

Risk Assessment of Breast and Ovarian Cancer

Breast cancer is a common disease affecting more than 180,000 women and 1,600 men each year. A woman's lifetime risk for developing breast cancer is about 1 in 8 or 12%. Common symptoms of breast cancer include an abnormal mammogram; detection of a lump, thickening, swelling, or tenderness in the breast; skin irritation or dimpling; nipple pain, scaliness, or retraction.

Ovarian cancer is diagnosed in approximately 22,000 women each year in the United States. The lifetime risk for ovarian cancer is 1 in 70 or 1.4%. The ovaries are located deep inside a woman's pelvic region and often times when cancer develops there are no symptoms in the early stages. Possible symptoms include bloating, loss of appetite, gas, indigestion, nausea, unexplained weight loss or feeling of fullness after a light meal. It is important to remember that only a small percentage of ovarian cancer cases are due to an underlying genetic cause. However, women with a family history of ovarian cancer may be at increased risk of breast cancer.

Because breast cancer is common, many women will have one, two or even more relatives with breast cancer just by chance. It is also possible for the cancer to be caused by an inherited genetic alteration in one of the genes for breast and ovarian cancer. These genes are known as ***BRCA1*** and ***BRCA2*** (for the first and second breast cancer genes to be identified). Individuals who have a genetic alteration in one of these genes will have a significant increase in their risk for breast and ovarian cancers. Only 5-10% of all breast and ovarian cancer is thought to be inherited.

The Genetics of Breast/Ovarian Cancer

We receive our genetic information from both of our parents. The genetic information tells our body how to grow and function. The individual pieces of genetic information are called genes. Each person has two copies of about 100,000 genes. Sometimes a change occurs in a gene which stops the gene from working properly. Such a change is called a "mutation" or "alteration". We know that some genes function to protect our body from developing cancer. If a person has a mutation in a cancer-protection gene, that gene does not work properly and the person has a higher chance of developing cancer. This is genetic susceptibility to cancer. If an individual has a genetic alteration that results in an increased susceptibility to cancer, they will have a 50% chance to pass this genetic alteration on to each of their children. This alteration can be passed down from the maternal or the paternal side of the family. Women with an alteration in ***BRCA1*** have an increased susceptibility to develop breast and/or ovarian cancer and men have an increased susceptibility for developing prostate cancer. Women with an alteration in ***BRCA2*** have an increased susceptibility to develop breast and/or ovarian cancer and men have an increased susceptibility for developing breast and/or prostate cancer.

Ashkenazi Jewish Ancestry

Alterations in ***BRCA1*** and ***BRCA2*** have been found in all races and ethnic groups but, in some populations, specifically the eastern European (Ashkenazi) Jewish population, mutations in these genes are more common. Individuals of Ashkenazi Jewish ancestry with one or more relatives with early onset breast cancer or with ovarian cancer at any age may be appropriate for

genetic testing. It has been estimated that approximately 1 in 40 (2.4%) individuals who are of Eastern European Jewish descent carry one of three alterations. Individuals who test negative for these three common genetic alterations may proceed to have full gene sequencing.

Researchers are now beginning to identify other common genetic alterations in the *BRCA1* and *BRCA2* genes in other ethnic populations such as Iceland, The Netherlands, Belgium, Finland, Sweden, South Africa, and France.

Characteristics of Hereditary Breast/Ovarian Cancer

Personal or family history of the following:

- Pre-menopausal breast cancer with or without ovarian cancer
- Breast cancer in both breasts (bilateral)
- Ovarian cancer at any age
- Breast and ovarian cancer in the same individual
- Breast cancer in a male
- Genetic alteration identified in *BRCA1* or *BRCA2*

Cancer Risk Assessment

Cancer risk assessment provides information about cancer risk, cancer screening, and genetic testing that is based on family and medical history evaluation. Genetic counselors, medical geneticists, and medical oncologists help individuals and their families understand how certain cancers cluster in families and what preventative measures are available to lessen the risk to individuals. The cancer risk team will help individuals and families explore the risks, benefits, and limitations of current genetic testing methods and will help determine whether a family is appropriate for genetic testing. Genetic testing, and the results that it provides, may alter your personal surveillance strategy and modify the risk for other family members to develop of cancer. When your cancer risk appointment is completed, you will receive a letter detailing appropriate cancer surveillance and prevention strategies. Genetic counseling and cancer risk assessment can be of benefit to anyone with concerns regarding their risk for developing cancer even if they do not desire to pursue genetic testing.

What to Expect During an Appointment for Cancer Risk Assessment

The risk assessment team will provide an estimation of a person's risks for specific cancers based upon age, family history, and other risk factors. It is important to provide the cancer risk team with accurate family history information including the types of cancers in your family and the ages at which they occurred. It is helpful to obtain medical records and death certificates whenever possibly in order to verify each cancer diagnosis. The cancer risk team will discuss the possible role of genetics in a person's family, the emotional issues regarding the risks of cancer, cancer screening and cancer risk reduction recommendations, and the availability of genetic testing for certain cancers. It may also be possible to have a physical examination by a clinical oncologist or gynecologist during your visit. While anyone can benefit from cancer risk assessment, it may be especially helpful for individuals who have 1) a parent or sibling with cancer, 2) relatives with breast and other cancers with early ages of occurrence, 3) multiple first or second-degree relatives with breast or ovarian cancer, 4) relatives with a genetic alteration in a *BRCA* gene, 5) male breast cancer in the family, or 6) anxiety about breast cancer in general.

Genetic Testing

Genetic testing to determine if an individual or family has a breast cancer gene alteration is offered to appropriate families following cancer risk assessment. Currently, genetic testing is available for *BRCA1* and *BRCA2* mutations. Mutation testing is most informative when performed on a family member who has had cancer. If a mutation is identified in that individual, this will assist with their cancer management. Once a mutation is identified in a family, other family members can be tested for that specific mutation. Traditionally, the consideration of genetic testing takes place in a multi-step format. We usually require that the individual considering testing have a complete educational session with a genetic counselor. At this appointment, the risks, benefits, and limitations of genetic testing are reviewed extensively. It is important that individuals being tested understand the value of the information that testing provides, how it will affect future surveillance for them and other family members, and the impact that this information may have on themselves and their children. After taking some time to think about the option of genetic testing, this individual can schedule a second appointment and return to the clinic to ask additional questions and have blood drawn. The results of testing typically take between 4 to 6 weeks, at which time a third appointment is scheduled to review these results.

If an alteration in the *BRCA1* and *BRCA2* genes is not identified, it is possible that a different cancer susceptibility gene is responsible for the cancer in the family. Options for cancer prevention and surveillance would be based on the genetic risk assessment.

Management Options for Patients at Moderate-to-High Risk for Breast and/or Ovarian Cancer

Cancer surveillance recommendations and strategies will be made based upon the outcome of a patient's cancer risk assessment appointment. For women who are *BRCA1* or *BRCA2* mutation carriers, the current management options are increased screening and prophylactic (preventative) surgery. Breast screening options include: monthly self-breast exams, breast exams annually or semiannually by a specialist, annual or semiannual mammography. Ovarian screening options include: annual pelvic exams, transvaginal ultrasound and CA-125 blood test. Preventative surgery options should be discussed with specialists. Additionally, a chemoprevention agent called Tamoxifen has been approved for use in women at increased risk for breast cancer. The risks and benefits of taking Tamoxifen should also be discussed with a specialist. There may also be clinical trials that eligible patients can enroll in to test treatments that may reduce their risk for breast or ovarian cancer.

Other Issues

Many people are concerned that genetic testing may be used by employers or insurance companies to discriminate against those at increased risk for cancer. Legislation exists to protect individuals in large group health insurance plans, but this has not been sufficiently tested in court. Furthermore, life and disability insurance policies are not protected. Many individuals choose not to inform their insurance companies about the testing and choose to pay for testing out of pocket. This is an important issue that can be discussed with the cancer risk assessment team. There is no reason to be concerned about insurance discrimination following a genetic counseling/cancer risk assessment appointment. Individuals seek genetic counseling for a multitude of reasons and counseling has not been known to adversely affect insurability.

Confidentiality is, of course, of paramount importance in cancer risk assessment. Most risk evaluation programs have careful safeguards to help ensure that family and medical history information, as well as genetic testing results, are not released to anyone without written consent from the individual concerned.

For more information or to schedule an appointment, please contact:

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