BRCA1 & BRCA2

GeneHealth UK
What is hereditary breast cancer?
Cancer is unfortunately very common, with 1 in 2 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. 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 BRCA1 & BRCA2, or in a different breast cancer associated gene. Currently we know that there are at least 10 genes which cause breast cancer.

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 45
- 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
- Triple negative breast cancer

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.
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 4 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 screening is based on the family history.

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 up to 60% risk of ovarian cancer. Men with BRCA1 mutations may have approximately a 20% risk of prostate cancer and a 5-10% risk of male breast 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 5-10% lifetime risk of developing breast cancer, and approximately a 40% risk of prostate cancer. 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 breast MRI from age 30 and annual mammograms from age 40. 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.
Cancer Treatment

Individuals diagnosed with breast cancer who also have a BRCA gene mutation may consider having a risk reducing mastectomy to lower their risk of future breast cancer (usually around 50%). Certain chemotherapy treatments may also be tailored on the basis of a BRCA mutation. For example, platinum based chemotherapy and PARP inhibitors can be beneficial in treating cancer associated with BRCA mutations.

Women with ovarian cancer related to BRCA mutations may also benefit from these chemotherapies.

Preventative medication

The medications Tamoxifen and Raloxifene have been shown to lower the risk of developing breast cancer in BRCA2 carriers as well as women at increased risk, 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.

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 should be breast aware and perform monthly self breast examination. Annual prostate screening with PSA tests should be arranged.

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, there is a moratorium ensuring that individuals do not need to disclose predictive genetic test results. This moratorium is valid until 2019. 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://brcaubrella.ning.com/
http://www.breastcancer genetics.co.uk/
http://www.youngsurvival.org
http://www.facingourrisk.org
www.cancercare.org
www.cancerresearchuk.org
www.lbcc.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.
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Please visit our website [www.GeneHealthUK.com/Clinics](http://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](http://www.GeneHealthUK.com) for more information and advice.

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