The Facts

• Breast cancer affects 1 in 8 women in the United States. Hereditary breast cancer accounts for approximately 5-10% of these breast cancers. Most cases of breast cancer are sporadic.
• Ovarian cancer affects about 1 in 70 women. Hereditary ovarian cancer accounts for 10-15% of these cases. Most cases of ovarian cancer are sporadic.
• A large proportion of hereditary breast and ovarian cancers have been shown to harbor mutations in the BRCA genes.
• Individuals of Ashkenazi Jewish (Eastern European Jewish) descent have a significant risk to have a mutation in the BRCA genes.

What is the BRCA Gene?

We have about 10,000 – 20,000 genes in every cell of our body. We have two copies of each gene, one inherited from our mother and the other inherited from our father.

Each gene in our body has a unique function or job. BRCA1 and BRCA2 are examples of two genes. They both have the same “job” -- to protect our bodies from cancer. Therefore, if someone has a mutation or mistake in either BRCA gene, then that gene does not work properly and that individual would have a higher-than-average risk to develop cancer. If an individual develops breast or ovarian cancer because she/he has a mutation in the BRCA1 or BRCA2 gene, the name of this condition is Hereditary Breast and Ovarian Cancer (HBOC). Individuals with a BRCA mutation are commonly referred to as “BRCA carriers”.

In the general population, the incidence of BRCA1 and BRCA2 mutations is between 1 in 400 and 1 in 800. Individuals of Ashkenazi Jewish descent, however, have a 1 in 40 to 1 in 100, or 1.0% - 2.5%, risk of having a mutation. In other words, Ashkenazi Jews have a higher-than-average risk to be BRCA carriers. The chance to be a BRCA carrier is 1 in 10 for an Ashkenazi Jewish woman who has already had breast cancer.
The Jews of Eastern Europe (“Ashkenazi Jews”) have lived in small insular communities for hundreds of years. Mutations in genes were present in these communities, but were not common. The communities changed over time; there was migration outside, isolation, and a decrease in size. As a result, the mutations that had been rare now became more prevalent, and a higher percentage of the population became carriers. This phenomenon is known as the “founder effect.” There are 3 common BRCA mutations in the Ashkenazi Jewish population due to the founder effect.

How one identifies with their religion does not define their ancestry. An individual does not need to practice Judaism to be considered Jewish. If an individual has at least one grandparent of Ashkenazi Jewish descent, that person is at risk of being a carrier for mutations associated with a Jewish genetic disease.

When someone is found to be a BRCA carrier, there are 2 major implications to consider: his or her own health and the health of the family.

1) Increased Risk for Cancer
   If a woman has a BRCA mutation, she has about a 55-85% risk to develop breast cancer (vs. the general population risk of about 12%). There is also an increased risk to develop a second cancer in the opposite breast. The risk to develop ovarian cancer is about 20-65% (vs. the general risk of about 1.5%).

   In addition to these cancers, BRCA carriers (both females and males) are also at increased risk to develop colon cancer, pancreatic cancer, melanoma. Male BRCA carriers are at increased risk for male breast and prostate cancers. We would expect BRCA carriers to develop cancer at a relatively young age since they are born with one non-working copy of their BRCA gene. Remember that BRCA carriers are increased risk to develop cancer, but there is no guarantee that a carrier will ever get cancer.
2) Risk of Transmitting Mutation to Offspring

BRCA carriers have one working copy of their BRCA gene and one non-working copy. Each time they have a child, there is a 50% chance they will transmit the working BRCA and a 50% chance they will transmit the one with the mutation. Each child of a BRCA carrier, therefore, has a 50% risk of inheriting the mutation. Another way to see it is that if someone is a carrier, each of his or her siblings has a 50% chance of being a carrier since at least one of their parents is a BRCA carrier. This pattern of inheritance is called autosomal dominant.

Males Can Be BRCA Carriers Too!

While women BRCA carriers have a heightened risk for breast and ovarian cancers, there are also potential implications for male carriers. Male BRCA carriers have up to a 10% risk of developing breast cancer and have an increased risk for developing pancreatic and prostate cancer. Annual checkups with a primary care physician is recommended for male carriers. Most males who are BRCA carriers will not develop cancer, but they still have the same 50% risk as a female carrier to transmit the mutation to their offspring. A male whose parent is a known carrier is encouraged to consider BRCA testing in part so that his children will know if they are at risk of being carriers as well.

How to Get Tested

BRCA testing involves a simple blood draw or saliva sampling. The sample is sent to a lab that looks for mutations in both BRCA1 and BRCA2. For individuals of Ashkenazi Jewish descent, there is a test that looks for the three common founder mutations only. About 90% of Ashkenazi BRCA carriers will have one of these three mutations. If someone is suspected to be a BRCA carrier and he or she does not have one of these common mutations, the genetic counselor may order a more comprehensive genetic test to look for different mutations.

If you are found to carry a BRCA1 or BRCA2 gene mutation, this means that you are at increased risk of cancer and will have to make decisions about how you would like to manage this increased risk of cancer. The level of risk will depend on a number of different factors (age, personal medical history, etc.). Carriers are advised to have a personalized genetic counseling appointment to discuss their risks, management and any necessary referrals.
However, we know it’s not all about the BRCA genes only. We have about 10,000 genes in the body, some of which protect us from cancer. We know that these “modifier genes” play a role in curbing the development of cancer, as well as other non-genetic and environmental factors. It may be more than just BRCA. For an Ashkenazi Jewish woman with no personal or family history of cancer, finding a BRCA mutation may indicate higher cancer risks, however, due to all of these other genetic and non-genetic factors, those cancer risks may not be as high as it is for women with a personal or family history of cancer.

If a BRCA mutation is identified through genetic testing, additional genetic testing may become available in the future which may help clarify cancer risks. At this time, however, we cannot personalize your risk to develop cancer. Please be in touch with us to stay updated on new developments in this realm.

Preventative Measures for BRCA Carriers

Once a woman has been identified as being a BRCA carrier, there are measures she can take to reduce her risk of developing cancer or to detect cancer at an earlier, more treatable stage:

1) **Increased surveillance:** It is recommended that female BRCA carriers be vigilant in their screening for breast cancer. Frequent monitoring for breast cancer includes: breast self awareness starting at age 18, annual or semi-annual clinical breast exams starting at age 25, annual mammography and breast MRI or ultrasound (depending on doctor’s recommendations) starting at age 25. Monitoring for ovarian cancer includes: annual or semi-annual transvaginal ultrasound, annual or semi-annual CA-125 blood test, and annual pelvic exams. Clinical decisions concerning surveillance may differ from woman to woman and consultation with a physician is encouraged.

2) **Prophylactic surgery:** A woman who is a carrier will be counseled about the option of having both of her breasts removed (mastectomy). This reduces her risk to develop breast cancer by up to 95%. Another risk-reducing surgery is the removal of the ovaries and fallopian tubes (bilateral salpingo-oophorectomy). This outpatient procedure would reduce her risk to develop ovarian cancer by 97-98%, and for breast cancer by about 50%. If a woman opts to have her ovaries removed, she will essentially be putting herself into menopause. For this reason, oophorectomy is recommended only once a woman is
done with child-bearing. The decision to have a mastectomy and/or oophorectomy is very personal one. A woman may decide to make this decision with the help of her physician, family, and spiritual leader.

3) **Preventative drug therapies:** Research has shown that certain medications have been implicated in reducing the incidence of breast and ovarian cancer in *BRCA* carriers. Tamoxifen, for example, has been proven to reduce the risk of breast cancer for women with *BRCA* mutations by more than half. In addition, oral contraceptive pills can reduce the risk of ovarian cancer in women with *BRCA* mutations by up to 60%.

**Important information regarding life insurance coverage for BRCA carriers**

It is important to be aware of potential non-medical implications of a genetic testing result. In 2008, Congress passed the Genetic Information Nondiscrimination Act (GINA). GINA was created to remove barriers to the appropriate use of genetic services by the public. It was designed to prohibit the improper use of genetic information in health insurance and employment. Since it was enacted, group health plans and health insurers are prohibited from denying coverage to a healthy individual or charging that person higher premiums based solely on a genetic predisposition to developing a disease in the future. The legislation also bars employers from using individuals' genetic information when making hiring, firing, job placement, or promotion decisions. GINA does not protect against insurance discrimination in the area of long term care insurance or life insurance. Genetic testing should not affect any insurance policies you already have in place. Also, if your test is normal this should have no effect on your current or future insurance policies.