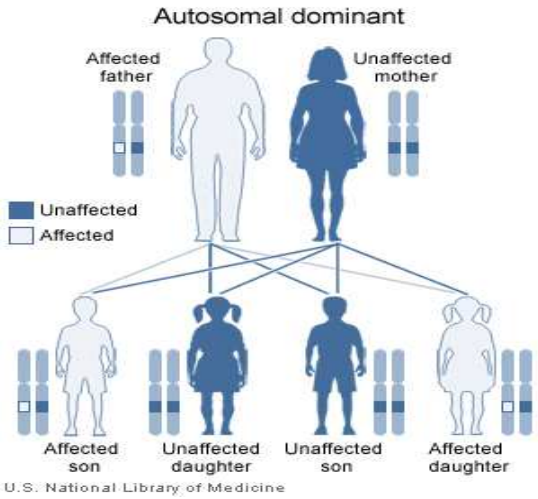
Lynch Syndrome

Genetics:
Hereditary cancer is typically suspected in families when several members over multiple generations develop cancer, often at a relatively young age (less than 50). Hereditary cancer is also suspected if a particular type of caner, or a recognizable pattern of cancers, cluster in a family. About 5-10% of all cancer cases are thought to be due to an inherited gene mutation. Therefore, most cancer is not hereditary.

Lynch syndrome (previously known as Hereditary Non-Polyposis Colorectal Cancer - HNPCC) is the most common hereditary colon cancer syndrome and accounts for approximately 2-3% of cases. Lynch syndrome is associated with mutations in 1 of 5 genes; MLH1, MSH2, MSH6, PMS2 and EPCAM. These genes are involved in correcting DNA damage.

Inheritance:
We have two copies of every gene in our body, one from our mother and the other from our father. Having one non-working copy of a Lynch syndrome gene is enough to increase the risk of developing cancer. When an individual has a Lynch syndrome mutation they have a 50% chance of passing the mutation on to each of their children. This is known as autosomal dominant inheritance.



Cancer risk up to age 70 years in individuals with Lynch Syndrome:

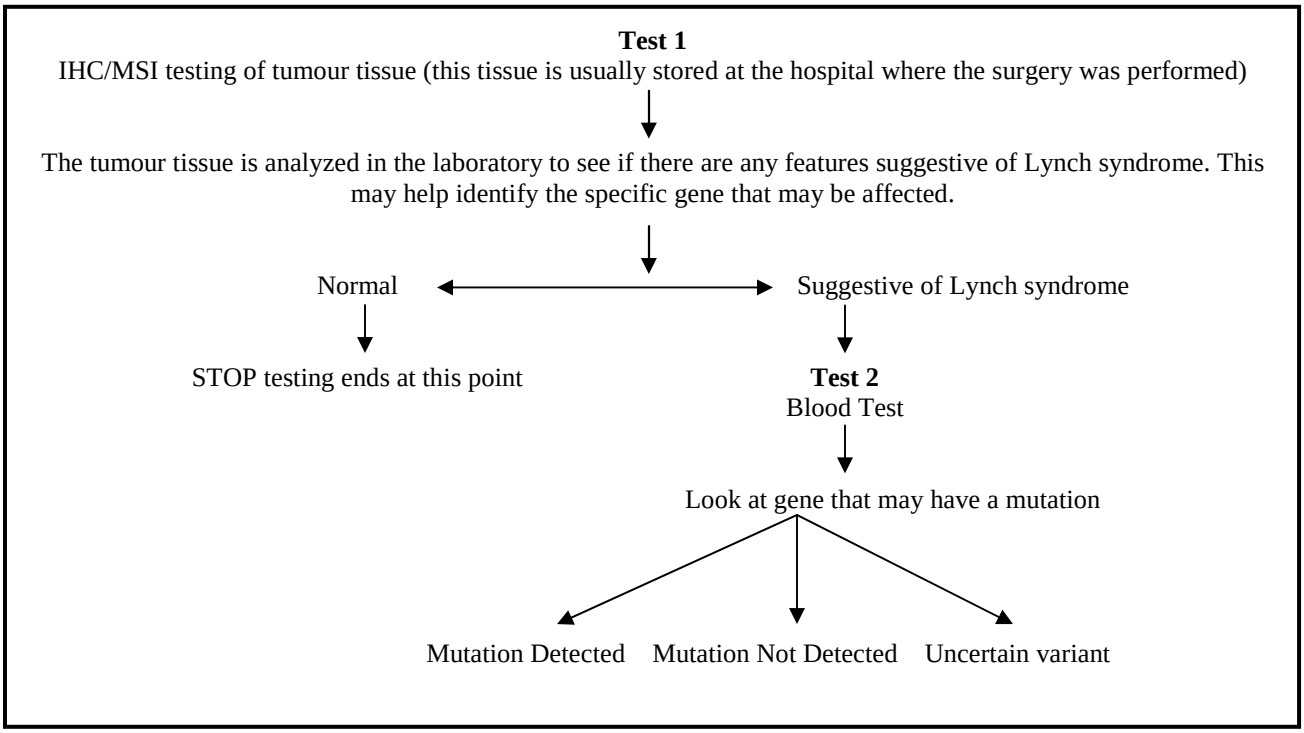
Type of Cancer	With a Mutation	General Population
Colon Cancer	Men: 27-74% Women: 22-53%	8% 6%
Uterine Cancer	14-54%	2.7%
Ovarian Cancer	4-20%	1.6%

(Giardiello et al Am J Gastroenterology 2014)

Men and women who carry a Lynch syndrome mutation have a smaller (<10%) increased risk for other cancers such as urinary tract, small bowel, pancreas, hepatobiliary tract brain and specific types of skin cancer.

MLH1 and MSH2 gene changes are the most common cause of LS. Cancer risks differ between mutation types, men and women and within and between families

Genetic Testing:
Due to the complexities of genetic testing, it is most useful to begin testing on a family member who has been diagnosed with colorectal cancer. For the first part of Lynch Syndrome testing, screening tests are performed on a tumor sample.



Mutation Detected: A gene change (mutation) known to increase cancer risk has been identified. This likely explains the family history of cancer. Genetic testing for this mutation would be available to other family members.

No Mutation Detected: A gene change in the specific Lynch Syndrome gene tested has not been identified. This does not rule out a hereditary cancer predisposition. It is still possible that the individual carries a mutation that the testing cannot detect or in another cancer predisposition gene. Screening and management decisions should be based on family history and other personal risk factors.

Uncertain variant: Testing identified a gene change, but the significance of the change has not yet been determined. Additional studies by researchers would be required to determine whether this gene change is part of normal gene variation or is a mutation which increases cancer risk.

Screening:
Everyone in the general population should have screening for colon cancer starting at age 50. Those with a family history of colorectal cancer may be recommended for more frequent screening beginning at an earlier age. Specific recommendations for you and your family will be discussed during your genetics appointment.