The Leeds Teaching Hospitals NHS Trust

Yorkshire Regional Genetics Service

Predictive genetic testing for Lynch syndrome

Information for patients

Yorkshire Regional Genetics Service

Lynch syndrome has been found to run in your family. Lynch syndrome is sometimes called Hereditary Non-Polyposis Colorectal Cancer (HNPCC).

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

We all have more than 20,000 genes. Each gene is an instruction within our body. Changes in that instruction can affect how it works. Lynch syndrome is caused by a change in one of several genes. We have two copies of every one of our genes, one inherited from each parent. A change in just one of those two copies will lead to Lynch syndrome.

When we have our children, we pass only one copy of each gene on, with the other copy coming from our partner. If a parent has Lynch syndrome, there is a 50% chance for each of their children of inheriting the gene change and a 50% chance of not inheriting it. Lynch syndrome affects males and females. There is no way at present to reverse the gene change but there is screening and surgery available to help protect against the chance of cancer developing, or detect it early.

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. The genes are called MLH1, MSH2, MSH6, PMS2 and EPCAM.

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 having regular screening. The risk of bowel cancer in the general population is about 6% to 7%;
- between 13% and 50% chance of developing cancer of the uterus (womb) in women. The risk of womb cancer in the general population is around 3%;
- between 11% and 17% chance of developing ovarian cancer. The risk in the general population is about 2%. Note that the risk with a PMS2 gene change is not increased;
- up to 20% chance of developing stomach or urinary tract (e.g. kidney, ureter or bladder) cancers; and
- a slightly increased risk of small bowel, gall bladder, bile duct, pancreas, skin and brain cancer.

Bowel polyps and bowel cancer

People with Lynch syndrome are more likely than the general population to develop bowel polyps. They tend to develop more polyps and at a younger age than people without Lynch syndrome. Bowel cancers can arise from polyps. Removal of the polyps in Lynch syndrome reduces the chance that a bowel cancer will develop.

People with a Lynch syndrome gene change are offered screening of their bowel by colonoscopy every 2 years, starting from the age of 25 or 35, depending on the specific cause of Lynch syndrome in your family.

To prepare for a colonoscopy, the bowel needs to be cleared with laxatives. During colonoscopy, a narrow tube with a small light and camera is carefully passed through the back passage into the large bowel. Polyps can then be removed, if seen. Colonoscopy can be uncomfortable but sedation is offered. It is usually done as an outpatient procedure.

The aim of colonoscopy screening is to prevent bowel cancer developing or to detect it at an early stage. The earlier a cancer is found, the better the chance of successful treatment.

It is important to be aware of bowel symptoms. If you have any of the following symptoms you should see your GP for a check-up:

- bleeding from the anus (back passage);
- increase in the amount of mucus in the stool (poo);
- change in bowel habit such as persistent diarrhoea or constipation;
- abdominal pain or bloating;
- unexplained weight loss; and
- feeling of incomplete emptying of the bowel.

There is increasing evidence that a diet low in animal fats (particularly red meat and processed meats) and high in fresh fruit and vegetable is protective for the bowel.

Stomach cancer

It is recommended to check 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.

This test can be organised through the GP. People with a Lynch syndrome gene change are not routinely offered endoscopy of their stomach.

Endometrial (uterine or womb) cancer

The chance of developing endometrial cancer in Lynch syndrome is low under the age of 35 but increases after this age. Symptoms to watch for include: any abnormal bleeding; for example, between periods or if periods become heavier than normal. After the menopause, any vaginal bleeding should be brought to the attention of the GP or gynaecologist so it can be investigated.

Surgery to remove the womb (hysterectomy) is an option to reduce the risk of endometrial cancer. It may be offered together with surgery to remove the ovaries (see below). It would not usually be considered until a person has reached their mid to late 30's and has finished their family.

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.

Ovarian cancer

Symptoms of ovarian cancer can be difficult to notice. They include persistent abdominal (tummy) pain, bloating, difficulty eating, feeling full very quickly and the need to pass urine more frequently. We do not have an effective screening test for ovarian cancer yet. The chances of developing ovarian cancer can be reduced by surgical removal of the fallopian tubes and ovaries (bilateral salpingo-oophorectomy (BSO)).

It would not usually be considered until a person has reached their mid to late 30's and has finished their family. BSO will cause an immediate menopause if it has not already occurred. This can increase the risk of other problems, including osteoporosis (thinning of the bones). Hormone Replacement Therapy (HRT) may be prescribed. BSO is not usually recommend for people with a PMS2 gene change.

Urinary tract screening

This is not proven to be of benefit but may be considered for some families, depending on their specific gene change, or if there is a strong family history of urinary tract cancer.

Aspirin

Research suggests that taking aspirin can reduce the risks of bowel cancer in Lynch syndome. 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.

Genetic testing

If the specific gene change causing Lynch syndrome has been found in a family member, others in the family can have a 'predictive' genetic test. This allows them to find out whether they have inherited it or not. This testing is usually only offered to adults. There is a 1 in 2 chance of inheriting the gene change from a parent who has Lynch syndrome.

If it has not been inherited, then the chances of developing the cancers discussed above are not increased and screening or surgery to reduce the risk is not needed. Someone who has not inherited the gene change cannot pass it on to their own children. If the gene change causing Lynch syndrome has been inherited, then all the options described above could be considered, where appropriate.

It is possible that genetic testing could have an impact on life insurance or critical illness cover. There is a voluntary code on genetic testing from the Association of British Insurers (ABI) that provides some protection. Everyone has to disclose their family history if asked but you may not have to declare your own genetic test result when getting these types of insurance. Please see the ABI website for more details.

Having a family

Most people with Lynch syndrome will have their children as usual. Some people with a Lynch syndrome gene change want to ensure that it is not passed on to the next generation. They may consider the possibility of testing a pregnancy or Pre-implantation Genetic Testing (PGT). This incorporates In-Vitro Fertilisation (IVF) with genetic testing, aiming to implant an embryo without a Lynch syndrome gene change.

It is a complicated process with a success rate of about 1 in 3 per cycle of IVF. Further information about these options are available on request.

This information may be relevant to other adult members of your family. If they wish to be seen in the Genetics Clinic to discuss Lynch syndrome, they can be referred by their GP quoting the family reference number given on your clinic summary letters.

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**

Association of British Insurers

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

Bowel Cancer UK

Tel: **020 7940 1760**

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

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Developed by: Department of Clinical Genetics (Chapel Allerton Hospital)
With thanks to The Department of Clinical Genetics at Guy's & St Thomas' Hospital
Produced by: Medical Illustration Services • MID code: 20191219_010/IH

LN002326
Publication date 06/2023
Review date 06/2026