The Leeds Teaching Hospitals NHS Trust

Yorkshire Regional Genetics Service

Genetic testing for Lynch syndrome

Information for patients

Yorkshire Regional Genetics Service

What is inherited bowel cancer?

Although cancer is a common disease, an inherited tendency to developing cancer is rare. Of all the people who develop bowel (colorectal) cancer, only a small proportion (about 1 in 20) have some form of inherited tendency to developing this cancer.

The pattern of cancer in your family may be due to an inherited condition called Lynch syndrome.

What is Lynch syndrome?

Lynch syndrome is an inherited condition which causes polyps to form in the bowel, which increases the risk of bowel cancer. People with Lynch syndrome also have an increased chance of developing certain other cancers.

Lynch syndrome is sometimes called Hereditary Non-Polyposis Colorectal Cancer (HNPCC).

Lynch syndrome is caused by an altered gene. There are several different genes linked with Lynch syndrome and the cancer risks are slightly different for each one.

Not everyone who has Lynch syndrome will develop cancer. Over a person's lifetime there is:

- Between 12% and 60% chance of developing bowel cancer for people who are having regular bowel screening. The risk of bowel cancer for the general population is 6 - 7%.

- There can be an increased chance of of developing stomach or urinary tract (e.g. kidney, ureter or bladder) cancers. Also, there may be a slightly increased risk of small bowel, gall bladder, bile duct, pancreas, skin and brain cancer. These cancer risks vary depending on the specific gene involved.

For women, there is also:

- Between 13% and 50% chance of developing endometrial cancer (lining of the womb). The risk of endometrial cancer in the general population is about 3%.
- Between 11% and 17% chance of developing ovarian cancer. The risk of ovarian cancer in the general population is about 2%. Carriers of a PMS2 gene change have a risk of ovarian cancer similar to the population level.

What are genes?

Genes are coded messages which give instructions for how cells grow and function. Genes come in pairs; we inherit one copy from each parent. A change in one of a number of genes can cause Lynch syndrome. The genes involved are MLH1, MSH2, MSH6, PMS2 and EPCAM. A person who has a change in any of these genes has an increased risk of developing Lynch syndrome-related cancers.

Who can have genetic testing for Lynch syndrome?

A test of tumour tissue may be offered first to clarify if genetic testing is going to be helpful for a family. Tumour tissue testing is now done routinely when a person is diagnosed with bowel or endometrial cancer. You may have been told that your tumour has features consistent with Lynch Syndrome but a genetic test is needed to diagnose the condition.

If genetic testing is indicated, this usually requires a blood sample from someone who has had a Lynch syndrome-related cancer. The genes will be examined to look for changes.

What are the possible results of genetic testing?

Testing can reveal one of three results:

No gene changes are found

This means it is less likely that the cancer is caused by Lynch syndrome; however, there may still be other genes that can cause bowel and other cancers which we are not yet able to offer testing for. For this reason, family members may still have an increased risk compared with the general population. No genetic testing will be available to other relatives but additional cancer screening may be recommended. If your initial tissue test showed features consistent with Lynch syndrome, we may need to offer a test to look for gene changes within the cancer cells that are not present in your blood.

A cancer causing gene change is found

This confirms that Lynch syndrome is running in your family. People with this gene change will be at higher risk of developing bowel and other Lynch syndrome-related cancers, even if they have had a previous diagnosis. Other family members can have a **'predictive test'** if they want to know whether they have inherited the same gene change (see separate information sheet). This is generally only offered to adults.

A variant of uncertain significance is found

This is a gene change of unknown significance which may be entirely harmless. The family may have an increased risk of certain cancers so we may still recommend additional cancer screening for relatives, but no genetic testing will be available for them at this time. Sometimes, research into the significance of the variant is possible and this will be discussed, if appropriate. We recommend that you seek advice again in around 2 to 5 years' time so that the evidence around the significance of the gene change can be reviewed.

What if I have a Lynch syndrome gene change?

People with a Lynch syndrome gene change are offered two yearly screening of their bowel, starting from the age of 25 to 35, by colonoscopy. Removal of any polyps during colonoscopy reduces the chance that a bowel cancer will develop. Other risk-reducing options will be discussed with you, once we have the results.

It is recommended that people with a Lynch syndrome gene change are checked for an infection (bacterium) called Helicobacter pylori, which may be found in the stomach and is linked to an increased risk of stomach cancer. If present, it can be treated with a course of antibiotics. People are not routinely offered endoscopy of their stomach.

The chance of developing endometrial or ovarian cancer in Lynch syndrome is low under the age of 35 but increases after this age. There is no screening proven to be effective for endometrial or ovarian cancer. Symptoms to watch for include any abnormal bleeding; for example, between periods or if periods become heavier than normal. Other symptoms include persistent abdominal (tummy) pain, bloating, difficulty eating, feeling full very quickly and the need to pass urine more frequently.

Surgery to remove the womb and ovaries (total hysterectomy) is an option to reduce the risk of these cancers. It would not usually be considered until a person has reached their mid to late 30's and has finished their family. People with a PMS2 gene change are offered surgery later (usually after age 45) and it does not include removal of the ovaries as the risks are lower with this type of gene change.

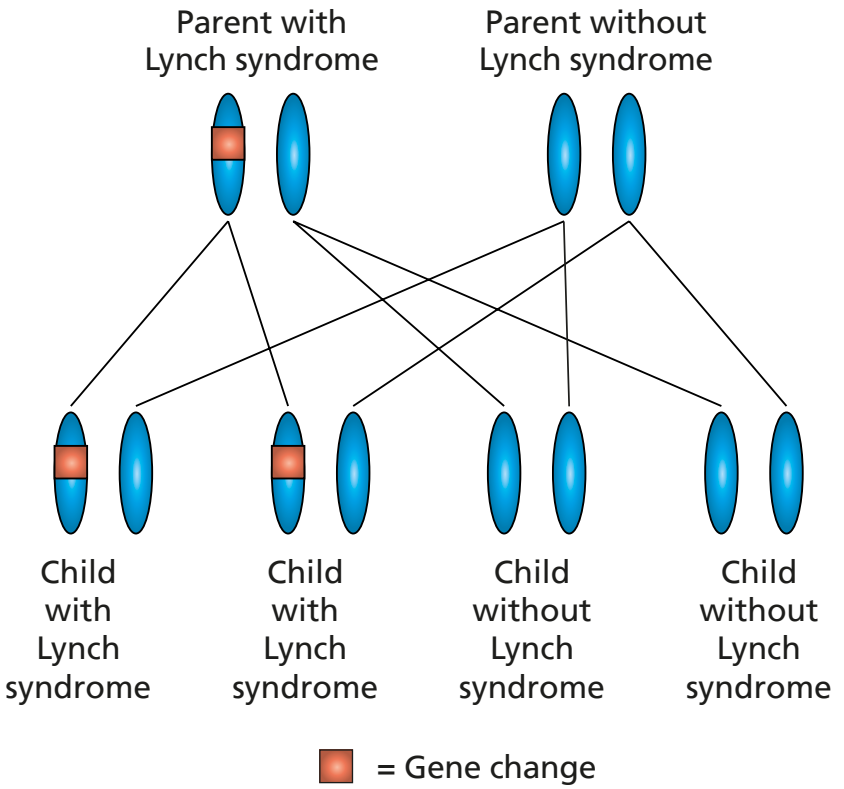
Although there is no proven effective screening for endometrial cancer in Lynch syndrome, from the age of 35, it may be possible to arrange annual checks with a local gynaecologist. This would continue until a hysterectomy is carried out.

Aspirin

Research suggests that taking aspirin can reduce the risks of bowel cancer in people with Lynch syndrome. This is not suitable for all people and the best dose has not yet been determined. Research studies are investigating this further but there are some expert recommendations allowing people with Lynch Syndrome to take aspirin while the research continues. Regular aspirin should only be taken on the advice of a doctor.

How is a Lynch syndrome gene change passed on?

If someone has Lynch syndrome, they have a change in one copy of the gene, as shown below.



Only one gene from the pair is passed on to a child in the egg or sperm. If someone with Lynch syndrome has children, each child has:

- a 50% (1 in 2) chance of inheriting the gene change, and being at risk of developing Lynch syndrome-related cancers. Their children will also then be at 50% risk; and

- a 50% (1 in 2) chance of not inheriting the gene change and therefore, not having Lynch syndrome. They cannot then pass it to their children.

Further information

You may find the following websites helpful:

Macmillan Cancer Support

Tel: **0808 808 0000**

http://**www.macmillan.org.uk**

Lynch Syndrome UK

http://**www.lynch-syndrome-uk.org**

Bowel Cancer UK

Tel: **020 7940 1760**

http://**www.bowelcanceruk.org**

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