**Lynch Syndrome**

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***Fact Sheet for Healthcare Professionals***

Patients with Lynch syndrome are at increased risk of developing colorectal cancer, endometrial (uterine) cancer, ovarian cancer, and other cancers. Lynch syndrome is caused by mutations in the mismatch repair genes, *MLH1, MSH2, MSH6,* and *PMS2*, and the *EPCAM* gene. About 3% of patients with colorectal cancer have Lynch syndrome. Identification of patients and their relatives with Lynch syndrome is important to allow them to take advantage of interventions that can significantly reduce their risk of cancer in the future and allow for early detection of cancer if it develops.

**Cancer Risks Associated with Lynch Syndrome:**

* 25- 82% risk of colorectal cancer by age 701
* 20-60% risk of endometrial cancer by age 702
* 11-19% risk of stomach cancer by age 702
* 9-12% risk of ovarian cancer by age 702
* 2-7% risk of cancers of the hepatobiliary tract by age 702
* 4-5% risk of cancers of the urinary tract by age 702
* Increased risks for cancers of small bowel, brain, and skin

**Evidence-Based Clinical Recommendation for Identifying Patients at Risk**

*The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Recommendation (2009)1*

The EGAPP Working Group found sufficient evidence to recommend offering tumor screening and genetic testing for Lynch syndrome to individuals with newly diagnosed colorectal cancer to reduce morbidity and mortality in relatives.

Screening for Lynch syndrome is done on the colorectal cancer tissue after surgery using immunohistochemistry (IHC) and/or microsatellite instability (MSI) testing. For those patients who screen positive for Lynch syndrome, genetic testing can be performed to diagnose Lynch syndrome by identifying the patient’s specific mutation. Other family members then can be tested for that mutation.

Other recommendations exist to help identify *unaffected*individuals who may be at risk for Lynch syndrome, including those from the National Comprehensive Cancer Network (NCCN)2 and the American College of Medical Genetics (ACMG)/National Society of Genetic Counselors (NSGC).3

Genetic counseling and testing for Lynch syndrome may be appropriate for patients who meet any of the following criteria:

* Diagnosed with colorectal cancer in the past
* Diagnosed with endometrial cancer (especially before age 50)
* Several family members with colorectal, endometrial, or other cancers associated with Lynch syndrome

**Genetic Counseling and Testing for Lynch Syndrome**

*Genetic Counseling*

Genetic counseling helps patients and their families better understand their risk for hereditary cancer so that they can make informed decisions about tumor screening, genetic testing, and follow-up care by:

* Reviewing an individual’s personal and family medical history
* Reviewing risk for Lynch syndrome and the chance of finding a mutation through tumor screening and genetic testing
* Interpreting tumor screening and genetic testing results and explaining what they mean for individuals and their relatives
* Outlining medical management implications of a positive or negative screen or test result
* Providing referrals to medical specialists, support resources, and research opportunities
* Addressing concerns about the privacy and confidentiality of personal genetic information

*Benefits and Risks of Genetic Testing*

* Individuals with a positive genetic test result can take steps to reduce their cancer risk through earlier, more frequent and/or additional screening or prophylactic surgery in some cases
* Genetic testing may provide a patient’s relatives with useful information, including which mutation relatives should be tested for.
* For relatives, a negative test result may provide a sense of relief and will help them avoid unneeded screens or surgeries.
* While the benefits of genetic testing greatly outweigh the disadvantages, test results may affect a person’s emotions, family relationships, finances, privacy, insurance, and medical choices.
* Genetic information cannot be used to deny someone health coverage or employment, because of a federal law called the Genetic Information Nondiscrimination Act of 2008 (GINA). However, this law does not cover life, disability, and long-term care insurance, and only applies to asymptomatic individuals (*not* those with a personal history of Lynch syndrome-related cancer).
* Treatments like prophylactic surgery have risks and possible serious long-term complications.

**Medical Management of Patients with Lynch syndrome**

*Several management options exist but the strength of evidence varies across types of interventions*

Interventions recommended by EGAPP:

* Patients diagnosed with Lynch syndrome should be informed of the advantages of contacting blood relatives to offer counseling and targeted testing for Lynch syndrome
* Relatives with Lynch syndrome should have earlier and more frequent colonoscopies
* Women with Lynch syndrome (with and without personal histories of Lynch syndrome-related cancers) should consider having additional surveillance for endometrial cancer

Recommendations from other groups include consideration of the following:2,3

* *Colon and Rectum*
  + Colonoscopy every 1-2 years starting at age 20-25 or 2-5 years before the youngest case in the family if diagnosed before age 25
  + Aspirin although optimal dose and length of time not determined
* *Endometrium and ovary*
  + Prophylactic hysterectomy and salpingo-oophorectomy when childbearing is completed
  + Patient education on gynecologic cancer signs (See CDC’s [Inside Knowledge](https://www.cdc.gov/cancer/gynecologic/knowledge/index.htm) campaign)
    - Abnormal vaginal or postmenopausal bleeding
    - Pelvic or abdominal pain or pressure
    - Bloating
    - Feeling full too quickly or trouble earing
    - Increased urinary frequency or urgency
  + Endometrial biopsy every 1-2 years
  + At clinician’s discretion: transvaginal ultrasound and serum CA-125
* *Gastric and small bowel*
  + Testing for *Helicobacter pylori* and treatment if present
  + Upper endoscopy at time of colonoscopy with visualization of the duodenum every 3-5 years starting at age 40 for those at higher risk of gastric or small bowel cancer
* *Urothelial*: Annual urine analysis starting at age 25-30
* *Central Nervous System*: Annual physical/neurological exam starting at age 25-30

References

1. Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Recommendations from the EGAPP Working Group: Genetic testing strategies in newly diagnosed individuals with colorectal cancer aimed at reducing morbidity and mortality from Lynch syndrome in relatives. *Genetics in Medicine* 2009; 11:35-41.

2. National Comprehensive Cancer Network. NCCN Guidelines Version 2.2019 Genetics/Familial High-Risk Assessment: Colon.

3. Familial risk-colorectal cancer: ESMO Clinical Practice Guidelines. American Society of Clinical Oncology Clinical Practice Guideline Endorsement of the Familial Risk- Colorectal Cancer: European Society for Medical Oncology Clinical Practice Guidelines. *Journal of Clinical Oncology*. 2014. 58. 1322.