What is Lynch syndrome?
Lynch syndrome, formerly known as hereditary non-polyposis colorectal cancer (HNPCC) syndrome, is a hereditary cancer predisposition condition caused by mutations in the \textit{MLH1, MSH2, MSH6, and PMS2}. All of these genes are involved in the repair of mistakes made when DNA is copied (DNA replication) in preparation for cell division. Mutations in any of these genes prevent the proper repair of DNA replication mistakes. As the abnormal cells continue to divide, the accumulated mistakes can lead to uncontrolled cell growth and possibly cancer. In addition, deletions affecting the epithelial cell adhesion molecule (\textit{EPCAM}) gene can also cause Lynch syndrome by epigenetic inactivation of the respective \textit{MSH2} allele.

Facts about Lynch syndrome

- Approximately 1 in 35 (2\%-3\%) of colon cancer patients has Lynch syndrome.
- People with Lynch syndrome have a 52\%-80\% chance of developing colon cancer in their lifetimes compared to 5\%-6\% for people in the general population.
- Women with Lynch syndrome have a 30\%-60\% chance of developing endometrial cancer in their lifetimes compared to a 2\%-3\% chance for women in the general population.
- Individuals with Lynch syndrome also have a slightly increased risk of developing stomach, ovarian, hepatobiliary, small intestine, and urinary tract cancers.
- The average age of onset of colon cancer in Lynch syndrome patients is between 42 and 61 years compared to 71 years in the general population.

Are there any screening tests for Lynch syndrome in a colorectal cancer patient?
There are several screening tests for Lynch syndrome, including microsatellite instability (MSI) testing and immunohistochemistry (IHC) testing. Either or both of these tests can be performed on a tumor from a person suspected of having Lynch syndrome. Such screening often is recommended prior to genetic testing.

Who is most likely to have a \textit{MLH1, MSH2} (including \textit{EPCAM}), \textit{MSH6}, or \textit{PMS2} mutation?
The likelihood is highest in families with a history of colorectal cancer and other Lynch syndrome-associated cancers (e.g., endometrial, stomach, small intestine, renal pelvis/ureter, ovarian, pancreatic, biliary tract, and brain, as well as sebaceous gland adenomas and keratoacanthomas); young age of onset; and synchronous or metachronous colorectal cancer. However, not every person in such families carries a harmful \textit{MLH1, MSH2} (or \textit{EPCAM}), \textit{MSH6}, or \textit{PMS2} mutation, and not every cancer in such families is linked to a harmful mutation in one of these genes but instead may be the result of a sporadic mutation. Furthermore, not every person who has Lynch syndrome will develop colorectal or endometrial cancer.

Specific indications for genetic counseling and testing vary among professional organizations. Guidelines are not a substitute for clinical judgment. Not all clinical scenarios can be anticipated, such as when there is a limited family structure or family medical history.
Why is genetic counseling important?
Genetic counseling helps people better understand their risk for hereditary cancer in order to make informed decisions about genetic testing and follow-up care.

What does genetic counseling entail?
Genetic counseling is a process that encompasses the following services:

- Reviewing an individual’s personal and detailed family medical history.
- Assessing and explaining risk for hereditary cancers and the chance of finding a mutation through genetic testing.
- Discussing the benefits, limitations, and other possible consequences of genetic testing.
- Outlining medical implications of a positive or a negative test result.
- Determining which family member is most appropriate to begin the genetic testing process in a family.
- Interpreting genetic test results and explaining what they mean for individuals and their relatives.
- Providing referrals to experts for follow-up screening and risk management.
- Providing referrals to support resources and research opportunities (including research on genetic testing, screening, treatment, etc.).
- Discussing risks and medical management options with a patient’s other health care provider(s).
- Addressing common concerns about the privacy and confidentiality of personal genetic information.

What are some of the benefits of genetic testing for Lynch syndrome?

- A positive test result can bring relief from uncertainty and allow people to make informed decisions about their futures. They can take steps to reduce their cancer risk through increased surveillance or other medical and lifestyle choices.
- A positive test result may help to explain why individuals or family members had cancer in the past, and, should they choose to share test results, may provide their family members with useful information.
- Those who have a positive test result may be able to participate in medical research that could, in the long run, help reduce deaths from colorectal cancer.
- A negative test result may provide a sense of relief and preclude the need for special preventive checkups, tests, or surgeries.

What are the disadvantages of genetic testing?
Test results may affect a person’s emotions, family relationships, finances, privacy, and medical choices.

- A positive result may make a person feel anxious, angry, or depressed. Medical treatments, such as surgery to try to prevent the cancer, could have serious, long-term implications and uncertain effectiveness.
- A negative result may make a person feel guilty because they escaped a disease that affected a loved one. They may also get a false sense of security that they have no chance of getting cancer, when, in fact, their cancer risk is the same as that of the general population.
- Because genetic testing can reveal information about more than one family member, the emotions caused by the results can create tension within families. The results also can affect personal choices, such as marriage and childbearing.
- Privacy and confidentiality of genetic test results are additional potential concerns. There is no guarantee that a person’s test results will remain private.
- Genetic testing can be expensive, depending on the extent of testing. Although many insurance plans cover the cost of the testing for individuals at high risk, coverage is unlikely for those not considered to be at high risk.