



National Hereditary Breast Cancer Helpline 01629 813000



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What is a Gene?

A single cell in the body is made up from thousands of genes (approximately 30,000) joined together on chromosomes. Genes are the instructions that help us be what we are. In fact they are the body's instructions to life. Genes come in pairs inherited from our parents – one copy from each parent. Our genes are responsible for everything that we are . . . the way we look, our characteristics and some inherited illnesses. If one of our parents carries a faulty gene then we have a 50/50 chance of inheriting it. Let us imagine one of our cells is a library. In this library there are several sections or Chromosomes. Each Chromosome comprises thousands of books or genes).
...each book (or gene) has thousands of words.

A spelling mistake in one of these words could confuse the understanding of this book . . . a missed chapter make it unintelligible. This is what happens sometimes. A fault may occur at any part of the gene . . . the effects of which may vary. In some cases it is not just a mistake but an entire chunk of the gene that is missing. It seems hard to imagine a single cell that is far too minute for the human eye to see, contains so much information.

What is Hereditary Breast Cancer?

Breast Cancer is the most common cancer in women in the UK, making up around 30% of all cancers in women. About 1 in 9-10 women in the UK will develop breast cancer at some time in their life. Most women develop breast cancer by chance however in a small percentage of women this can be due to a faulty gene. So far 3 genes have been identified that give a high risk of breast cancer.

These are BRCA1 BRCA2 and TP53. A fault in one of these genes usually confers around an 80% lifetime risk of breast cancer. The normal population lifetime risk is around 10%. What is important to realise therefore is that most women who have a relative who has breast

cancer will **NOT** be at increased risk. With just one family member with the disease it is much more likely that theirs will be a 'chance' breast cancer. However, in some families there are more breast cancers than would be expected by chance alone (particularly at young ages). This may be due to a faulty gene, especially if there are any other related cancers such as ovarian cancer, or, a family member with breast cancer in both breasts. If there is a family member affected with breast cancer still living who can give a blood sample, a genetic test may be performed to look for a faulty gene. (for further information see **Gene Testing**)

Am I at risk?

Most people who have a relative with breast cancer will not be at increased risk. However in families where there are two or more breast cancers occurring under the age of 50, in close family members, then this may be a reason to take a closer look at the family history. Typically, a family affected by one of the high risk genes will often be self evident, with multiple breast cancers occurring.

Of course sometimes families are of predominantly male descent and therefore it may be difficult to recognise the trend. In some families there are instances of male breast cancer, however most males will be unaffected by the fault.

Family histories are usually considered significant if there are:

- 1 Two cases of breast or ovarian cancer under the age of 40 – especially a case of breast cancer in both breasts.
- 2 Three breast or ovarian cancers under the age of 50.
- 3 Four breast or ovarian cancers occurring under 60.

(NB 1-3: the ovarian cancers can occur at any age)

If this is the case then your GP will refer you, if appropriate, to your nearest Family History Clinic.

There you should receive specialised genetic counselling and risk assessment. There are many different courses of action available to you from screening, drug trials, surgical interventions, or of course, doing nothing. There is no right or wrong thing to do...its all a matter of individual choice.

The most important thing is being aware of the risk and the choices so that you personally can make an informed decision of how you would like to handle your situation. There are organisations who will help you trace your family history (see Useful Contacts section at the end of this Fact sheet).

Gene Testing

Recent developments have made gene testing a very real possibility, however in some families it can be extremely difficult. Usually a gene test will only be offered if the family history is strong enough (at least a 20% chance of identifying a faulty gene), and if there is a living affected family member who can be tested first. The reason for this is that looking for a fault in a gene is rather like looking for a needle in a very large haystack.

If the blood of an unaffected family member is tested and no fault is found immediately, then this only means that nothing was found, it does not mean that there is no fault. However, if a family member is tested whose history suggests very strongly that their breast cancer is genetic, but a fault is not found immediately, then deeper investigation would be warranted.

Once the fault has been identified in a family then it is a relatively easy task to test subsequent unaffected family members. In other words, what and where the fault is can be exactly identified.

Remember that an affected parent has a 50/50 chance of passing this fault on to their children. Equally if a child does not inherit the fault then there is no chance at all of future generations inheriting it.

Before you receive a genetic test you will be seen by the genetic counsellors team. This is to establish that you really do want the test and that you are prepared for the outcome. If of course it is good news and you have not

inherited the fault, then that gives peace of mind immediately. Many people want to have the test just so they know, not that they have any particular strategy in mind before the result. Some find it more stressful not knowing than actually finding that there is a fault so being able to take control and deal with it.

We are all different and our reactions will differ enormously from person to person, even within a family. It is important to remember that having the test alters nothing . . . we are what we are from conception.

WHAT OPTIONS ARE AVAILABLE?

The main options available to a woman at risk are screening and preventive measures.

Screening

Mammography:

A mammography is an x-ray of the breast. This screening procedure can detect a breast cancer at an early stage in development. It can detect precancerous changes such as small lumps of calcium.

Mammography is proven to be effective in women after 50 years of age and is available on a three-yearly basis to women as part of the National Screening Programme. Women at moderate risk or above are entitled to annual screening between 40 and 49 years. Women at high risk especially due to mutations in the genes BRCA1 or BRCA2 are usually entitled to screening at a younger age but not before 30 years of age.

Magnetic Resonance Imaging (MRI):

MRI uses a strong magnetic field and radio waves to produce detailed pictures of the inside of your body.

MRI scans can show muscles, joints, bone marrow, blood vessels, nerves and other structures within your body. The images the scans produce are usually two-dimensional, but in some cases several different scans can be taken to build up a three-dimensional image that can be displayed on a computer screen. The process usually takes about 30-45 minutes.

Patients may also have an injection of a dye which helps highlight any tumours.

Some studies show that MRI is superior to mammography in detecting early breast cancer in BRCA1 and BRCA2 carriers.

Preventative Measures

Studies have shown that surgery can reduce the risk of developing breast cancer by approximately 90%.

Mastectomy:

Essentially there are three main options. The first would be a straightforward mastectomy, which would mean leaving someone with a scar across the chest.

The second option would be to have a full mastectomy with reconstruction although the results of this would obviously not be cosmetically very good.

The third option would be to have a skin sparing mastectomy where most of the skin envelope, were retained and where you either used your own tissue or an implant under the muscle to replace the area where the breast tissue has been removed. With reconstruction this is going to mean two and possibly three procedures and obviously there are risks involved with general anaesthetic and with complications from the operation.

The operations are not without at least some small amount of pain also. Risk reducing mastectomy will decrease your risks by at least 90% so this would reduce the risk to around 8% for a BRCA mutation carrier. A complete mastectomy would reduce the risks to very low levels indeed.

Removal of the ovaries:

In view of the uncertainty about ovarian screening and the lower likelihood of cure for ovarian cancer, women who are at risk of a BRCA1 or BRCA2 mutation and particularly if they test positive often opt to have their ovaries removed preventatively. This is a major operation and involves being in hospital for a week or two. It is often performed at about 40 years of age when the main risk period starts. As such this will inevitably put a woman into an early menopause.

Some women have little or no symptoms from this, but others may have substantial and prolonged menopausal symptoms (they may have had these anyway only later with the natural menopause). HRT can be given to relieve these symptoms and as long as this is not for a prolonged period (5 years or more) may still leave a woman protected against breast cancer due to the early menopause. If

women opt for a full hysterectomy rather than just removal of the ovaries and tubes (bilateral salpingo-oophorectomy) they would qualify for oestrogen only HRT which is much safer to the breast tissue.

Removal of the ovaries and tubes will reduce the risk of an ovarian type cancer by 90-95%. Dietary and other prevention It is likely that keeping fit and being close to the weight that you were at aged 20 years when entering or through the menopause will reduce your risks. Certain elements in the diet may be risk factors such as animal fats and certain fruits and vegetables may be protective. New research initiatives continue to be developed in this area, to reduce the risk of cancer in high-risk individuals.

New treatment trials/studies for BRCA

There are some new treatment studies for BRCA carriers whose cancer has returned.

Platinum agent study:

Women whose breast cancer has returned, and who carry a BRCA1 or BRCA2 mutation, are potentially eligible for a new treatment study using platinum chemotherapy. It is very important that the oncologist involved in the care of you/your affected family member is aware of the genetic status so that eligibility for this treatment can be assessed. Platinum agents have been shown to have an increased sensitivity in treating cancers from BRCA carriers with ovarian cancer and there are laboratory tests that confirm this. If you think that you or a relative is eligible with newly diagnosed metastatic (cancer returned in other parts of the body) that hasn't yet been treated or treatment has failed please contact your oncologist.

Parp inhibitor study:

Women and men whose cancer has returned who carry a BRCA1 or 2 mutation are potentially eligible for a new treatment study using a brand new agent called a PARP inhibitor. It is very important that the oncologist involved in the care of you/your affected family member is aware of the genetic status so that eligibility for this treatment can be assessed. If a cancer has returned and you think that you or a relative is eligible with newly diagnosed metastatic (cancer returned in other parts of the body) that has not yet been treated or treatment has failed please contact your oncologist.

Herceptin treatment:

Herceptin is a therapy for women with metastatic breast cancer whose tumours have too much HER2 protein. (HER2 is a growth factor receptor, and is generally associated with a more aggressive breast tumour and resistance to some types of chemotherapy.) Herceptin is not chemotherapy.

There has been much publicity about the use of herceptin for early stage breast cancer. Women who have activation of the nuclear estrogen receptor (NER) in their breast cancer could potentially qualify for treatment. BRCA carriers and in particular BRCA1 carriers very rarely have involvement of the Human Epithelial Growth Factor Receptor (HER) and are therefore unlikely to qualify for herceptin treatment.

The Future

The Human Fertilisation and Embryology Authority (HFEA) the fertility watchdog decided in May this year to extend genetic screening of human embryos used in IVF treatments to check for faulty genes that increase the risk of breast, ovarian and bowel cancers.

The HFEA issues licences permitting fertility clinics to use the embryo screening technique, called pre-implantation genetic diagnosis (PGD), where a cell from a three-day old embryo is tested.

Whilst this news has pleased some, others have expressed reservations about the idea. This controversial issue will always raise ethical concerns.

The HFEA's decision will be reviewed in 2008. It is hoped that progress of screening and prevention will continue to improve and will be made available through research. Efforts are being made on ways of preventing breast cancer through natural means as well as through drug trials.

To find out more about or to take part in research trials and studies, see Further Information section at the end of this fact sheet.

USEFUL CONTACTS:

The National Hereditary Breast Cancer Helpline and Information Centre

St Anne's Cottage, Over Haddon, Derbyshire.
DE45 1JE

Tel 01629 813000 (available 24 hours)

Email: canhelp@btopenworld.com

Website: www.breastcancergenetics.co.uk

The Helpline has been running now for over 10 years, and has taken thousands of calls worldwide. It aims to provide help and information for those concerned about their family history of breast cancer, and also has a useful database of women prepared to share their own experiences with others.

The Genesis Appeal

PO Box 320 • Manchester M20 2HT

Home 4 • Withington Hospital • Manchester M20

Tel: 0870 623000

Website: www.genesisuk.org

Provides information about the latest news on trials and treatments. Launched in 1996 to support vital work into breast cancer prevention and early diagnosis, The Genesis Appeal is a registered charity which is solely dedicated to the prevention of the disease.

Dietary and exercise studies have been initiated at the GENESIS prevention centre at the Nightingale Centre. A National treatment trial with the drug arimidex to prevent breast cancer in post-menopausal women is underway (IBIS2). Genesis hopes that arimidex will reduce breast cancer risk by as much as 70%. Women at moderate risk of breast cancer are eligible can contact the IBIS centre on 0207 014 0235.

New evidence, which shows a clear connection between breast cancer and diet and exercise, has provided the basis for a new book, due to be published this year.

Following studies funded by Genesis, "The Breast Cancer Prevention Diet" is written by Research Dietician Dr Michelle Harvie, and is an extension of work carried out by Professor Tony Howell, Professor Gareth Evans and Professor Nigel Bundred.

Breast Cancer Care

Kiln House, 210 New Kings Rd, London.

SW6 4NZ

Website: www.breastcancercare.org.uk

Tel: 0808 800 6000 (open 9am-5pm Monday - Friday, Saturday 9am-2pm)

Provides information, practical assistance and emotional support for anyone affected by breast cancer.

My Family Health

c/o St Anne's Cottage • Over Haddon

Derbyshire. DE45 1JE

Website: www.myfamilyhealth.co.uk

Tel: 01629 813867

Family Tree tracing service designed to discover genetic predispositions within the family.

Cancer BACUP

3 Bath Place, Rivington Street, London EC2A

3JR

Tel: 0808 800 1234 (open Monday-Friday, 9am-7pm)

Provides up-to-date information about cancer, practical advice and support for cancer patients, their families and carers.

Cancer Research UK

P.O. Box 123, Lincoln's Inn Fields

London WC2A 3PX

(Supporter Services) 020 7121 6699

(Switchboard) 020 7242 0200

Website: www.cancerresearchuk.org

Supports research into all aspects of cancer through the work of more than 3,000 scientists, doctors and nurses.

NHS Direct Online

Website: www.nhsdirect.nhs.uk

Online help and information on all aspects of health or call 0845 4647 (24 hours).