Gynecologic Cancers of Lynch Syndrome

What is Lynch Syndrome (LS)?

LS, which has also been referred to as hereditary nonpolyposis colorectal cancer (HNPCC), is an inherited condition that increases the risk of colorectal cancer (cancer of the large intestine and rectum). It is also common for people with LS to have benign growths, called polyps, in the colon.

LS also increases the likelihood of other cancers including, those of the endometrium (uterus), stomach, ovaries, urinary tract, small intestine, liver, gall bladder, brain, and skin.

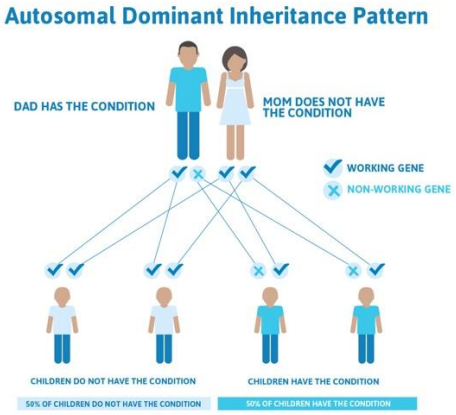
What causes Lynch syndrome?

The genes associated with LS are *MLH1, MSH2, MSH6, & PMS2.* These genes are in charge of repairing DNA when a mistake has been made. If a mistake goes uncorrected, cancer can develop.

How is it inherited?

LS is inherited as an autosomal dominant condition. It is caused by a mutation in one of several different genes. Like chromosomes, genes also come in pairs. An individual with Lynch syndrome has one working gene copy and one that has a change (mutation) that prevents it from working properly. To be at increased risk for a LS-associated cancer, it is only necessary to have one copy of the gene with the mutation.

The majority of individuals with this condition inherit the altered gene copy from a parent in an autosomal dominant pattern. This means an individual with Lynch Syndrome has a 50% chance of passing on their mutated copy of the gene to their offspring. Children who inherit the working copy of the gene will not have Lynch Syndrome. The children who inherit the mutated copy of the gene will be at higher risk to develop the condition.



What gynecologic cancers are associated with LS?

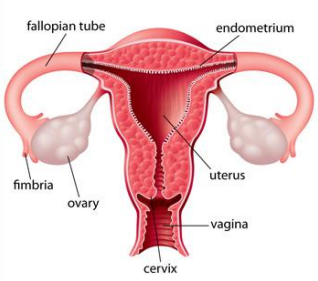
LS is associated with two gynecologic cancers.

Endometrial (Uterine) Cancer

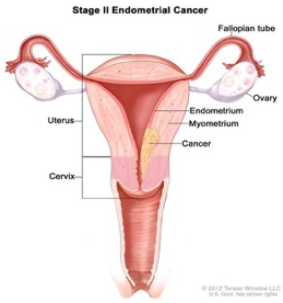
- Women with LS have an increased risk of developing cancer of the endometrium, the inner lining of the uterus.
- Average age of onset is about 40-years-old.
- Risk for developing endometrial cancer in LS is equal to or greater than the risk for developing colon cancer (see chart).

Ovarian Cancer

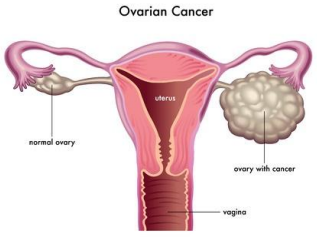
- Women with LS also have an increased risk of cancer of the ovaries, the reproductive glands that produce eggs in females.
- Average age of onset is about 42-years-old.



+Normal Endometrium & Ovaries



+ Endometrial Cancer



+ Ovarian Cancer

Gynecologic Cancers of Lynch Syndrome

LS Gynecologic Cancer Risks

Cancer Type	Endometrial	Ovarian
General Population Risk[1]	2.7%	1.6%
Familial Mutation Based Risk[1]:		
MLH1 or MSH2	25-60%	4-24%
MSH6	16-26%	1-11%
PMS2	15%	+

1. Cancer risk up to age 70 years
+ Combined risk for renal pelvic, ovary, small bowel, ureter, and brain is 6% to age 70

Symptoms of gynecologic cancers?

Gynecologic cancers may not produce symptoms until the disease has become more severe. It is important to know the signs and talk to your doctor if you experience any of the following symptoms:

- Abdominal and/or pelvic pain
- Bloating
- Feeling full quickly when eating
- Changes in urinary frequency or urgency
- Abnormal vaginal bleeding
- Pain with intercourse
- Fatigue

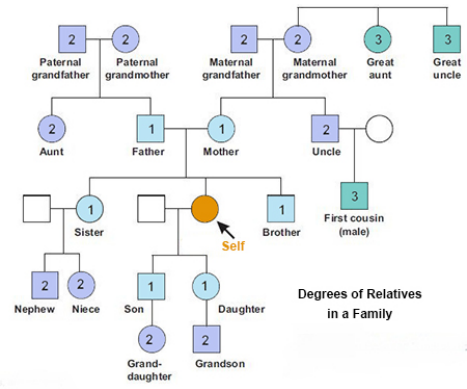
Reducing your Risk

Hysterectomy and bilateral salpingo-oophorectomy (BSO)

- Involves removal of uterus, cervix, ovaries, and fallopian tubes
- Should be considered following completion of childbearing

Birth control pills

- Associated with reduced risk for ovarian cancer when taken on average 3-5 years
- Discuss risks and benefits with your doctor.



+Pedigree showing 1st degree relatives

Screening Guidelines

According to the National Comprehensive Cancer Network, the following are guidelines for the screening and management of gynecologic cancers associated with Lynch syndrome.

All screening should begin at the age advised by your doctor or 10 years before the age of the earliest diagnosed cancer in the family, whichever is earlier.

- Evaluation of abnormal bleeding or pain
- Annual gynecologic/pelvic exam
- Annual endometrial biopsy starting age 30-35
- Transvaginal ultrasound
- CA-125 for ovarian screening (protein cancer antigen 125 produced by cancer cells)

It should be noted that there is not sufficient evidence for the usefulness of these methods for early stage detection.

Which other family members should consider testing?

- If you have a mutation in a gene associated with LS, it is important to notify your close relatives that they are at increased risk.
- Your first degree relatives should be offered genetic counseling and genetic testing. This includes your children, siblings, and parents.
- Anyone else in the family with a history of cancer should be offered genetic counseling and genetic testing, along with their first-degree relatives.
- Healthcare providers with expertise in LS, such as genetic counselors and geneticists, can assist in determining who in your family is at risk. Discuss with them your options for communicating the diagnosis and coordinating genetic testing.
- Relatives who decline genetic testing should still be informed of their risks of cancer and the screening options available.

References

NCCN Guidelines. Genetic/Familial High-Risk Assessment: Colorectal. (n.d.). Retrieved March 20, 2016, from http://www.nccn.org/professionals/physician_gls/f_guidelines.asp

Lu, K. H., & Broaddus, R. R. (2005). Gynecologic Cancers in Lynch Syndrome/HNPCC. *Fam Cancer, 4*(3), 249-254.

Lu, K. H. (2008). Hereditary gynecologic cancers: differential diagnosis, surveillance, management and surgical prophylaxis. *Fam Cancer, 7*(1), 53-58.

Schulman, L. (2015, May 8). ACOG Guidelines at a glance: Lynch syndrome. Retrieved March 20, 2016. http://contemporaryobgyn.modernmedicine.com/contemporary-obgyn/news/acog-guidelines-glance-lynch-syndrome?page=full