

## **Genetic Testing for BRCA1 and BRCA2: Information for Texas Health Care Professionals**

### **How common are BRCA1 and BRCA2 mutations in the general population?**

Inherited mutations in BRCA1 and BRCA2 are relatively uncommon in the general population. The carrier frequency is estimated to range from 1 in 300 to 1 in 800.<sup>1,3</sup> Certain ethnic groups have been shown to have a higher carrier frequency (i.e., 1 in 40 for individuals of Ashkenazi Jewish descent).

### **What percentage of breast and ovarian cancer cases are estimated to be caused by BRCA1 and BRCA2 mutations?**

Five to 10 percent of all breast cancer cases and up to 14 percent of all ovarian cancer cases are thought to be caused by BRCA1 and BRCA2 mutations.<sup>1,2,3,4</sup>

### **Can BRCA1 and BRCA2 mutations be inherited from either side of the family?**

Yes, either parent can pass along a BRCA1 or BRCA2 mutation. Therefore, it is important for clinicians to obtain a complete cancer history on both the maternal and the paternal sides of the family when assessing genetic risk.<sup>4</sup>

### **Which patients should I consider referring to a genetic counselor for risk assessment and to discuss the option of genetic testing for BRCA1 and BRCA2 mutations?**

Most individuals do not have a mutation in the BRCA1 or BRCA2 gene. While specific indications for genetic counseling and testing vary among professional organizations, certain aspects of your patient's personal and/or family history may increase his or her likelihood of carrying a BRCA1 or BRCA2 mutation. The indications below are to be used as a guide and are not a substitute for clinical judgment. Not all clinical scenarios can be anticipated. For instance, genetic testing guidelines may not take into consideration a situation where the family history is limited.<sup>6</sup> In addition; individual insurance companies have their own criteria for reimbursement for genetic testing, which may not match the indications list below.

Indications include<sup>1,2,3,5</sup>:

- A personal history of:
  - Breast cancer at a young age (younger than age 50) or ovarian cancer at any age,
  - Bilateral breast cancer or two or more primary tumors of the breast,
  - Breast and ovarian cancer (in the same individual), or
  - Breast cancer in a male;

AND/OR

- A maternal or paternal family history of:
  - Two or more individuals in the family (parent, child, sibling, grandparent, aunt/uncle) with breast and/or ovarian cancer,
  - One or more close male relatives with breast cancer,
  - Early onset breast or ovarian cancer (before age 50) in a close relative, or
  - Confirmed BRCA1 or BRCA2 mutation.

Note: Individuals who belong to ethnic groups with increased mutation prevalence, such as those of Ashkenazi Jewish descent, may be appropriate candidates for referral even if they have a less striking personal or family history of breast and/or ovarian cancer.

Ideally, the decision to test should start with the patient's family member affected with either breast or ovarian cancer, since this helps determine if the cancer is associated with one of the mutations and makes test interpretation more straightforward.<sup>1,2,3,4</sup>

You may find it helpful to refer to specific genetic testing guidelines published by professional organizations, some of which are listed on the third page of this document.

Genetic testing for breast cancer risk may be complicated by:

- The possibility of false negative results, since other genes and mutations carrying similar cancer risk, but not yet discovered or tested for, may be present;
- The possibility of test results with mutations noted to have “uncertain clinical significance” (some mutations in the BRCA genes may or may not be of clinical significance);
- Cost of BRCA gene testing, which ranges from \$385 (single-site analysis) to \$3,120 (for full sequencing of both genes); or
- The fact that results do not provide an individual patient information regarding if or when or where cancer may develop.<sup>4</sup>

### **What are the advantages and disadvantages of BRCA1 and BRCA2 testing?**

Test advantages:

- Testing may clarify risk of specific cancers.
- Testing may lead to an increased sense of control and decreased stress for the patient.
- For families with a known mutation, a negative test result reduces the patient's risk of breast and ovarian cancer to that of the general population.
- Testing may help patients focus on the medical and lifestyle choices available to them (earlier/increased screening, chemoprevention, surgical options).
- Testing may help inform other family members about their potential risk.
- For cancer patients, a positive test result may decrease feelings of self-blame.
- Patients with a BRCA gene mutation would benefit from prophylactic surgeries.

Test disadvantages:

- Testing may cause a patient to experience stress.
- Testing positive may result in guilt or fear over possibly passing a mutation to children.
- Individuals with a negative test result may think they have no chance of getting cancer and thus forgo appropriate screening tests.

### **What are the benefits of genetic counseling when offering BRCA1 and BRCA 2 testing?**

Patient education and informed consent are critical aspects of the genetic testing process and will help individuals decide if genetic testing is right for them. Pretest counseling, usually done by genetic counselors, addresses the implications of potential test results, medical management, psychosocial aspects, other options for testing, and testing costs. If help is needed, a genetic counselor also can provide assistance with dissemination of relevant information to at-risk family members.

### **What is the risk for breast and ovarian cancer in individuals found to have a BRCA1 or BRCA2 mutation?**

For women with a mutation in either BRCA1 or BRCA2, studies have shown the lifetime risk of breast cancer to range between 50 and 87 percent. The lifetime risk of ovarian cancer has been noted to range between 15 and 44 percent, depending on the specific mutation.<sup>1</sup>

Men with a BRCA mutation have a 5- to 10-percent lifetime risk of developing breast cancer. Men without such mutations have a 0.1 percent lifetime risk.<sup>1</sup>

### **How can I find a genetic counselor in my area for my patients?**

Genetic counselors are master's-trained individuals who are board certified by the American Board of Genetic Counselors. You can locate a genetic counselor or genetic nurse in your area from the following organizations:

- National Society of Genetic Counselors at [www.nsgc.org/](http://www.nsgc.org/) (click on Find a Counselor)
- International Society of Nurses in Genetics at (412) 344-1414 or [www.isong.org/](http://www.isong.org/)
- National Cancer Institute at (800) 4-CANCER (Cancer Information Service) or [http://www.cancer.gov/search/genetics\\_services/](http://www.cancer.gov/search/genetics_services/) (Cancer Genetics Service Directory)
- Texas Society of Genetic Counselors at [www.tsgc.org](http://www.tsgc.org) (Find a Genetic Counselor currently under construction)

### **What is GINA — Genetic Information Nondiscrimination Act?**

GINA is a new federal law passed by President George Bush in May 2008 that provides patients additional protection against genetic discrimination in regards to health insurance and employment. Other Texas and federal laws provide this protection as well. GINA paves the way for people to take advantage of the promise of personalized medicine without fear of

discrimination. However, currently no state or federal legislation protects against genetic discrimination in life insurance and disability insurance.

## FOR MORE INFORMATION

### BRCA1 and BRCA2 testing and risk management guidelines:

- National Comprehensive Cancer Network — *Genetic/Familial High-Risk Assessment: Breast and Ovarian* at [www.nccn.org/professionals/physician\\_gls/PDF/genetics\\_screening.pdf](http://www.nccn.org/professionals/physician_gls/PDF/genetics_screening.pdf). (These guidelines also contain information on managing patients found positive for BRCA1 or BRCA2.)
- U.S. Preventive Services Task Force — Genetic Risk Assessment and *BRCA* Mutation Testing for Breast and Ovarian Cancer Susceptibility at [www.ahrq.gov/clinic/uspstf/uspstfbrgen.htm](http://www.ahrq.gov/clinic/uspstf/uspstfbrgen.htm)
- National Cancer Institute — Genetics of Breast and Ovarian Cancer (PDQ®) at [www.cancer.gov/cancertopics/pdq/genetics/breast-and-ovarian/healthprofessional](http://www.cancer.gov/cancertopics/pdq/genetics/breast-and-ovarian/healthprofessional)

### About genetic testing for breast and ovarian cancer risk:

- National Cancer Institute fact sheets —
  - Genetic Breast and Ovarian Cancer Risk: It's Your Choice at [www.cancer.gov/cancertopics/Genetic-Testing-for-Breast-and-Ovarian-Cancer-Risk](http://www.cancer.gov/cancertopics/Genetic-Testing-for-Breast-and-Ovarian-Cancer-Risk)
  - Genetic Testing for BRCA1 and BRCA2: It's Your Choice at [www.cancer.gov/cancertopics/factsheet/Risk/BRCA](http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA)
- Centers for Disease Control and Prevention, National Office of Public Health Genomics, at [www.cdc.gov/genomics/training/perspectives/factshts/breastcancer.htm](http://www.cdc.gov/genomics/training/perspectives/factshts/breastcancer.htm).
- National Institute of Health — Genetics Through a Primary Care Lens (a Web-based resource for faculty development) at [www.genetests.org](http://www.genetests.org). (Click on “Genetic Tools” in the right-hand tool bar.)

### References:

1. Berliner JL et al (2007). Risk Assessment and Genetic Counseling for Hereditary Breast and Ovarian Cancer: Recommendations of the National Society of Genetic Counselors. *Journal of Genetic Counseling*, 16:241-260.
2. Centers for Disease Control and Prevention. *Fact Sheet on Genetic Testing for Breast and Ovarian Cancer Susceptibility*. Located July 5, 2007, at [www.cdc.gov/genomics/training/perspectives/factshts/breastcancer.htm](http://www.cdc.gov/genomics/training/perspectives/factshts/breastcancer.htm).
3. National Cancer Institute. *Genetic Testing for BRCA 1 and BRCA 2: It's Your Choice*. Located June 11, 2007, at [www.cancer.gov/cancertopics/factsheet/Risk/BRCA/print?page=&keyword](http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA/print?page=&keyword).
4. Pinsky LE et al (2001). Why Should Primary Care Physicians Know About Breast Cancer Genetics? *Western Journal of Medicine*, 175:168-173.
5. Guidelines listed in above resource list.
6. Weitzel JN et al (2007). Limited Family Structure and BRCA Gene Mutation Status in Single Cases of Breast Cancer. *JAMA*, 297(23):2587-2695.