HNPCC information sheet

Hereditary Non Polyposis Colorectal cancer (HNPCC) was initially the term used to define families who had a strong family history of bowel cancer but where the bowel cancer in these families was not associated with hundreds of bowel polyps. One of the other familial bowel cancer syndromes, Familial Adenomatous Polyposis (FAP), is associated with hundreds of bowel polyps. The term "Non Polyposis" was used to separate HNPCC families from these families.

A family was considered to have HNPCC when they met the Amsterdam Criteria listed below.

Amsterdam (1991)

Three or more relatives with colorectal cancer, plus all of the following:

- One affected patient should be a first-degree relative of the other two;
- Colorectal cancer should involve at least two generations;
- At least one case of colorectal cancer should have been diagnosed before the age of 50 years.
- All confirmed by medical records.

These criteria helped facilitate research to find genetic mutations (spelling mistakes in the genes) associated with familial bowel cancer. As a result of this research we now know that there are a number of different types of familial bowel cancer within families previously labeled as having HNPCC.

A number of modifications to the Amsterdam criteria were made over the years to allow the inclusion of cancers outside the bowel, namely cancers of the uterus, small bowel, and ureter that can be associated with one of the strongly inherited bowel cancer syndrome, Lynch Syndrome, which is talked about in the next paragraph.

Lynch Syndrome

Approximately half of families meeting the Amsterdam criteria have been identified to have a DNA spelling mistake in a mismatch repair genes. These genes are responsible for correcting genetic spelling mistakes that occur when normal cells in the body divide. Where we have been able to identify that a DNA spelling mistake in one of the four mismatch repair genes is responsible for the bowel cancer in the family this is now called Lynch Syndrome. This means that genetic testing is available for the family. This syndrome can be associated with cancers outside the bowel, namely cancer of the uterus, small bowel or ureter. There is a separate information sheet on Lynch Syndrome.

Presumed Lynch Syndrome (or Likely Lynch Syndrome)

A This term is used for families who meet the Amsterdam criteria and in whom specialised tests, on removed bowel cancer samples, have indicated that a DNA spelling mistake in a mismatch repair gene is likely to be the reason why bowel cancer is developing in these families BUT we cannot identify the exact genetic spelling mistake to confirm a diagnosis of Lynch Syndrome. Sometimes this is because current genetic testing techniques cannot detect all spelling mistake even though we suspect one to be present. However, sometimes this is because there is no one in the family with cancer who is alive and able to have genetic testing.

In this situation, because we suspect Lynch Syndrome, we make the same recommendations for families as if they had Lynch Syndrome. As genetic testing is not available for these families we are not able to identify which family members are at increased risk, and therefore we recommend colonoscopy at two yearly intervals, at least initially, for family members who have a first degree relative who developed a bowel or other Lynch Syndrome cancer .

B Sometimes, a person develops bowel cancer at or under the age of 50 years ***but*** they do not have (or are not aware of) a family history of bowel or other cancers that can be associated with Lynch Syndrome. Given the young age at which they have developed bowel cancer, specialised tests on their bowel cancer samples are routinely performed to see if the results indicate the possibility that a spelling mistake in the mismatch repair genes is reason why they developed bowel cancer at a young age. If the tests indicate this possibility, then even though they do not have a family history of bowel or other cancers, genetic testing to detect the specific spelling mistake in the mismatch repair genes is advised. Sometimes however, we cannot identify this to confirm a diagnosis of Lynch Syndrome, even though we still suspect one may be present. These people are therefore still managed as Presumed Lynch or Likely Lynch Syndrome, even though they have no known family history of bowel cancer and therefore cannot meet the Amsterdam Criteria.

HNPCC

In some families meeting Amsterdam Criteria there is no bowel or other cancer tissue available to do specialised tests. These families have a history of bowel and other cancers that indicates they have a significantly increased risk of developing cancer compared to the general population. We still call these families HNPCC because we do not have enough information to either confirm or rule out the possibility of Lynch Syndrome. However, we usually manage these families as Presumed Lynch Syndrome or Likely Lynch Syndrome families.

Familial Colorectal Cancer Type X / Syndrome X

In some families meeting Amsterdam Criteria (and previously labeled as having HNPCC) we find, after specialised testing on bowel cancer tissue , that there is no evidence that the mismatch repair genes associated with Lynch Syndrome are involved in causing the bowel cancer in these families.

In these families bowel cancer occurs on average at an older age than in Lynch Syndrome and bowel cancer does not develop as quickly. This means that screening or surveillance colonoscopy can start at an older age (10 years before the youngest age at diagnosis in the family) and, providing no abnormality is found at colonoscopy, the interval between colonoscopy procedures can be extended to five yearly.

Sometimes we have families like this (with no evidence of mismatch repair gene involvement) who do not meet the Amsterdam criteria (usually because a family member has not been affected with bowel cancer at or under the age of 50 years) and we then say these families have **familial clustering of colorectal cancer or familial colorectal cancer**

In families with Syndrome X and familial clustering of colorectal cancer the risk of cancers outside the bowel are the same as for the general population and therefore increased screening for other cancers is not advised.

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