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Genetics of Hereditary Colon, Uterine and Ovarian Cancer

The majority of cancer cases are not attributable to hereditary causes. However, cancer can be hereditary in some families. There are many factors that can increase the probability that cancers in a family may be hereditary. Some of these factors are: early onset of cancer (colon cancer <50), more than one primary (new) cancer in an individual, the same cancer in two or more close relatives, unusual presentation of cancer, and related cancers (such as colon/uterine/ovarian/other gastrointestinal cancers) found in the same family.

Several gene changes (mutations) have been discovered which predispose individuals to cancer. In review, the genetic instructions for our bodies are stored in our cells in tiny structures called chromosomes. A normal individual has 23 pairs of chromosomes: one chromosome from each pair is normally inherited from the mother, and the other from the father. There are now 5 genes that, when mutated, are known to cause a hereditary colon cancer syndrome called Hereditary Non-polyposis Colorectal Cancer (HNPCC). This syndrome is also called Lynch syndrome. Clinical testing is available for several of the most common genes involved in HNPCC, including MLH1 (on chromosome 3) and MSH2 (on chromosome 2).

HNPCC is passed down in families in an autosomal dominant pattern of inheritance. This means that an individual who carries a mutation has a 50% chance of passing the mutation on to each of their children. It also means that siblings of an individual who carries a mutation have a 50% chance of carrying the same mutation.

Individuals who carry a mutation in the MLH1 or MSH2 gene are at risk for several types of cancer. Both men and women who carry a mutation are at increased risk to develop colon cancer. It is estimated that the risk for colon cancer approaches 75% by age 65. Individuals who carry a mutation are also at increased risk for a second primary colon cancer. The available data suggest that women who carry a mutation have a 30-40% lifetime risk of uterine cancer, and up to a 10% lifetime risk of ovarian cancer. Individuals with HNPCC may also be at some increased risk for a variety of other types of cancers including cancers of the head and neck, small intestine, stomach, and urinary tract.

Individuals who learn they have HNPCC are offered special surveillance and risk reduction options.