cancer.

When reviewing your family history, it is important to consider both your father's and your mother's side of the family since an altered gene can be inherited from either parent. Gather information on all types of cancer because other cancers can occur as part of hereditary non-polyposis colorectal cancer. Certain "red flags" may suggest a higher risk for hereditary non-polyposis colorectal cancer. These include:

- The diagnosis of colon or rectal cancer before age 50
- The presence of several family members with colorectal cancer
- Having several family members with colon polyps
- The occurrence of ovarian, uterine, stomach, ureter, or small intestine cancers in family members
- A relative with a positive genetic test for colorectal cancer

What Can You Do?

Talk with your health care provider about options for prevention, screening, genetic counseling and genetic testing.

If you have a family history of colorectal cancer, experts may recommend more frequent screening examinations beginning at an earlier age than recommended for the general population. These tests may include

- Colonoscopy
- Sigmoidoscopy
- Barium enemas and x-rays
- Fecal occult blood tests

Your physician may recommend additional screening exams to detect cancer in different organs including

- Annual physical exams with standard blood tests (heme-8, prothrombin time, SMA-6, and SMA-12)
- Urinalysis
- Urine cytology
- For affected/at-risk females:
    - Yearly Pap smear and pelvic exams
    - Yearly transvaginal ultrasound (with or without endometrial biopsy)

Options for preventing colon cancer can include certain medications or surgery. Talk with your health care provider to determine if these are right for you.

Genetic testing and genetic counseling for HNPCC is currently available. Genetic counselors interpret information about genetic diseases or disorders, analyze inheritance patterns and risks of occurrence, identify high-risk family members, and review available options for prevention, screening, genetic testing, and treatment. For more information about hereditary colorectal cancer or for a referral, please call the **Mid-Atlantic Cancer Genetics Network** toll free at 1-877-880-6188 or visit our Web site at http://www.MACGN.org

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