12: BOWEL CANCER IN FAMILIES

12.1 INTRODUCTION TO GENETICS AND INHERITANCE

The human body is made up of billions of cells (such as skin cells, brain cells, nerve cells, etc). Almost every cell in the body contains a complete set of genetic instructions (chromosomes). These genetic instructions are made up of almost 100,000 genes, all linked together like tiny beads on a necklace and wound up into tight little packages that fit inside the centre (or nucleus) of a cell. Each gene in the body is made of DNA (deoxyribonucleic acid) and they carry the instructions that control how our bodies grow, develop and work. For example there are genes whose job is to make sure our cells grow at the right time, or genes that control the colour of our eyes, or hair.

Inheritance is the transfer or ‘passing on’ of genetic information from a parent to a child. Genes come in pairs, and sperm cells and egg cells contain only half the genes needed to make a new human being. When the two come together, the new life contains a complete set of genetic information, half being from the mother and the other half from the father. Sometimes the genes act together in the same way, but if the two genes contain conflicting information, one gene may dominate over the other, eg a gene for dark hair and a gene for light hair will result in the darker hair being dominant.

When we talk about cancer that ‘runs in the family’ we often assume that everyone in the family will develop the cancer. This is not true. In fact, if your parent has an altered gene that causes bowel cancer, you are at risk of having the altered gene—that is, you have a 50:50 chance of having the altered gene that can cause cancer. If you have a brother or sister with the altered gene, you may also be at risk of having the altered gene.
If you have an altered gene that causes a high risk of bowel cancer, all your children are at risk. Each has a 50:50 chance of inheriting the altered gene from you—like tossing a coin, heads or tails. Remember that because genes are inherited in pairs, if you have an altered gene that causes a high risk of bowel cancer, you will have one copy of the altered gene and one copy of the normal gene. When you have a child you will pass on one or the other of the two genes but not both.

12.2 HAVE I INHERITED AN INCREASED RISK OF BOWEL CANCER?

Most people with bowel cancer will not have inherited a high risk altered gene from their parents. In fact 98 per cent of the population have only an average risk of developing bowel cancer. These are people who have never had a history of bowel cancer or a condition known as ulcerative colitis, and have no confirmed family history of bowel cancer. People with only one first-degree relative (parent, sibling or child) or second-degree relative (grandparent, aunt, uncle, niece or nephew) with bowel cancer diagnosed after the age of 55 are at a slightly increased risk.

**Recommendation:**

Based on family history, people who have an average (or slightly above) risk of developing bowel cancer should have an FOBT every year and consider having a sigmoidoscopy every five years from the age of 50.

Some people are thought to be at a moderately increased risk of getting bowel cancer. This accounts for only 1 to 2 per cent of the population. These are people who have a first-degree relative (parent, sibling or child) with bowel cancer diagnosed before the age of 55, or two first-degree or one first-degree plus one second-degree relative (grandparent, aunt, uncle, niece or nephew) on the same side of the family with bowel cancer diagnosed at any age. If you are at increased risk, consult your doctor about having regular bowel checks.

**Recommendation:**

Based on family history, people who have a moderately increased risk of developing bowel cancer should have a colonoscopy every five years starting at age 50 or at age ten years younger than the first diagnosis of bowel cancer in the family, whichever comes first. You should have an FOBT in each of the intervening years.

Other people are at a potentially high risk of getting bowel cancer. This accounts for less than 1 per cent of the population. These are people with three or more family members who have been diagnosed with bowel cancer, and people whose families have the inherited disorders known as hereditary non-polyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP). These conditions are described in more detail below. If you are at high risk of developing bowel cancer,
you will need to have regular bowel checks. Your doctor may advise genetic testing.

People with relatives who have had bowel cancer can consider having tests that diagnose signs of early bowel cancer. You will have a better chance of being cured if a cancer is detected at an early stage (see p61 ‘Screening tests for bowel cancer’).

12.3 TYPES OF INHERITED BOWEL CANCER

Two types of inherited conditions, if left untreated, may result in bowel cancer. These are familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC).

FAP accounts for less than 1 per cent of all bowel cancers and is very rare. HNPCC is only marginally more common, accounting for about 1 per cent of all bowel cancers. These figures show that it is uncommon to actually have inherited an altered high risk gene associated with bowel cancer.

Familial adenomatous polyposis (FAP)

Familial adenomatous polyposis (FAP) is caused by a change in a gene known as the APC gene. People with this change in every APC gene in their body are referred to as ‘having the FAP gene mutation’.

FAP causes polyps to grow inside the bowel. These polyps always turn into cancer if left untreated. Polyps are small growths, often on stalks like a mushroom, and they vary in size from a tiny pinhead to 2 centimetres or more.

Polyposis simply means a lot of polyps. The polyps in FAP are ‘adenomatous’, which means they can develop into cancer. FAP is also ‘familial’ which means the condition is passed on through families. If one of your parents has FAP, you have a 50:50 risk of developing FAP.

Most people with FAP develop bowel polyps during their late teens or early adult years. The polyps may start at any age, but rarely before the age of 10.
Bowel cancer in families

What can be done?
There is much that can be done for someone with FAP.

Gene testing
For most people at risk of FAP, gene testing is now available. This can tell you whether you have the altered gene which causes FAP. People without the gene will not develop FAP, and their risk of developing bowel cancer is the same as the rest of the population (that is, it increases with age). Gene testing is discussed in more detail on p70 'Genetic testing for bowel cancer'.

Regular check-ups
People with FAP, and at-risk people who have not yet had gene testing, should have regular check-ups with the doctor. These should start when you are around 12 years of age, well before bowel cancer is likely to appear. When you have a check-up for FAP, it will generally involve having a sigmoidoscopy and maybe a barium enema (see p19 'Sigmoidoscopy', and p20 'Barium enema').

There is evidence showing that deaths due to bowel cancer are significantly reduced in families with FAP that have regular check-ups.

Treatment to prevent cancer
Treatment can remove polyps by removing all or most of the large bowel (the colon and sometimes the rectum) through surgery. The aim is to prevent cancer from developing, and at the same time, to keep your digestive system working as normally as possible. It is important to discuss the impact of this surgery with your doctor or professional counsellor before and/or after the operation. This type of help can be obtained through your hospital, or by phoning the Cancer Information Service on 13 11 20.

**Recommendation:**
Individuals having surgery for FAP should have an operation to remove all or most of the large bowel. It is not recommended that people with FAP routinely take nonsteroidal anti-inflammatory drugs.

Hereditary non-polyposis colorectal cancer (HNPCC)
Hereditary non-polyposis colorectal cancer (HNPCC) is also caused by an altered gene (as with FAP).

The normal function of the HNPCC gene is to repair any problems within the cell, but when a person carries an altered HNPCC gene, the problems are not repaired and this causes bowel cancer to develop. Currently there are five known HNPCC genes, all of them called mis-match repair genes. Each family has a unique HNPCC gene mutation.
People with HNPCC have very few, or no, polyps, which can make this condition more difficult to diagnose than FAP. The cancers which occur in individuals with HNPCC however, do still tend to develop from polyps.

HNPCC most commonly occurs when people are in their thirties or forties or older. Sometimes it occurs in the twenties, and very rarely in teenage years. Unfortunately, without genetic testing, it is impossible to tell in advance who will get bowel cancer, and genetic tests cannot tell when cancer will develop.

What can be done?

Many things can be done for families with HNPCC.

Gene testing

For some families, the altered gene can be identified. However, present tests will not identify the altered gene for all families, so regular check-ups are vital. New tests will become available in the future.

Regular check-ups

For those who are known to carry an altered HNPCC gene and for people from HNPCC families who have not yet been able to have genetic testing, regular bowel check-ups are vital. It is recommended that testing begin at the age of 25 years, well before the cancer is likely to appear. These check-ups need to continue for life and should involve having a colonoscopy every one to two years (see p21 'Colonoscopy'). If you decide to have a colonoscopy every two years, it is important that every alternate year when you are not being screened, you have an FOBT (see p61 'Faecal occult blood test') to ensure a cancer does not grow during this period. Sometimes other tests might be needed and your doctor will provide more information if you need to have them.

For women with HNPCC, it is also important from the age of 35 to have regular gynaecological check-ups as having HNPCC can also increase your chances of developing uterine, ovarian, and other cancers. Your doctor will discuss these additional tests with you, or you can contact the Cancer Information Service on 13 11 20.

Treatment to prevent cancer

Cancers cannot develop if organs are removed. One option for people with HNPCC is to remove all or most of the large bowel (the colon and sometimes the rectum). The aim of surgery is to prevent cancer, and at the same time, to keep your digestive system working as normally as possible.

Women can also choose to have a hysterectomy (removal of the uterus) and possibly an oophorectomy (removal of the ovaries) to prevent gynaecological cancers, although this can be delayed until after they have had a family. It is important to discuss the impact of any preventative surgery with your doctor or professional counsellor before and/or after the operation. This type of help can be obtained through your hospital, or by phoning the Cancer Information Service on 13 11 20.
Recommendation:

Members of families with a proven link to HNPCC should be screened by yearly or two-yearly colonoscopy from the age of 25 years.

12.4 GENETIC TESTING FOR BOWEL CANCER

Genetic testing can tell you whether or not you have the altered FAP or HNPCC gene(s) that may lead to bowel cancer.

The mutation in the particular HNPCC or FAP gene can differ from one affected family to another. Laboratory scientists need to find out which mutation is present in your family. The best way to do this is to take a blood sample from someone in the family who definitely has HNPCC or FAP, and identify the gene mutation. This is difficult to do, can take some time, and is not always successful.

Once the gene mutation has been found, anyone else in the family who is at risk of FAP can have the gene test once they reach the age of 12, or for HNPCC at 18. This involves only a blood test, and must be done at a specialist genetic clinic which will ensure you receive all the advice, support and help you need. Your doctor can arrange an appointment for you.

There are many implications to having genetic testing. These include:

• what if I do or don’t have the altered gene?
• what if the scientists can’t find the altered gene?
• when can I have genetic testing?
• how much does it cost?
• how long will it take?
• what if I don’t want to know the result?
• what should I tell other family members?
• what if they don’t want to know?
• what effects will a positive test result have on my life insurance?
• who needs to know the result?

All of these questions need to be considered before an individual or family has genetic testing. Genetic counsellors can help you work through these issues, answer questions, and help you come to a decision about having the test.

For more information on genetic testing, contact the Cancer Information Service on 13 11 20.
Recommendation:
Genetic testing should only be carried out under the supervision of a clinical genetics or cancer genetics specialist, and should always be supported by counselling.

The FAP and HNPCC registers
The FAP and HNPCC registers have been set up so that information about these genetic disorders can be recorded. Family trees of people with FAP or HNPCC are checked to identify people at risk of inheriting the altered gene. It could help the future medical care of you and your family if your gene test result is recorded on the FAP or HNPCC register.

If no one else in your family has had a gene test for FAP or HNPCC, your result will help give the correct advice to other family members. Your test could enable the laboratory to identify the family-specific HNPCC gene mutation. In any event, knowing that you do indeed have—or do not have—FAP or HNPCC could help others understand who else in the family may be at risk.

All information kept at both the registers is strictly confidential. It is never given to outside enquirers, including family members, without your permission.
Guidelines for the prevention, early detection and management of colorectal cancer: A guide for patients, their families and friends

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