



COMMENTARY

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## Hereditary Nonpolyposis Colorectal Cancer: its Treatment, Symptoms and Causes

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### Description

The inherited condition known as Lynch syndrome, also known as Hereditary Nonpolyposis Colorectal Cancer (HNPCC), raises the risk of a variety of malignancies, especially those of the colon (large intestine) and rectum, which are together referred to as colorectal cancer. In addition to endometrial cancer, which is the second most common type of cancer, stomach, small intestine, hepatobiliary tract, upper urinary tract, brain, and skin cancers. These tumours are more common because of hereditary mutations that hinder Deoxyribonucleic acid (DNA) mismatch repair. It is a particular kind of cancer syndrome. The name HNPCC has lost favour since people with Lynch syndrome can develop polyps.

### Treatment

Surgery is still the first line of treatment for HNPCC. A partial colectomy or a total colectomy with ileorectal anastomosis may be used to treat patients with Lynch syndrome who develop colorectal cancer. Total colectomy may be the preferred course of treatment for HNPCC, particularly in younger individuals, due to the higher risk of colorectal cancer after partial colectomy and the comparable quality of life after both surgeries. Anti-PD-1 antibody treatment has shown promise. Today, the chosen first-line treatment for advanced Microsatellite-Instability-High colorectal cancer is checkpoint inhibition with anti-PD-1 therapy.

### Symptoms

HNPCC is known that Lynch syndrome increases the risk of sebaceous neoplasms, brain cancer, biliary tract cancer, ureter/renal pelvis cancer, small bowel cancer, pancreatic cancer, and sebaceous neoplasms. Lynch syndrome has also been linked to an increased risk of breast and prostate cancer, however the exact nature of this connection is unclear. Blood in the

stool, diarrhoea or constipation, and unintentional weight loss are typical signs and symptoms of colon cancer, which affects the proximal colon in two-thirds of cases. Endometrial cancer is the most frequent sentinel cancer in Lynch syndrome, occurring in nearly half of women with HNPCC who had both colon and endometrial cancer.

### Causes

People with Lynch syndrome have been shown to have mutations in the (*MLH1*) mutL homolog1, (*MSH2*) mutS homolog2, (*MSH6*) mutS homolog 6, (*PMS2*) PMS1 homolog 2, or epithelial cell adhesion molecule gene. The *MLH1*, *MSH2*, *MSH6*, and *PMS2* genes have a role in correcting mistakes that arise during DNA duplication prior to cell division. These genes are collectively referred to as mismatch repair (MMR) genes because they cooperate to correct DNA mistakes. Any of these genes can have variations that hinder the correct repair of DNA replication mistakes. The cumulative mistakes can cause unchecked cell proliferation and possibly cancer when the aberrant cells continue to proliferate. Variants in the *MSH6* or *PMS2* genes have a decreased chance of acquiring cancer (25% to 60%), whereas variants in the *MLH1* or *MSH2* genes tend to increase the risk (70% to 80%) of having cancer in a person's lifetime. DNA repair is further hampered by variations in the gene for the epithelial cellular adhesion molecule (EPCAM), despite the fact that this gene is not directly engaged in DNA repair. On chromosome 2, the EPCAM gene is located close to the *MSH2* gene, and specific EPCAM gene variations result in the inactivation of the *MSH2* gene. As a result, the *MSH2* gene is less effective at repairing DNA, which can result in the accumulation of DNA mistakes and the development of cancer. Although people with these variants are more likely to develop malignant tumours, not everyone with these mutations does.

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