BRCA1 & BRCA2
What is hereditary breast cancer?
Cancer is unfortunately very common, with 1 in 3 people developing cancer at some point in their lifetime. Breast cancer occurs in 1 in 8 women; with 80% being diagnosed after age 50; while ovarian cancer occurs in about 1 in 75 women. Most of these cancers are not inherited, but occur randomly. Men can also develop breast cancer although this is rarer, accounting for only 1% of all breast cancer. Most breast cancer occurs by chance however about 5-10% is inherited. When breast cancer is inherited it may be caused by a mutation (fault) in one of the breast/ovarian cancer genes, known as BRCA 1&2, or in a different breast cancer associated gene.

Characteristics of Families with BRCA mutations
Families with BRCA1 & BRCA2 mutations generally have one or more of the following:

- Several close relatives with breast cancer
- Breast cancer diagnosed before the age of 50
- Bilateral breast cancer (cancer in both breasts)
- Ovarian cancer
- Increased frequencies of other cancers such as prostate and pancreatic cancer
- Male breast cancer
- Ashkenazi (Eastern European) Jewish ancestry

It is important to be aware that hereditary breast or ovarian cancer can be present on either the maternal (mother’s) or paternal (father’s) side of the family.
What are genes?
We have approximately 25,000 genes in every cell of our body. Genes are our body’s instructions and determine how our body functions, develops and is maintained. Genes come in pairs and each gene has a code, which can be thought of as a long sentence with thousands of letters. Changes in this code can stop the gene working and are called mutations. Mutations in some genes, such as BRCA1 & BRCA2 can increase the risk of certain types of cancer because normally these genes prevent cancer by repairing mistakes in the cells.

How are BRCA mutations inherited?
Our genes come in pairs. This means that we inherit two copies of BRCA1; one from our mother and one from our father. The same is true for the BRCA2 gene. BRCA gene mutations can therefore be inherited from either parent. If a parent has a genetic mutation, there is a 50% chance that it will be passed on to each child.

This diagram shows how a BRCA gene mutation can be inherited

Genetic testing for BRCA1 & BRCA2 Mutations
Genetic testing is performed on a saliva or blood sample and analyses the BRCA1 & BRCA2 genes to identify mutations which are likely to lead to an increased risk of developing cancer. There are three different tests available depending on an individual’s personal and family history:

Predictive testing
In families where the BRCA mutation has already been found it is possible to test for just the familial mutation. If the mutation is not present then the relative is not at increased risk of cancer.

Ashkenazi Jewish mutation test
In Jewish families it is possible to test for 3 common mutations. These mutations are responsible for 97% of BRCA mutations in Jewish families. Results will show the presence or absence of these 3 mutations.

Comprehensive BRCA sequencing
Comprehensive sequencing, examines the entire DNA code of the BRCA1 & BRCA2 genes in detail. It is preferable to test a living relative who has been diagnosed with breast or ovarian cancer first. When this is not possible an unaffected person can have genetic testing if they wish.

Genetic testing usually takes several weeks, at which point a follow up appointment is scheduled.

There are three possible outcomes of Comprehensive genetic testing:

1. A mutation is identified which is known to increase the risk of breast and ovarian cancer. Appropriate screening or treatment can be arranged and predictive testing offered to other relatives after appropriate counselling.
2. A genetic variation is found, but whether or not this is the definite cause of cancer is unknown. Further studies may be necessary.
3. No mutation is found. It is possible that there may be a mutation that is unidentifiable by current laboratory techniques. There may also be other genes that increase the risk of breast cancer and therefore if no mutation is found breast screening may still be required, particularly when an unaffected person is tested.

When a family has a history of only breast cancer and no BRCA1 & BRCA2 mutation is identified, there is usually no increased risk of ovarian cancer.
Cancer Risks Associated with a BRCA mutation

It is important to remember that not everyone who inherits a BRCA gene mutation will develop cancer and the estimated cancer risks associated with BRCA mutations vary. BRCA1 mutations are estimated to have up to an 85% risk of breast cancer and a 40-60% risk of ovarian cancer. Men with BRCA1 mutations may have a slightly increased risk of prostate cancer.

Women with BRCA2 mutations have up to a 90% risk of breast cancer and up to a 26% risk of ovarian cancer. Men with BRCA2 mutations have a 7% lifetime risk of developing breast cancer, and an increased risk of prostate cancer (2-5 times the general population risk). Individuals with BRCA2 mutations also have an increased risk of pancreatic cancer and possibly other cancers.

Occasionally, a baby will inherit two BRCA2 mutations and will therefore have the congenital condition known as Fanconi Anemia.

Early detection for women with BRCA mutations

Women with BRCA gene mutations should have annual mammograms and annual breast MRI from age 30. It is also important for all women to be ‘breast aware’ which means becoming familiar with how your breasts look and feel and noticing any changes unusual for you. Many women have lumpy breasts, which naturally change depending upon the time in your menstrual cycle and therefore it is best to check yourself at the same time each month (mid-cycle). If you notice a change in your breasts it is important to seek medical advice.

Ovarian screening has not been shown to be beneficial and therefore some women may consider risk-reducing surgery.
Preventative medication
The medications Tamoxifen and Raloxifene have been shown to lower the risk of developing breast cancer in moderate and high risk women and BRCA2 when taken for 5 years. These medications have some side effects and it is important to discuss these with a genetics expert or breast specialist, who should be able to discuss the benefits and side effects in detail and then prescribe the medication if required.

Risk-reducing surgery
Some women who are found to have a BRCA mutation choose to have risk-reducing surgery to lower their risk of cancer.

Surgery to remove the ovaries can be carried out from about 40 years of age, when women have completed their families, and when the risk of ovarian cancer starts to increase. Removing a woman’s ovaries before the menopause is also known to reduce the risk of breast cancer. If a woman decides to have her ovaries removed before the menopause she should consider taking hormone replacement therapy to help treat the symptoms.

Risk-reducing surgery to remove healthy breast tissue (risk-reducing mastectomy) may also be considered by some women. This is a very individual decision and obviously needs careful consideration. If a woman wishes to consider this option, her breast surgeon can provide further information.

Early detection for Men with BRCA mutations
Men with BRCA mutations could have annual clinical breast examinations performed by a doctor. It is also important that they are breast aware and perform monthly self breast examination. Prostate cancer screening includes an annual blood test called PSA (prostate specific antigen). Recent research has shown that other biomarkers can improve the accuracy of the PSA test and this method of screening is offered by ProstateHealth UK.

Hormonal Factors
Some hormonal factors have been suggested as breast cancer risk factors. In particular, it is known that early menarche (first period) and late menopause increase the risk of breast cancer. Breast-feeding lowers the risk of breast cancer, as does early childbirth (before the age of 30). It is known that the pill lowers the risk of ovarian cancer when taken for 5 or more years. However, there may be a slightly increased chance of developing breast cancer for women who take the pill for prolonged periods, although this risk decreases once women stop taking the pill.

Hormone replacement therapy (HRT) increases the risk of breast cancer when used after a natural menopause however it may be helpful for women who have an early surgically induced menopause.

Lifestyle Factors
It is known that a healthy diet can promote good general health and lower the risk of cancer. In particular, maintaining a normal body weight and avoiding abdominal weight gain will lower the risk of breast cancer. Limiting alcohol intake and doing regular physical exercise will also lower the risk of breast cancer.

Financial Issues
Some individuals may be concerned about difficulties with obtaining insurance coverage following genetic testing. Currently, this is not a problem as there is a moratorium ensuring that individuals do not need to disclose genetic test results, unless a very large policy is being taken out. This moratorium is valid until 2017. More information about insurance can be found at:

http://www.abi.org.uk

Further information and support can be found at:-
http://www.breastcancercare.org.uk/
http://brcaumbrella.ning.com/
http://www.breastcancer.genetics.co.uk/
http://www.youngsurvival.org
http://www.facingourrisk.org
www.cancercare.org
www.cancerresearchuk.org
www.lbhc.org
www.cancerbacup.org.uk
www.menagainstbreastcancer.org

Our knowledge of cancer genetics is rapidly growing, and the information given summarises this to date. Please keep us informed of any significant changes in your family in the future as this may alter our advice to you. Please do not hesitate to contact us if you have any questions or concerns.
GeneHealth UK

Head office
GeneHealth UK
1 The Mill
Copley Hill Business Park
Cambridge Road
Cambridge
CB22 3GN

www.GeneHealthUK.com
Info@GeneHealthUK.com

Appointments
Call 0800 331 7177
Mon-Fri 08.00-20.00
Sat 09.00-12.00

Clinics - Locations
Please visit our website www.GeneHealthUK.com/Clinics for an up-to-date list of clinic locations and directions. Please be aware that most genetic counselling sessions are undertaken by phone so a clinic may not be needed.

GeneHealth UK is the leading provider of genetic tests and offers national and international counselling and testing services. We have designed our services to be comprehensive and to detect all of the clinically relevant mutations, however no genetic test will pick up all genetic mutations. If your results are abnormal you may be eligible for referral to an NHS clinic via your GP, or to a consultant in one of our private clinics throughout the UK. This may be funded by either self-pay or private medical insurance.

Please visit www.GeneHealthUK.com for more information and advice.

GeneHealth UK is part of Check4Cancer Ltd.