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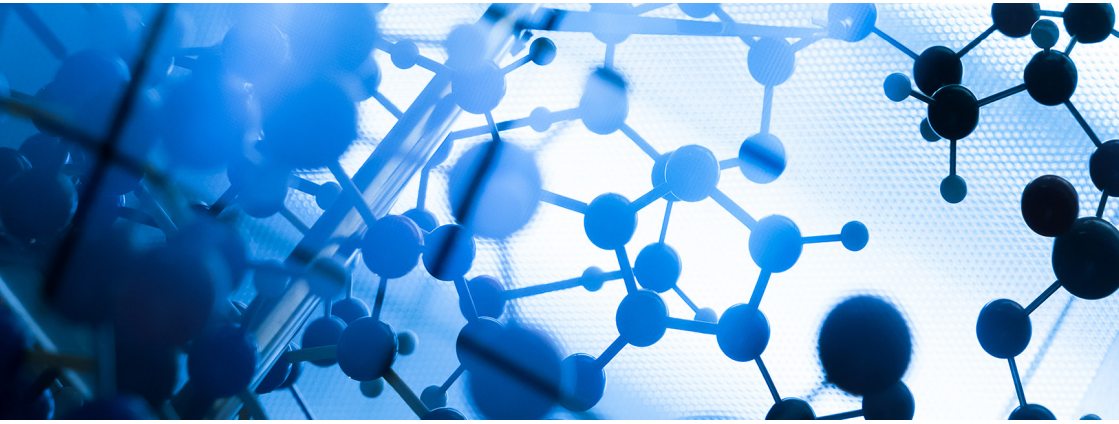
LYNCH SYNDROME



PREDICTIVE GENETIC TESTING

LYNCH SYNDROME
PREDICTIVE GENETIC TESTING

This booklet has been written for people who have a family history of Lynch syndrome and a genetic change has been identified. This leaflet contains general information about the condition, but it needs to be considered in combination with our clinic discussions and the covering letter that relates to the specific history in your own family.

WHAT IS LYNCH SYNDROME

Lynch syndrome, which is sometimes referred to as Hereditary Non-Polyposis Colorectal Cancer (HNPCC), is a hereditary condition which is associated with an increased risk of developing certain types of cancer. Men and women who have Lynch syndrome have an increased risk of developing colorectal cancer, which is cancer of the large bowel (colon) and rectum. Women who have Lynch syndrome also have an increased risk of developing cancer of the lining of the womb (endometrium). Some people with Lynch syndrome can have an increased risk of other cancers, these are detailed below. Lynch syndrome is caused by pathogenic (disease causing) variants in the mismatch repair (MMR) genes.

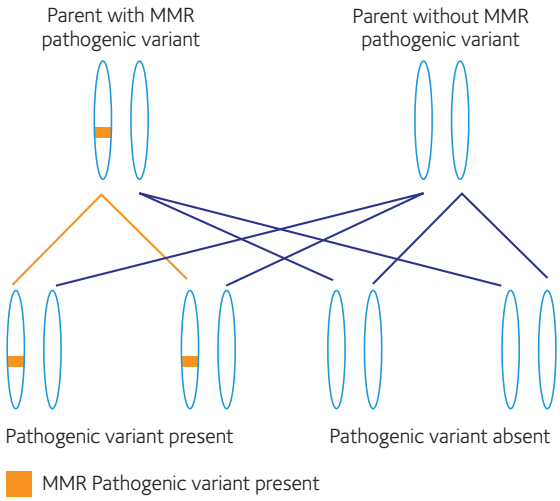
WHAT ARE MISMATCH REPAIR (MMR) GENES?

The MMR genes help to protect us from developing certain forms of cancers. A pathogenic variant can affect the function of the gene and this can increase the chance of developing these forms of cancer, which may occur at a younger age than these cancers usually occur in the general population. There are four MMR genes which have been linked to Lynch syndrome; these are MLH1, MSH2, MSH6 and PMS2. The risks of different cancers vary depending on which gene is affected and so not everyone with Lynch syndrome will have the same screening recommendations

HOW IS LYNCH SYNDROME INHERITED?

All of our genes come in pairs; we inherit one copy from our mother and the other from our father. When we have children we randomly pass on one of each pair. If a person has a pathogenic variant in one copy of a MMR gene, each of his or her children (male or female) has a 50% (1in 2) chance of inheriting it.

AUTOSOMAL DOMINANT INHERITANCE



IF I DO NOT HAVE LYNCH SYNDROME CAN I STILL GET CANCER?

Yes, there is still a chance of developing cancer; however this risk is similar to any other individual in the general population. We still recommend that individuals who have not inherited the family pathogenic variant still participate in the national cancer screening programmes which are open to everyone.

DOES EVERYONE WITH LYNCH SYNDROME DEVELOP CANCER?

No, not everyone with Lynch Syndrome will develop cancer. Individuals with Lynch syndrome are at an increased risk of developing certain cancers, compared to the general population.

We do not yet know why some people with Lynch syndrome develop cancer and some do not. Lifestyle or other genetic factors are likely to play a role. Knowledge about what can be done to reduce the risk of cancer developing or identifying it at the earliest and most treatable stage is always improving.

WHAT ARE THE CANCER RISKS ASSOCIATED WITH LYNCH SYNDROME?

This table outlines the approximate cancer risks by age 70 associated with each of the four MMR genes and compares that risk to the population risk.

Cancer Site	MLH1 Carriers	MSH2 Carriers	MSH6 Carriers	PMS2 Carriers	General Population
Colorectal Cancer	50-65%	35-75%	20-70%	15-20%	5-6%
Endometrial Cancer (women)	20-25%	30-40%	25-70%	15%	2%
Ovarian Cancer (women)	10-15%	10%	1-2%	1-2%	1-2%
Gastric	<10%	<10%	<1%	<1%	<1%
Urinary Tract	3-5%	10-30%	<1%	<1%	<1%
Small Bowel	3-5%	3-5%	<1%	<1%	<1%

IF I HAVE INHERITED THE FAMILY MMR GENE PATHOGENIC VARIANT SHOULD I HAVE ADDITIONAL SCREENING?

Cancer	Risk Management Options
Bowel	• 2 yearly Colonoscopies from from 25 for MLH1 & MSH2 carriers from 35 for MSH6 & PMS2 carriers
Gastric	• There is no convincing evidence to support the use of endoscopy (Oesophago-gastro-duodenoscopy OGD) as a screening test for gastric cancer, in all Lynch Syndrome families but it may be recommended in some situations (eg. where there is a significant family history) • Helicobacter pylori (an organism found in the stomach of some individuals) is known to be associated with gastric cancer generally Screening for H. Pylori & treatment- usually a course of antibiotics can be arranged by your GP.
Gynaecological	• Endometrial cancer surveillance may sometimes be offered. A referral to gynaecology to discuss options is recommended from 35 • Ovarian screening is not routinely recommended • Some women with Lynch syndrome opt to have a total abdominal hysterectomy (removal of the womb) with bilateral salpingo-oophorectomy (removal of both ovaries and fallopian tubes) as this reduces the risk of developing endometrial and ovarian cancer.

We recommend that everyone maintains a healthy lifestyle including a diet high in fibre and low in saturated fat. We also recommend that you maintain a healthy body weight, exercise regulary and do not smoke. Even if you are having regular screening it is important to report any symptoms of concern promptly to your GP.

DOES ASPIRIN REDUCE THE RISK OF DEVELOPING COLORECTAL CANCER?

Several research studies have reported that individuals with Lynch Syndrome who take aspirin long term have lower rates of bowel cancer, compared to those who were taking a placebo. Studies are still ongoing to try and establish the optimal dose of aspirin. Currently we recommend that people should take 150mg of Aspirin if they have a BMI less than 25kg/m^2 (approximately 70kg or 11 stone). 300mg is recommended for anyone over that weight following a discussion with their GP regarding any possible contraindications.

WHAT ARE THE IMPLICATIONS OF PREDICTIVE GENETIC TESTING

Some people may worry that genetic testing will affect their insurance prospects (e.g. health, life, disability). Insurance companies may consider an individual's personal medical history and family history, but at present they are not permitted to ask about predictive genetic testing, and you are not obliged to disclose that you have undergone genetic testing for Lynch Syndrome or the results. However, it is possible that this may change in the future.

Some people experience a range of emotions when they are told they have Lynch syndrome. They may feel angry, shocked, anxious, or guilty about possibly passing the pathogenic variant on to children. Some people may also feel guilty if they do not have Lynch syndrome when other close family members do. Genetic testing can affect other family members, they may need to be told that they may have an increased risk of cancer.

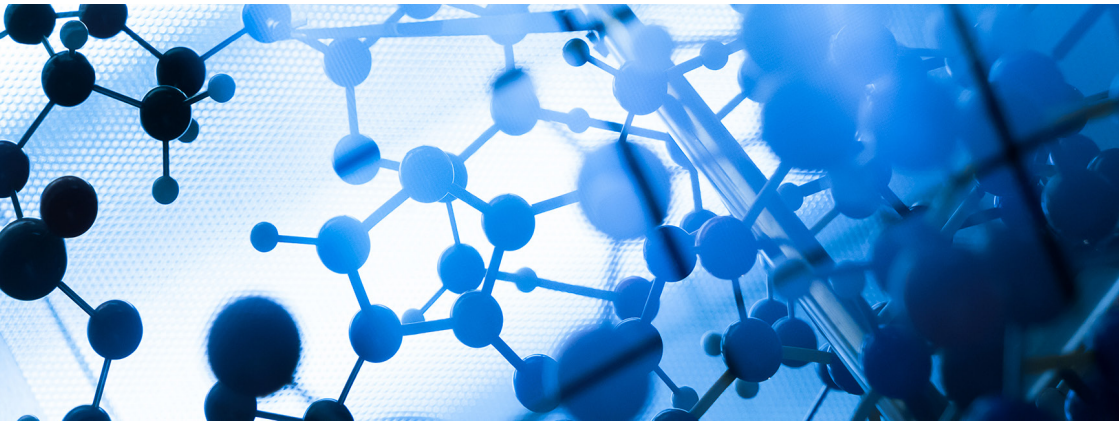
Some people who have Lynch syndrome consider a specialist technique called pre-implantation genetic diagnosis (PGD). This is a technique used to create embryos and test them for the familial genetic condition. Please discuss this further with the genetics department if you wish to find out more.

IS THERE AN ALTERNATIVE TO GENETIC TESTING?

You may decide not to have genetic testing. Whether or not you are tested, you should talk to your clinician about screening options.

ARE THERE ANY SUPPORT GROUPS FOR PEOPLE WITH LYNCH SYNDROME?

There is a UK based support group for individuals with Lynch syndrome that can provide information and peer support. Their website is http://www.lynch-syndrome-uk.org



The health professionals involved in your case are:

Genetic Counsellor: _____

T: _____

Consultant: _____

T: _____

If you have any feedback or comments regarding the contents of this leaflet we would be pleased to receive them at genetic.medicine@belfasttrust.hscni.net
If your relative has given you this leaflet and you would like to discuss testing for yourself please ask your GP to refer you to your local genetics service

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