Understanding genetic testing for bowel cancer

Genetic testing is offered to families who:
• are at high risk of getting bowel cancer
• doctors suspect might be at high risk.

These families have a history of cancer that may be due to a change in a gene that has been passed down through their family.

Some families have a clustering (grouping) of bowel cancer in their family that is not due to any of the known gene changes linked to bowel cancer. We are still learning about genes and bowel cancer and we do not know all of the genes that can lead to bowel cancer.

In Victoria, genetic testing for bowel cancer is usually only offered through Family Cancer Centres. In most cases, genetic testing is government funded.

There are different types of tests for familial bowel cancer to see if a person and their family has an altered gene (gene change) that may increase their risk of bowel cancer. The type of testing that is done depends on:
• the family history of cancer
• the features of the bowel cancer a person has had
• whether they have had multiple polyps or not.

Pre-genetic testing on tumour tissue

*Immunohistochemical test (IHC)*
This is a test done on a cancer tissue sample from somebody in the family who has had:
• bowel cancer or
• a cancer that may be related to bowel cancer.

This test is requested by the surgeon on tissue taken from the cancerous tumour. This may be sent to the pathologist at the time of surgery to remove the bowel cancer or at a later time (as tumour tissue may be stored for up to 14 years after removal).

If the result is ‘normal’ (about 80 per cent of the time) it means you most likely do not have an inherited type of bowel cancer and no further testing is required.

If the test comes back ‘abnormal’ (with signs that it may be inherited) further tests will be done to determine if you have signs of an inherited bowel cancer.

If the tumour test suggests a genetic cause, usually there are two options:

1. If the patient with bowel cancer was diagnosed at an older age, and there are no other relatives with bowel or related cancers, the first step may be to do another test on the tumour sample. This test is called the *Microsatellite Instability Test (MSI).* This test can help work out if further genetic testing, with a blood test, is needed.

2. If the patient tested is under the age of 50 and/or has a family history of bowel cancer, the next step may be to offer the patient genetic testing on a blood sample.
What are genes?
Genes are tiny and complex pieces of information that are in each cell. They tell our bodies how to grow and work. Each person has around 20,000 to 30,000 genes. These are in pairs, as we get (inherit) one copy from each parent. Genes usually correct mistakes that happen in our genetic material; they act like a ‘spell-checker’ on a computer. Genes can become faulty and when this happens cells may grow uncontrollably and become cancer.

What gene mutations (changes) can we test for?
There are a number of genes we know about that make people more likely to get bowel cancer.

There are at least four genes (MLH1, MSH2, MSH6 and PMS2) that can cause an inherited bowel cancer condition called Lynch Syndrome [previously known as Hereditary Non Polyposis Cibrectal Cancer (HNPPC)].

There are at least two genes that can cause people to get multiple polyps in the bowel:
1. APC – This gene causes a condition known as Familial Adenomatous Polyposis (FAP)
2. MYH – This gene can also cause people to get polyps in the bowel. We are still learning about the MYH gene. We do know that, unlike the other bowel cancer genes, both copies of the MYH gene have to be affected to get the polyps.

There are other genes which are rare but can also lead to a higher risk of bowel cancer. Your doctor or Family Cancer Centre staff will be able to talk about these with you if they apply to your situation.

What is genetic testing?
Genetic testing, normally on a blood sample, looks for changes (also called mutations) in a gene. These changes may stop the gene from working properly.

Looking for a gene change for the first time in a family is known as ‘mutation detection’. It’s a bit like looking through a book for one spelling mistake. Results may therefore take some months. This type of testing is usually offered to somebody in the family who has had bowel cancer. When possible, this is usually the person diagnosed at the youngest age.

What do the results of genetic testing mean?
There are three possible results from genetic testing.

Gene change (mutation) found
For the individual tested, this confirms that there is an inherited reason for their bowel cancer. This may place them at higher risk of other new cancers. It also means that other family members are eligible to have tests to find out if they are at higher risk of getting cancer (see What is predictive testing?).

Gene change (mutation) not found
Where a mutation cannot be found, the result may be due to limits to the tests we have at this time. There may be other gene mutations present that we don’t yet know about and are unable to test for. The family may still be seen to be at high risk of cancer.

Variant found
• This result gives us no useful information.
• A gene change has been found but it is not clear whether it gives you a higher risk of cancer.
• If a variant is found, it is not possible to offer testing to other family members.

What is predictive testing?
When a gene change is found in a family member who has had cancer, it is possible to offer testing to other members of the family. This is known as predictive testing. It can show if they have a higher risk for cancer.

Results of this testing are quicker as the laboratory is looking only for the specific change that has been already found in the family.
There are two possible results:

- A ‘positive’ result means that the change in the gene has been inherited. The person is at a higher risk for bowel cancer and possibly for other types of cancer. Staff at the Family Cancer Centres will be able to talk about how to manage this risk. Depending on the gene, this finding may also affect the children of the person tested.

- A ‘negative’ result (i.e. normal) means that the gene change has not been inherited. This usually means the person tested is now at average risk (same as the general population) for bowel cancer. However if the person tested has had bowel polyps in the past or if they have a history of cancer on the other side of their family, their risk may still be higher than average. The children of a person who has a negative test result (normal) cannot inherit the gene change. They do not need testing.

There are many things to consider when making a decision about genetic testing, such as the effects on your emotional wellbeing and your family, as well as on certain types of insurance.

Ask your doctor or Family Cancer Centre for more information.

What that word means

average risk This means that someone’s chance of getting a disease is the same as any other person in the population. This may also be called population risk.

high risk This means that someone’s chance of developing a disease in the future is higher than average. This is due to:
- a family history of the disease and/or;
- a change in a gene known to make that person more likely to get that disease.

People in the high risk group should think about ways to lower their risk.

Family Cancer Centres (FCC) A centre where people can get information about a family history of cancer. The centre offers:
- genetic counselling
- genetic testing
- medical advice

- psychological support
- information about research to individuals and families.

family history A careful look at the medical history of family members of an individual who has bowel cancer. This may involve:
- getting information from death certificates
- questioning of other family members.

This information helps your medical team understand your family’s level of risk for getting cancer.

gene change A change somewhere in a gene. A change may be:
- inherited
- caused by a mistake while a cell is reproducing itself
- caused by some chemicals or viruses
- caused by events that science is yet to find.

A change in a gene may lead to the gene not working in the right way. This can make the person more likely to get cancer. A gene change is also known as a gene alteration or gene mutation. Not all people with gene changes get cancer.

genetic testing Testing for gene changes which may explain why a disease has happened or whether a disease is more likely to happen.

polyp A small growth in the bowel that can be flat or look like a mushroom. Polyps are common and there are different types. Some polyps can become cancerous whereas others do not.

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