Lahey CLINIC

# Hereditary Breast & Ovarian Cancer

*Last Updated: November 2011*

## BACKGROUND INFORMATION

It is estimated that one out of every three Americans will develop cancer sometime during their lifetime. Women have a 1 in 8 (10-12%) chance of developing breast cancer and a 1 in 57 (1 to 2%) chance of developing ovarian cancer over the course of a lifetime. While it is difficult to determine the exact cause of cancer in an individual, the majority of cancer is thought to be sporadic. Sporadic cases of cancer could be due to a combination of factors such as chance events, the aging process, or environmental exposures. About 15-20% of cases of cancer appear to cluster in families, suggesting that the cancer in the family may be due to a combination of familial factors and other sporadic factors. Only 5-10% of cancer cases are caused by a hereditary predisposition that is passed on within a family.

Inherited traits are characteristics, such as eye color or hair texture, that are passed from one generation of a family to the next. These traits are passed on in the form of genes. Genes are located on structures called chromosomes. Individuals typically have 46 chromosomes in every cell of the body, and they come in pairs. The chromosome pairs numbered 1 through 22 are the same between men and women and the last pair determines our gender: XX for female and XY for male. One copy of each chromosome pair (and therefore each gene) comes from our mother and the other from our father. Similarly, we pass on one copy of each chromosome pair to our children.

There are hundreds of genes located on each chromosome. Genes make proteins that are necessary for the proper growth and development of the body. Each gene is made up of DNA, which is the information that codes for a particular trait or condition. If you think of a gene as being a very large book, DNA is like the alphabet that makes up the words and sentences in the book. When a gene is altered, it simply means there is a typographical error (typo) in the book. This alteration makes the gene unable to function properly. Alterations can be as large as an entire chapter missing from the book, or as small as a single letter change within a word.

## GENETICS OF BREAST AND OVARIAN CANCER

We know of a few genes that when altered, may give an individual in increased chance to develop certain types of cancer. These types of genes are called cancer predisposition genes. *BRCA1* and *BRCA2* are two cancer predisposition genes that are responsible for the majority of cases of inherited breast and ovarian cancer. However, there are other known genes that can cause a predisposition to breast and ovarian cancer. There are other rare cancer syndromes that are associated with an increased predisposition to breast cancer, including Cowden syndrome and Li-Fraumeni syndrome. Research is ongoing to discover other cancer predisposition genes.

While the function of the *BRCA1* and *BRCA2* genes is not completely understood, it is believed that these genes prevent cancer. Individuals have two *BRCA1* genes and two *BRCA2* genes. During the course of an individual's lifetime, these genes can acquire alterations and stop functioning properly. Gene alterations can be acquired for a variety of reasons, including the aging process, chance, etc. If one copy of a gene pair in a cell becomes altered, that cell will remain healthy because there is still one copy of the gene pair that is working properly.

However, as the cell ages, it is possible that the working copy of the gene pair may also acquire an alteration. At this point, both copies of the gene in the cell no longer work and the cell could become a cancer cell and grow into a tumor. This is called "sporadic" cancer and is the way most cancers develop (see Figure 1). An individual is born with two working copies of the gene and both need to be altered in order for the cell to become a cancer cell.

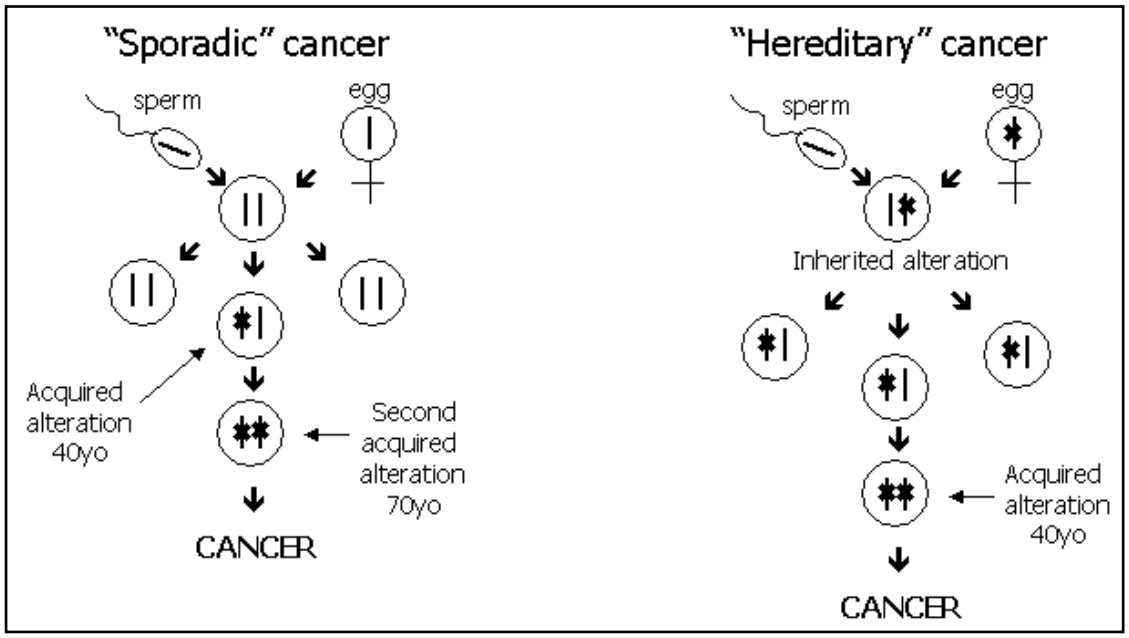


Figure 1: "Sporadic" cancer vs "Hereditary" cancer

Some individuals are born with one altered copy of the *BRCA1* or *BRCA2* gene, and therefore have only one working copy of the gene in all of the cells of their body. The altered gene could have come from either the egg or the sperm. These individuals only require one alteration in the working gene to occur for the cell to become a cancer cell. This explains why individuals with "hereditary" cancer tend to have cancer at an earlier age and may develop more than one cancer during their lifetime because only one alteration is needed to develop cancer (see Figure 1). Individuals with hereditary cancer are *predisposed* to developing cancer, but some may never acquire an alteration in the working gene and therefore never develop cancer.

We look for several features in families to try to determine whether or not there is a hereditary cancer predisposition in the family. These include:

- Multiple family members affected with the same cancer (such as breast cancer) or related cancers (such as breast and ovarian cancer)
- Earlier than average ages of diagnosis
- Multiple primary cancers in the same individual (such as cancer in both breasts)
- Cancer occurring in multiple generations

**INHERITANCE**

If an individual is found to have an alteration in the *BRCA1* or *BRCA2* gene, there is a 1 in 2 (or 50%) chance that each child could inherit the altered gene (see Figure 2). Both men and women can have alterations in these genes and have a chance to pass on the alteration to a child.

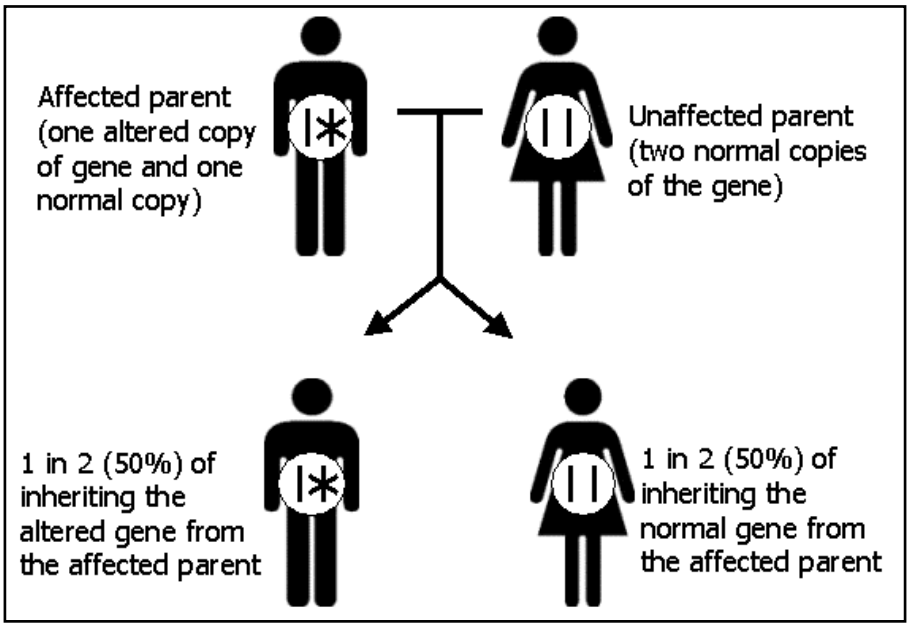


Figure 2: Autosomal dominant inheritance

**GENETIC TESTING**

Genetic testing involves taking a blood sample and checking the DNA pattern of a gene for an alteration. The cost of genetic testing is often covered by health insurance, but is dependent upon the individual insurance plan. Coverage information can usually be determined prior to proceeding with the test. Results of genetic testing are most informative if an individual who has been diagnosed with cancer is tested first. Genetic testing for cancer predisposition gene mutations should be accompanied by genetic counseling to determine the appropriateness of genetic testing based on the personal and family history of cancer, as well as the pros, cons, and limitations of testing.

**CANCER SUSCEPTIBILITY**

The cancer risks associated with a *BRCA1* or *BRCA2* alteration are listed below. The percentages cited are estimates and may change as more research is done. There are different cancer risks associated with Cowden syndrome and Li-Fraumeni syndrome.

> ***BRCA1* gene alterations:** A woman with an altered *BRCA1* gene has a 50-80% lifetime chance of developing breast cancer, and a 20-40% chance of developing ovarian cancer in her lifetime. There is an increased chance of developing a second breast or ovarian cancer as well in these individuals. In comparison, women in the general population have a 10-12% lifetime risk for breast cancer and 1-2% lifetime risk for ovarian cancer. Men who carry an altered *BRCA1* gene may have a slightly increased risk for breast and prostate cancer, although these risks are not well defined.

***BRCA2* gene alterations:** A woman with a *BRCA2* alteration has a 40-70% lifetime chance of developing breast cancer and a 10-20% chance of developing ovarian cancer in her lifetime. There is an increased chance of developing a second breast or ovarian cancer as well in these individuals. A man with an altered *BRCA2* gene has about a 6-7% lifetime risk of developing breast cancer and also has an increased chance of developing prostate cancer. The risk for a man to develop breast cancer in the general population is about 0.1% or 1 in a 1000 and prostate cancer is about 17% or 1 in 6. There may also be a slightly increased chance of developing melanoma, pancreatic, stomach, esophageal, and bile duct cancer for both men and women with a *BRCA2* mutation.

**OTHER ISSUES**

There are advantages and disadvantages to having genetic testing for hereditary cancer predisposition gene mutations. These issues will affect individuals differently, which is why we encourage you to consider the possible ramifications before proceeding with genetic testing.

*Potential advantages*

- The results of the test can help individuals tailor their cancer screening and management appropriately. For example, an individual who has a positive test result may be recommended to have more frequent screening or prophylactic surgery.
- Results can also help family members clarify their risks of developing cancer and alter their current screening, if indicated.
- The uncertainty of potentially having a gene alteration can also be alleviated by genetic testing results.

*Potential disadvantages*

- Individuals may be more anxious if they find they have a gene alteration because of the uncertainty of when and if cancer will develop.
- An individual's test result can have an impact on other family members and might lead to strained relationships within the family.
- While insurance companies will often cover the cost of genetic testing, the test can be quite expensive if an individual is responsible for covering all or part of the cost of testing.

Another concern for some individuals is the possibility of genetic discrimination. Genetic discrimination is the misuse of genetic information (genetic test results, for example) by employers, health insurers, life insurers and disability insurers. To date, there have been no documented cases of individuals suffering from genetic discrimination due to hereditary cancer syndrome genetic testing in terms of health insurance. There are federal laws that provide protection against genetic discrimination in heath insurance and employment. Unfortunately, these laws do not yet protect against genetic discrimination in life insurance, disability insurance, or long-term care insurance.

**If you are interested in scheduling an appointment to discuss this information with a genetic counselor at Lahey Clinic, please call 781-744-3982.**