Lynch syndrome

A guide for primary care health professionals

Lynch syndrome is a genetic condition with no known cure, that increases a person's lifetime risk of bowel cancer by up to 80%. It is estimated to cause around 3% of bowel cancer cases in the UK every year, many of them in people under the age of 50.

Currently, less than 5% of people with Lynch syndrome have been diagnosed. It is estimated that around 175,000–200,000 people across the UK have Lynch syndrome and are unaware they are at high risk of developing bowel, and other cancers.

People with Lynch syndrome have a 50% chance of passing the condition on to their children, meaning whole families can be devastated by the impact of bowel cancer.

Identifying those at risk

Bowel cancer is the fourth most common cancer in the UK, with 29% of the population having a family history in a first- or second-degree relative.

When a family member has a known hereditary bowel cancer syndrome, referral to local clinical genetics services is indicated.

Even when hereditary bowel cancer syndromes have not been identified, if a patient has a family history of bowel cancer, they themselves carry an increased risk of up to six times that of the general population.

Underlying flags for a genetic diagnosis include:

- cancer diagnosis at an early age;
- multiple affected family members (two or more first-degree relatives or one first-degree relative diagnosed at under 50 years of age);
- personal or family history of bowel polyps at an early age; and
- presence of other associated cancers such as endometrial, liver, gastric or brain.

Lynch syndrome predisposes to certain cancer types

The main concerns are:

- Colorectal
- Endometrial
- Other associated cancers:
  - Ovarian
  - Urinary tract
  - Gastric
  - Small intestine
  - Hepato-biliary and pancreatic
  - Sebaceous gland (and adenoma)

Diagnosing Lynch syndrome

Diagnosing Lynch syndrome begins with molecular testing of tumours for specific genes related to DNA repair. Mismatch repair (MMR) genes are responsible for fixing DNA errors in the body. If these genes have faults, DNA mistakes can build and lead to cancer over time.

Lynch syndrome is caused by germline pathogenic variants in one of the DNA Mismatch Repair (MMR) genes: **MLH1, MSH2, MSH6, PMS2, EPCAM**: which may inactivate MSH2.

Around 15% of people with bowel cancer are estimated to have defects to these genes, and approximately 25% of those with MMR defects have Lynch syndrome. Because these faults can happen in cancers unrelated to Lynch syndrome, two more tests are carried out. If no changes are found, further testing of DNA called germline testing is necessary to definitively diagnose Lynch syndrome.

Before getting a diagnosis, every patient must undergo genetic counselling. Counselling helps people to make informed decisions by providing information on the genetic condition, the implications of being diagnosed, and the measures that would be put in place to care for them after a Lynch syndrome diagnosis (also known as 'wraparound care').

Preventing bowel cancer

The new bowel cancer screening programme will offer a colonoscopy to people with Lynch syndrome every two years. They will be eligible to join the programme from age 25 or 35, depending on the gene variant they have that causes the condition, as some variants can result in the disease developing at a younger age than others.

Offering people with Lynch syndrome regular colonoscopies will allow precancerous cell changes to be identified and treated before cancer develops, as well as diagnosing cancers that do arise at the earliest possible stages, when treatment outcomes are best.

Effect of aspirin on the chance of getting bowel cancer: results of the CAPP3 study

CaPP3 is the third trial in the Colorectal Adenoma/Carcinoma Prevention Programme.

The CaPP2 trial showed aspirin reduced the risk of CRC in people with Lynch syndrome, however, CaPP2 did not identify the best dose, meaning people could be taking unnecessary high doses of aspirin.

Following the results from CaPP2, the CaPP3 trial was established to compare 3 doses of aspirin, with the aim to reduce the risk of potential harm from high dose aspirin. CaPP3's results show that taking as little as 75 to 100mg of aspirin each day can halve the risk of CRC in people with Lynch syndrome.

We're now engaging with regulators to change prescribing guidelines so that aspirin can be used more widely for people with a high risk of bowel cancer.

References

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Free training on Lynch Syndrome is available on the RM Partners website