

Genetics of Hereditary Colon, Uterine and Ovarian Cancer (Lynch syndrome)

Updated August 2020

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 or uterine cancer <50 years), 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. In addition, abnormal results on screening tests performed on a tumor (i.e. microsatellite instability (MSI) or immunohistochemistry (IHC)) may also suggest a higher likelihood that the tumor is due to a hereditary cause.

Several gene changes (mutations) have been discovered which predispose individuals to cancer. The most common form of hereditary colorectal cancer is called Lynch syndrome. Clinical testing is available for several genes involved in Lynch syndrome including *MLH1*, *MSH2*, *MSH6*, *EPCAM* and *PMS2*. Genetic counseling is particularly important as the cancer risks and thus management recommendations can vary greatly between the different genes associated with Lynch syndrome.

Lynch syndrome is passed down in families in an autosomal dominant pattern of inheritance. This means that an individual who has 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 has a mutation have a 50% chance of having the same mutation.

Individuals with Lynch syndrome are at increased risk for several types of cancer. Both men and women with Lynch syndrome are at increased risk to develop colorectal cancer with a lifetime risk of ~10-60% (vs. ~4-5% general population). Individuals with Lynch syndrome are also at increased risk for a second primary colon cancer. The available data suggest that women with Lynch syndrome have a ~13-57% lifetime risk of uterine cancer (vs. ~3% general population), and a ~4-38% lifetime risk of ovarian cancer (vs. 1-2% general population). Individuals with Lynch syndrome may also have some increased risk for a variety of other types of cancers, including stomach, small bowel, pancreas, urinary tract, prostate, sebaceous skin cancers, and brain tumors. Again, the risks for particular cancers can vary greatly between the different genes associated with Lynch syndrome; however, in general, the overall lifetime risks for many of these other cancers are relatively small.

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

References

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