

## Hereditary Breast Cancer

Most people develop breast cancer due to chance or as a result of multiple risk factors that occur over the course of a lifetime. Risk factors for breast cancer include increasing age, hormonal factors (early age at first menstrual period, later age at first live birth, and menopause), prolonged use of hormone replacement therapy after menopause, increased alcohol intake, obesity, low physical activity, family history, and others. However, approximately five to 10 percent of people who are diagnosed with breast cancer develop it due to a hereditary breast cancer syndrome (HBC). HBC is an inherited increased risk to develop breast cancer and possibly other cancers. Inherited conditions can be passed to an individual from one or both of their parents. People who have an HBC gene mutation are at an increased risk to develop breast and possibly other cancers compared to the general population.

### What Causes Hereditary Breast Cancer?

HBC is caused by an inherited change, called a mutation, in a gene. Genes are the set of instructions that tell all of the cells in our bodies what to do. Genes determine physical characteristics, such as our hair and eye color, the shape of our nose, and our blood type. A mutation is a change in a gene that causes it to stop working. In the case of HBC, a gene that normally helps to prevent cancer has stopped working. Therefore, certain types of cancer are more likely to develop and are also more likely to occur at a younger age than usual.

The majority of HBC is due to a mutation in either the BRCA1 or BRCA2 genes. A person who has a BRCA1 or BRCA2 mutation has “Hereditary Breast and Ovarian Cancer” syndrome and thus has an increased risk for breast, ovarian, prostate, male breast, pancreatic, skin (melanoma), and other cancers. There are also a number of other genes associated with HBC. Some of these genes, like BRCA1 and BRCA2, greatly increase breast cancer risk. Other genes only moderately increase breast cancer risk or are not well studied so that the level of increased breast cancer risk is not yet known.

Hereditary breast cancer genes		
High risk	Moderate risk	Potential increased risk
<i>BRCA1</i>	<i>ATM</i>	<i>BRIP1</i>
<i>BRCA2</i>	<i>BARD1</i>	<i>MLH1</i>
<i>CDH1</i>	<i>CHEK2</i>	<i>MSH2/EPCAM</i>
<i>PALB2</i>	<i>NF1</i>	<i>MSH6</i>
<i>PTEN</i>	<i>RAD51C</i>	<i>PMS2</i>
<i>STK11</i>	<i>RAD51D</i>	
<i>TP53</i>		

## How Is Hereditary Breast Cancer Passed On Through A Family?

Each person inherits two copies of most genes: one from their mother and one from their father. Inheriting a mutation in just one copy of a hereditary breast cancer syndrome (HBC) gene increases the risks for breast and possibly also other types of cancer. There is a 50 percent chance that a person with an HBC gene mutation will pass it to each of his or her children. However, if a person does not inherit the HBC gene mutation present in his or her family member(s), that person is usually at general population risk to develop breast cancer.

## Why Is It Important To Diagnose Hereditary Breast Cancer In A Family?

For someone who already has been diagnosed with breast cancer, an HBC diagnosis may indicate a higher risk of developing another cancer, including another breast cancer. Therefore, diagnosing HBC may impact treatment and management options.

Because HBC is inherited, the diagnosis also affects family members. If genetic testing identifies the specific mutation causing the increased risk for breast cancer in a family, then other family members can be tested for that same genetic mutation.

It is very important for people with HBC to consider specialized cancer screening. Cancer screening may help identify cancers at their earlier, more treatable stages. There may also be medical options that can lower the risk of developing cancer. Usually, a team of specialists will tailor a cancer screening and risk reduction plan to each patient and his or her family members.

## How Is Hereditary Breast Cancer Diagnosed?

A genetics evaluation includes a review of a person's medical and family history. A multi-generation family tree, called a pedigree, is often drawn during the evaluation. This information is used to determine the likelihood that the person has HBC. A genetic counselor usually conducts this evaluation. Some signs that suggest breast cancer may run in a family include:

- Close relatives with breast, ovarian, pancreatic, prostate, or other related cancers.
- Pre-menopausal breast cancer.
- Triple negative breast cancer.
- Multiple related cancers in an individual, such as breast and ovarian cancer.
- Male breast cancer.
- Ashkenazi Jewish ancestry.

## Genetic Testing

A person's blood or saliva sample can be tested to search for a genetic mutation that causes HBC. In general, there are three types of results:

- **Positive for a mutation.** If a mutation is found, then the diagnosis of HBC is confirmed. Next, other family members may have a genetic test to learn whether or not they carry the same mutation and have the same hereditary breast cancer syndrome.
- **Negative for a mutation.** The cancer in the family may not be hereditary. However, a negative genetic test result does not eliminate the possibility of HBC in the family, as current genetic testing technology is not able to identify all mutations that cause HBC. It is also possible that the HBC is being caused by a gene that was not included in the test.

- **Variant of unknown significance.** A variant is a genetic change that does not provide clear information regarding cancer risks. A variant may represent benign genetic differences from one person to the next or may actually represent a true genetic mutation. Until more information regarding the variant is collected by researchers, it remains unknown whether a genetic variant increases cancer risk. Thus, a variant result should not be used to make medical decisions.

If you are concerned about the possibility of a hereditary cancer syndrome in your family, you are encouraged to discuss your personal and/or family history with your health care provider. Your physician may refer you to the Cancer Genetics Program at MD Anderson Cancer at Cooper for genetic evaluation and discussion of your genetic testing options. If genetic testing is warranted and you choose to proceed, a blood or possibly saliva sample will be taken during your visit to the Cancer Genetics Program to start the genetic testing process. Please note that health insurance companies may cover most if not all of the cost of genetic testing.

### **Where Can I Find More Information?**

#### **Hereditary Breast and Ovarian Cancer**

FORCE is a nonprofit organization for women who are at high risk of developing breast and/or ovarian cancer due to their family history and genetic status and for members of families in which a BRCA mutation may be present. Check out the “Resource Guide”, “Message Board”, and “Chat” sections. Visit [www.facingourrisk.org](http://www.facingourrisk.org).

Be Bright Pink is a national non-profit organization that provides education and support to young women who are at high risk for breast and ovarian cancer. Visit [www.bebrightpink.com](http://www.bebrightpink.com).

The Basser Center for BRCA is the first comprehensive center for the research, treatment, and prevention of BRCA-related cancers. Visit [www.basser.org](http://www.basser.org).

#### **Breast and Ovarian Cancer**

National Ovarian Cancer Coalition’s (NOCC) mission is to raise awareness and to promote education about ovarian cancer. The coalition strives to improve the quality of life for ovarian cancer survivors. The site includes sections on detection, treatment, coping, surviving, and more. Visit [www.ovarian.org](http://www.ovarian.org).

Susan G. Komen Breast Cancer Foundation and the “Komen Facts for Life” features a section on genetics and breast cancer. Check out “Komen Connection, ABCs of Breast Cancer, and Resources and References.” Visit [www.breastcancerinfo.com](http://www.breastcancerinfo.com).

The Young Survival Coalition (YSC) is dedicated to the critical issues unique to young women and breast cancer. YSC works with survivors, caregivers, and the medical, research, advocacy, and legislative communities to increase the quality of life for women diagnosed with breast cancer ages 40 and under. Visit [www.youngsurvival.org](http://www.youngsurvival.org).

#### **General Cancer and Genetics**

National Cancer Institute has valuable cancer related health information on more than 200 cancer types, clinical trials, cancer statistics, prevention, screening, risk factors, genetics, and support resources. Information is available in Spanish. Visit [www.cancer.gov](http://www.cancer.gov).

American Cancer Society (ACS) is a voluntary national health organization that supports research, provides information about cancer, and offers many programs and services to patients and their families. Information is available in Spanish. Visit [www.cancer.org](http://www.cancer.org).

Genetic Alliance, Inc., supports individuals with genetic conditions and their families, educates the public, and advocates for consumer-informed public policies. This site provides information on genetic policy, research, and a helpline for people with genetic questions. Visit [www.geneticalliance.org](http://www.geneticalliance.org).