HEREDITARY

BREAST CANCER

BRCA1

Faulty gene

INFORMATION LEAFLET

How Do I Reduce My Risk?

CONTENTS

Part A

1 What is BRCA1
2 How does BRCA1 affect a person's risk of cancer?
3Testing for BRCA1
4Benefits and risks of genetic testing
5 Genetic testing and Insurance

Part B

Options for people with BRCA1 faulty gene

1 Screening- Breast and ovarian
2 Breast and ovarian awareness
3 Prophylactic surgery
4 Chemo prevention

Part C

RISK AVOIDANCE
1 Age
2 Family History
3 Medical History
4 Hormonal influences
5 Contraceptives
6 HRT
7 Obesity
8 Physical Activity
9 Alcohol
RESEARCH

PART A

1 What is BRCA1?

BRCA1 stands for Breast cancer susceptibility gene 1.Breast cancer is the commonest of all malignant diseases in women with 46000 new cases in the UK each year. A small number 5-10% of these are due to an inherited family gene.
This faulty gene also increases the women's risk of developing ovarian cancer. Ovarian cancer is the deadliest of all the gynaecological cancers with 6,800 women diagnosed in UK each year
BRCA1 is a human gene that belongs to a class of genes known as tumour suppressors. In normal cells BRCA1 helps to prevent uncontrolled cell growth. A mutation or fault of these genes has been linked to the development of hereditary breast and ovarian cancer.

2 How does BRCA1 affect a person's risk of cancer?

A woman's lifetime risk of developing breast and ovarian cancer is greatly increased if she inherits a harmful mutation /fault in BRCA1. She would have an increased risk of developing breast and/or ovarian cancer at an early age (before menopause) and often has multiple, close family members who

have been diagnosed with these diseases. Men with the faulty gene also have increased risk of breast cancer however breast cancer in men is at most, only 1% as common as women.
About 11% of women in the general population will develop breast cancer sometime during their lives compared to 70-80% of women with the BRCA1 faulty gene. Lifetime risks of ovarian cancer in the general population are 1.4% compared to 40% of women with BRCA1 faulty gene.
However not every women with a faulty BRCA1 gene will develop breast or ovarian cancer.

3. Testing for BRCA1 faulty gene

In a family with a history of Breast and/or ovarian cancer, it may be more informative to first test a family member who has breast or ovarian cancer. It involves a simple blood test to look for changes in BRCA1 DNA and/or look for changes in the proteins produced by these genes. It usually takes several weeks to get the test results. If that person is found to have a fault BRCA1 gene then other family members can be tested to see if they also have the faulty gene.
Genetic counselling is recommended before and after a genetic test. This involves a risk assessment based on the individuals personal and family

medical history and discussions about the appropriateness of genetic testing, the specific tests that might be used and the technical accuracy of the tests, the medical implications of a positive or negative test result, the psychological risks and benefits of genetic test results and the risk of passing a fault on to children.
The blood test is free in Northern Ireland and information regarding it is available from your GP or the Regional Genetic Centre BCH 02890236911.
A positive test means the person has inherited a harmful mutation or fault in BRCA1 gene and therefore an increased risk of developing breast and ovarian cancer. Both men and women with BRCA1 faulty gene have 50% chance of passing it on to their children.

4 Benefits and risks of genetic testing

Potential benefits of a negative result include a sense of relief and the possibility of preventive checkups, tests or surgeries will not be needed.
A positive result can bring relief from uncertainty and allows people to make informed decisions about their future, including taking steps to reduce their cancer risk.
However people who receive a positive result may feel anxious, depressed or angry. They may choose to undergo preventive measures such as

prophylactic surgery that have serious long term implications. People who receive a negative result may experience “survivor guilt”. The emotions caused by test results can create tension within families.

5 Genetic testing and insurance

Insurance companies may take genetic test results into account when making decisions about coverage. However there is a voluntary agreement between the Department of Health and the Association of British Insurers (ABI) that you can apply for up to £500 000 of life insurance or £300 000 of critical illness insurance without having to tell the insurer the results of any predictive genetic test.

PART B
Options for People with BRCA1 faulty gene

SCREENING

Cancer screening is a way of detecting the disease early; however it does not change the risk of developing cancer. The aim is to find the cancer early when it may be most treatable

.

Breast cancer screening

This involves yearly mammography, MRI and clinical breast examinations.
Mammography for women under the age of 35 may not be sensitive to detecting cancer due to the dense nature of younger breast tissue.
MRI is the most sensitive tool for screening women who are at high familial risk of breast cancer however there are cost implications

.

Ovarian cancer screening

Method may include transvaginal ultrasound, blood tests for CA125 antigen and clinical examination. However the benefits of screening are limited as

the tests are not sensitive enough to detect the cancer early when a cure is possible. Smear tests do not detect ovarian cancer.

BREAST AWARENESS

A person should know what is normal for them and check monthly for any changes.

Appearance:

Look for change in size, outline of either breast, especially those caused by arm movement, any puckering of the skin or veins that stand out more than usual.

Feelings:

Pain or discomfort in one part of either breast or in your armpit, particularly if new or persistent.

Lumps:

Any lumps or thickening in either breast that feels different from the other breast, any swelling or lumps under your armpit or around your collar bone.

Nipple change:

A nipple that has become pulled in or changed shape or shows signs of any discharge, bleeding or rash.

If you find a change see your GP. With careful screening many breast cancers will be diagnosed early enough to be successfully treated.

MALE BREAST CANCER

Most common symptoms are lump in the breast, swelling of the breast, tender indurate nipple often with crusting or discharge, sometimes blood stained, lumps under arm and sore that won't heal.

OVARIAN AWARENESS

Symptoms are vague but persistent and are more likely to be caused by more common ailments which make it difficult to diagnose
Symptoms include:
1 A constantly swollen abdomen.
2 Ongoing excessive fatigue.
3 Changes in bowel and bladder function that are constant and progressive.
4 Onset of unexplainable indigestion or nausea.
5 Unexplainable back or abdominal pain.

PROPHYLACTIC SURGERY

This type of surgery involves removing as much of the "at risk" tissue as possible in order to reduce the chance of developing cancer.

Bilateral prophylactic mastectomy (removal of healthy breasts) and prophylactic salpingo-oophorectomy (removal of healthy fallopian tubes and ovaries) reduces the risk of developing breast and/or ovarian cancer to <5% from 70-80% and 40% respectively.

Reconstruction can be done at the same time as the mastectomy and can reduce the psychological disturbance.
Removal of the ovaries will mean the woman will develop early menopause if surgery is carried out before the menopause.

CHEMO-PREVENTION

A few studies have evaluated the effectiveness of Tamoxifen in women with BRCA1 faulty gene. Data from studies have shown that Tamoxifen may be able to lower the risk of breast cancer in BRCA1 carriers however more research needs to be done.

RISK AVOIDANCE

Certain behaviours have been associated with breast and ovarian cancer risk in the general population.
However, research results on the benefits of modifying individual behaviours to reduce the risk of developing cancer among BRCA1 faulty gene carriers are limited.

AGE

Risks of breast and ovarian cancer increase with age. Most breast and ovarian cancers occur in women over the age of 50. Women with BRCA1 faulty gene often develop breast or ovarian cancer before age 50.

FAMILY HISTORY

Women with first degree relative (mother, sister, daughter or other close relative) with breast or ovarian cancer may be at increased risk.

MEDICAL HISTORY

Women who already had breast cancer are at increased risk of developing it again or of developing ovarian cancer.

HORMONAL INFLUENCES

Oestrogen is a hormone that is naturally produced in the body and stimulates the normal growth of

breast tissue. It is thought that excess oestrogen may contribute to breast cancer risk because of its natural role in stimulating breast cell growth.
Women who have their first menstrual period before age 12 or experienced menopause after 55 have a slightly increased risk of breast cancer, as do women who had their first child after age 30. Each of these factors increases the amount of time a woman's body is exposed to oestrogen.
Removal of a woman's ovaries, which are the main source of oestrogen production, reduces the risk of breast cancer.
Breast feeding also reduces the breast cancer risk as well as the number of children a women has.

CONTRACEPTIVE PILL

Most studies show a slight increase or no change in risk of breast cancer among women taking birth control pills.
In contrast numerous studies have shown that taking contraceptive pill decreases a woman's risk of developing ovarian cancer. This protective benefit appears to increase with the duration of oral contraceptive use and persists up to 25 years after discontinuing use. It also appears that the use of birth control pills lowers the risk of ovarian cancer in women with BRCA1 faulty gene.

HRT

Studies have shown HRT to be associated with increased risk of breast cancer and a small increase in ovarian cancer.

OBESITY

Substantial evidence indicates that obesity is associated with an increased risk of breast and ovarian cancer.

PHYSICAL ACTIVITY

Numerous studies have shown that physical activity reduces the risk of breast cancer especially strenuous exercise for 4 hours a week. This decrease is more pronounced in premenopausal women.

ALCOHOL

There is substantial evidence that alcohol consumption is associated with increased breast cancer risk.

RESEARCH

Research studies are being conducted to find better ways of detecting, treating and preventing cancer in BRCA1 faulty gene carriers.

REFERENCES

Ovarian cancer leaflet BCH

Breast cancer screening leaflet HPA (NI)

US National Cancer Institute

McPherson K et al Breast cancer, epidemiology, risk factors and genetics. Br MedJ 2000; 321:624-8

Kauff ND et al Risk reducing salpingo-oophorectomy in women with BRCA1 or BRCA2 mutation. New Eng J Med 2002; 346:1609-15

Marsden J Hormone Treatment and Breast cancer Lancet Oncology 2002 3: 330-11

Collaborative Gp on Hormonal factors in Breast Cancer Lancet 2002; 360:187-95

Narod SA Brunet JS, et al Tamoxifen and risk of contra lateral breast cancer in BRCA1 And 2 mutation carriers A case-control study Lancet 2000;356(9245):1876-1881

Hamajima N et al Alcohol, tobacco and breast cancer-collaborative re-analysis of individual data from 53 epidemiological studies .Br J Cancer 2002 Nov 18:87(11):1234-45

Leach MD et al. Screening with MRI and mammography of a UK population at high risk of Breast Cancer: a prospective multicentre cohort study. Lancet 2005 May 21-27; 365(9473):1769-78

Duffy SW, Nixon Estimates of the likely prophylactic effect of tamoxifen in women with high risk BRCA1and 2 mutations.

Brown PO Palmer C the Preclinical natural history of serious ovarian cancer; defining the target for early detection. Plos med 2009 Jul: 6 (7): e 1000114

Thompson D, Easton DF the Breast Cancer Linkage Consortium in BRCA1 mutation carriers. Journal of the National Cancer Institute 2002 94(18): 1358-1365

Lynch et al Hereditary Breast cancer: Part 1 Diagnosing Hereditary breast cancer syndromes The Breast Journal 2008; 14(1):3-13

Palma M et al BRCA! And 2; The Genetic Testing and the current management options for mutation carriers. Critical reviews in Oncology? Haematology 2006; 57(1):1-23.

King et al Tamoxifen and Breast Cancer Incidence among women with inherited mutations in BRCA1and 2. (NASPB) Breast care prevention trial. Journal of the American Medical Association 2001; 286(18):2251-2256.

Whittlemore AS et al. Oral contraceptive use and ovarian cancer risk among carriers of BRCA1 or BRCA2 mutations British Journal of Cancer 2004; 91(11):1911-1915.

Anderson GL et al. Effects of estrogen plus progestin on gynaecologic cancers and associated diagnostic procedures: The Women's Health Initiative randomized trial. Journal of the American Medical Association 2003; 290(13):1739-1748.

Kotsopoulos J et al HRT and the risk of ovarian cancer in BRCA1 andBRCA2 mutation carriers. Gynaecologic Oncology 2006; 100(1):83-88.

Calle et al. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. New England Journal of Medicine 2003; 348(17):1625-1638.