UT Southwestern
Harold C. Simmons
Comprehensive Cancer Center

NCI Designated Comprehensive Cancer Center

Lynch syndrome: *MLH1* Mutations

What You Should Know About Lynch Syndrome (*MLH1* Mutations)

Lynch syndrome is the most common type of hereditary colon cancer and accounts for 2-4% of all colon cancers. Families with Lynch syndrome often have multiple family members with colon, uterine or other cancers, typically diagnosed before age 50. Lynch syndrome is caused by mutations in one of five different genes, and the specific cancer risks and management recommendations depend on the gene.

Cancer Risks Associated with Lynch Syndrome (*MLH1* Mutations)

Individuals with Lynch syndrome due to a mutation in the *MLH1* gene have a 46-49% risk to develop colorectal cancer throughout their lifetime. Females have a 43-57% risk for uterine cancer, and a 5-20% risk for ovarian cancer. Men and women with Lynch syndrome also have an increased risk for other types of cancer, including stomach, small bowel, pancreatic, urothelial, bladder, prostate and brain cancers. These cancers tend to occur at a younger age.

Risks to Family Members

Mutations in the *MLH1* gene are inherited in an autosomal dominant fashion. This means that children, brothers, sisters, and parents of individuals with an *MLH1* mutation have a 1 in 2 (50%) chance of having the mutation as well. Individuals with an *MLH1* mutation may develop one cancer, more than one cancer, or none at all. Both males and females can inherit a familial *MLH1* mutation and can pass it on to their children.

When an individual inherits two *MLH1* mutations (one from each parent), this causes a syndrome called Constitutional Mismatch Repair Deficiency (CMMRD). CMMRD is associated with an increased risk for childhood colon cancer, lymphoma, brain tumors, and café au lait spots.

Managing the Cancer Risks

Colon Cancer

- Colonoscopy every 1-2 years starting at age 20-25
- If colon cancer is detected, partial or complete removal or colon should be considered

Uterine/Ovarian Cancer

- Screening via uterine biopsy every 1-2 years can be considered
- CA-125 screening and transvaginal ultrasound can be considered (these tests have limited ability for early detection of ovarian cancer)
- Removal of ovaries and uterus after child-bearing is complete can be considered to reduce the risk

Other Cancers

- Annual physical examination at age 25-30
- Annual urinalysis beginning at age 30-35
- Upper endoscopy every 3-5 years, beginning at age 40
- Additional screenings may be considered based on personal risk factors and family history

Last updated 01/03/2020

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