NHS
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Genetic testing for BRCA1 and BRCA2

This information explains how we test for genetic factors known as BRCA1 and BRCA2 which relate to breast and ovarian cancers. This will be explained to you at your appointment but this leaflet acts as a reminder.

How do I know I am at risk of having the BRCA1 and/or BRCA2 gene?

Cancer is a common disease and occurs in just over one in three people in the general population. Only a small proportion of all cancers are due to an inherited factor called a gene/genes and so clustering in families can occur due to chance alone. When assessing how likely it is that there may be an inherited predisposition (tendency) to breast and ovarian cancer in a family there are several factors that we consider.

These include:

1. A young age at diagnosis of breast cancer, significantly below that which occurs in the general population.
2. Particular types of breast cancer ('triple negative') occurring below a certain age.
3. A number of people on the same side of the family who are affected with cancer.
4. Other features, such as the occurrence of several cancers in one individual.
5. An unusual situation such as breast cancer in a male.

People from certain ethnic backgrounds may also be at higher cancer risk.

Looking at this in relation to you and your own family we believe it to be possible that a gene predisposing to breast and ovarian cancer is present. However, it is also possible that the cancers have arisen for other reasons.

How does having these genes result in an increased risk of cancer?

An inherited predisposition to breast and ovarian cancer is caused by an alteration in a gene. There are two major genes currently known to be involved in inherited breast and/or ovarian cancer, known as BRCA1 and BRCA2. Everybody has two copies of each of these two genes, one inherited from their mother and one inherited from their father. These genes work to protect against breast and ovarian cancer; however, when an alteration occurs in one copy of one of these genes it does not function properly and the person carrying that alteration has a higher risk of developing breast and ovarian cancer.

More rarely, other cancers can occur in such families.

If there is a gene predisposing to breast cancer in your family, then a person who has the gene has a 50/50 (or 1 in 2) chance of passing it on to any child of theirs.

It is possible to perform a test to determine if a person carries an alteration in BRCA1 or BRCA2. Many different alterations can occur in these genes and each family may have a different alteration. Currently, in order to identify the specific alteration within any given family, it is necessary in most instances to first test a family member who has been affected by cancer.

What can testing identify?

Testing is done using a blood sample that you have consented to give.

There are three main outcomes of this testing:

1. We may find a cancer-causing alteration in one of these genes. This would be highly likely to explain the occurrence of cancers in your family.
2. We may not find an alteration in either of these genes. This could mean that either:
    - an as yet unidentified gene/genes is involved in causing cancer in your family;
    - there is an alteration in BRCA1 or BRCA2 but due to current technical limitations we could not detect it;
    - there is no inherited gene involved and the cancers in your family have arisen purely by chance.
3. Occasionally, we may find a variation in the genetic code, the significance of which is uncertain at this time (called a 'variant of uncertain significance').

What happens if you find the BRCA1 or BRCA 2 genes?

If and when we were able to identify an alteration that is highly likely to have caused the cancers in your family, then testing would be available to unaffected family members. This type of testing is called predictive genetic testing as it can tell people whether or not they carry the familial cancer predisposition gene. We recommend that anyone considering genetic testing should have genetic counselling to consider all the implications for themselves and their family.

If you have a cancer-causing change in a BRCA1 or BRCA2 and have already had breast cancer, then you would have an increased risk of developing breast cancer again. It is difficult to place a precise figure on this, as there is still much we do not know about these genes, although the risk is substantially higher than the background risk in the general population which is 10% over a lifetime (or 1 in 10 women). In addition, you would also have a substantially higher risk of developing ovarian cancer than the average woman, although this risk is lower than that for breast cancer. Finally, your children would have a 50% chance of inheriting the breast cancer predisposing gene and a 50% chance they would not.

Self checks

All women should be 'breast aware'. This involves being aware of changes in the breast and feeling the breast with the flat of the hand in a systematic way once a month, 5-10 days after you have finished your period (or at around the same time each month if post-menopausal). It is also important to take time to look at your breasts in different positions. If there are any changes at all you should inform your doctor. All women should practice this from their early twenties.

Screening

Most breast screening is done by mammography. You will be followed up by the breast unit regarding this.

With regard to ovarian screening; at present we do not have good evidence that ovarian cancer screening will detect cancers any earlier than usual. Therefore, it is important to report new and

persistent abdominal symptoms promptly. Individuals with a change in BRCA1 or BRCA2 can discuss their options with a gynaecologist.

Preventative surgery

Breasts

Many women at high risk of breast cancer want to consider prophylactic mastectomy. This is the removal of the breast tissue to try to prevent the development of cancer. There are various types of operation, but in general, as much as possible of the breast tissue is removed. Some operations leave the nipple behind and some remove this and reconstruct a new nipple. An implant may be inserted to recreate the shape of the breast and one of the major disadvantages is numbness in the operation area. In addition, not all the breast tissue can ever be removed and so there is always some breast tissue remaining which may be at risk of developing breast cancer, though this risk is small.

Ovaries

Because of the problems associated with ovarian screening, many women affected by a cancer causing BRCA gene change would consider prophylactic oophorectomy. This is the removal of the ovaries to try and prevent the development of ovarian cancer. This may be done by keyhole surgery, in which case the ovaries and fallopian tubes are removed, or it may be done at the same time as a hysterectomy (removal of the womb). This should be discussed with your gynaecologist.

There have been rare instances where ovaries have been removed and ovarian cancer has subsequently developed in the cells lining the abdomen, since these are from the same origin as those cells covering the surface of the ovary. The incidence of this occurring is not known precisely, but is thought to be quite low (about 2 3%). There is also some evidence that women who have their ovaries removed before they go through their natural menopause reduce their subsequent risk of developing breast cancer, perhaps by as much as 50%.

Women who have a prophylactic oophorectomy at a younger age may be offered hormone replacement therapy to prevent undue menopausal symptoms which may include hot flushes, night sweats, tiredness, loss of libido, vaginal dryness and mood changes. This also protects against some of the complications of early menopause, which include bone thinning and increased rates of cardiovascular disease. This should be discussed with your oncologist.

Women who have an earlier menopause are at risk of developing osteoporosis (loss of bone density). We would therefore recommend that if you chose to have a prophylactic oophorectomy that your bone density is monitored afterwards. There are a number of alternatives to HRT for the prevention and treatment of osteoporosis and these can also be discussed with your GP or oncologist.

Results of your BRCA1 and BRCA 2 test

The blood test for BRCA1 and BRCA2 usually takes about 2 months to come back. The results may help decide the most appropriate on-going treatment for you in terms of further surgery and/or radiotherapy. If appropriate, you will be offered an appointment in the clinical genetic department in the future to discuss your result.

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Further information

- www.macmillan.org.uk/information-and-support/diagnosing/causes-and-risk-factors/genetic-testing-and-counselling/inherited-cancers-breast-ovarian.html
- www.cancerresearchuk.org/about-cancer/type/breast-cancer/about/risks/breast-cancer-genes
- Oxford Cancer Centre, Churchill Hospital www.ouh.nhs.uk/

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