

When the Patient Asks

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Q: Should I be tested for the *BRCA* gene?

According to current estimates for the year 2009, 192,370 women and 1,910 men will develop breast cancer,¹ and 21,550 women will develop ovarian cancer.² *BRCA1* and *BRCA2* gene mutations are responsible for 5% to 10% of these cancers.^{3,5}

▶ ABOUT *BRCA1* AND *BRCA2*

Everyone has the *BRCA1* and *BRCA2* genes. A mutation in either gene increases the risk of certain cancers. In women, a mutated *BRCA* increases the risk of breast and ovarian cancer.³ In men, a *BRCA* mutation increases the risk of breast and prostate cancer.³ Although much less common, mutations in *BRCA2* may increase a patient's risk of lymphoma, melanoma, and cancers of the pancreas, gallbladder, bile duct, and stomach.^{3,4,6} A mutated gene is autosomal dominant and may be inherited from the patient's mother or father.^{3,5,7}

In the general population, 12% of women are likely to develop breast cancer and 1.4% of women will develop ovarian cancer.³ If a woman has a *BRCA* mutation, her risk of breast cancer is five times that of a woman without the mutation, or 60%, and the risk of ovarian cancer in a woman with the mutated gene is 15% to 40%.³

▶ GROUPS AT HIGH RISK

Certain ethnic groups, such as people of Ashkenazi Jewish, Norwegian, Dutch, French Canadian, or Icelandic descent, have a higher predisposition toward cancers caused by a *BRCA* gene mutation.^{3,4,7,8} Patients with a strong family history of certain cancers are also likely to be carriers of *BRCA1* or *BRCA2* mutations and should be tested.^{5,7,8}

- These groups include those with a
- Personal history of breast cancer before age 50
- Personal history of two primary breast cancers

- Personal history of both breast and ovarian cancer
- Family history of a male breast cancer
- Family history of breast cancer before age 50
- Family history of breast or ovarian cancer in more than one relative
- Family history of both breast and ovarian cancer in one relative
- Known *BRCA1* or *BRCA2* mutation in the family.

▶ TESTING FOR A *BRCA* MUTATION

If a patient wishing to be tested for a *BRCA* mutation has a family history (as opposed to a personal history) of cancer, the sensible approach is to first test the relative who has been diagnosed with breast or ovarian cancer.^{4,7} The cost of testing is typically covered by health insurance for patients with known or approved risk factors. If insurance does not cover the cost of the test or the patient does not have the appropriate risk factors, the out-of-pocket expenditure can be as much as a few thousand dollars.

▶ MANAGEMENT OF *BRCA* CARRIERS

In women with a *BRCA* mutation, prophylactic mastectomy reduces the risk of breast cancer by 90%, and prophylactic salpingo-oophorectomy reduces the risk of ovarian and breast cancer by 90% and 50%, respectively.⁸ For women who choose not to undergo these procedures, close follow-up is recommended. Mammography and/or breast MRI should be done every 6 to 12 months, a clinical breast examination should be performed every 6 months, and breast self-exams should be done monthly (to detect breast cancer as early as possible).^{3,7,8} There is controversy regarding the use and effectiveness of tamoxifen (Nolvadex, generics) and raloxifene

(Evista) in the prevention of *BRCA*-related breast cancer.^{3,8} Surveillance for ovarian cancer includes an annual or biannual clinical examination, transvaginal ultrasonography, and measurement of cancer antigen (CA) 125.^{3,7,8}

Men with *BRCA* gene mutations should also be followed more closely. Prostate cancer screening should begin between ages 40 and 50 and includes a prostate examination and PSA determinations.⁴ Because these men are also at an increased risk of developing breast cancer, clinical examinations and mammography should be performed.⁴

A patient with a negative *BRCA* result on testing has the same risk for developing cancer as the general population.^{3,7,8} JAPPA

Jill Gore is a PA with Cancer Care Centers of South Texas in San Antonio. She has indicated no relationships to disclose relating to the content of this article.

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Patient Information

Q: Should I be tested for the *BRCA* gene?

Breast cancer is the most common cancer among women, while ovarian cancer is less common. Genetic alterations, known as *mutations*, are responsible for 5% to 10% of breast and ovarian cancer. The mutations most commonly related to breast and ovarian cancer occur on the *BRCA1* and *BRCA2* genes. Women who have a mutated *BRCA1* or *BRCA2* gene have an increased risk of developing breast and ovarian cancer. Men with a mutation have an increased risk of developing breast and prostate cancer.

▶HOW ARE THE *BRCA* MUTATIONS INHERITED?

BRCA1 and *BRCA2* mutations are inherited from an affected parent. Each person has a 50% chance of inheriting a mutated gene from that parent. Therefore, if neither of your parents is known to have a mutated *BRCA* gene, the likelihood that you will have a gene mutation that increases your risk for breast or ovarian cancer is very low.

▶ARE OTHER CANCERS LINKED TO *BRCA1* AND *BRCA2* GENE MUTATIONS?

Besides the increased risk of cancers associated with mutations in either the *BRCA1* or the *BRCA2* gene, a *BRCA2* mutation can also, but less commonly, be associated with lymphoma, melanoma, pancreatic cancer, bile duct cancer, and stomach cancer.

▶ARE ANY GROUPS OF PEOPLE MORE LIKELY TO HAVE A *BRCA* MUTATION?

Yes. Factors that contribute to increased risk of a *BRCA* mutation include

- A personal history of breast cancer diagnosed before age 50 years, breast cancer affecting both breasts, or breast and ovarian cancer
- Two or more close family members (grandparents, parents, siblings,

and/or children) who were diagnosed with breast cancer before age 50 years

- A male relative with breast cancer
- A close family member who has had both breast and ovarian cancer or breast cancer in both breasts
- A close family member who has tested positive for a *BRCA1* or *BRCA2* gene mutation
- A close family member who is of Ashkenazi Jewish ancestry or Dutch, Norwegian, Icelandic, or French Canadian heritage and has a known *BRCA* gene mutation.

If any of the above factors describes you, then you may be at increased risk of having inherited a *BRCA* mutation and developing certain cancers. Talk to your health care provider to determine if you qualify for testing.

▶HOW IS TESTING DONE?

A blood sample is sent to a laboratory. Results are usually available within a few weeks. No breast or ovarian tissue is needed to detect a mutation. If more than one family member wants to be tested, the person who is known to have (or who has had) cancer should be tested first. If this person is no longer alive, then his or her closest living relative should be tested first.

▶WHAT DO THE TEST RESULTS MEAN?

A negative result means that no *BRCA* mutation was found and that you are not at increased risk of developing any of the cancers associated with such a mutation. This does not mean that you will never develop cancer, but your risk of getting cancer is the same as that of the general population.

A positive test result means that a mutation in the *BRCA1* and/or the *BRCA2* gene has been detected and you have an increased risk of developing certain cancers, including breast and ovarian can-

cer. The test does not mean that you will definitely develop one of these cancers, nor can it determine at what age you might develop them.

▶WHAT IF MY TEST RESULT IS POSITIVE?

Women whose test results are positive are advised to have more frequent screening, including breast examinations every 6 months and mammograms every year, and to do breast self-examinations every month to detect breast cancer early. Screening measures for ovarian cancer in women with a known *BRCA* mutation include a pelvic examination; transvaginal ultrasonography; and a blood test every 6 to 12 months for a substance known as CA 125, which is released by cancer cells. Your health care provider may give you a medication called tamoxifen (Nolvadex) or raloxifene (Evista), which may help to reduce the risk of developing breast cancer. Another option for women is to undergo surgery to remove the breast (mastectomy) and ovarian tissue (oophorectomy). Removing the tissue that may become cancerous is likely to provide the greatest success in reducing the risk of breast or ovarian cancer. However, surgery does not guarantee prevention.

Men who test positive for a *BRCA* mutation should also undergo more regular screenings. This includes a yearly prostate examination and measurement of a substance produced by the prostate (prostate-specific antigen, or PSA), beginning at age 40 years. Men should also have breast examinations and, if possible, mammograms.

Talking to your health care provider about your risk of having a *BRCA1* or *BRCA2* mutation is the best place to start. He or she can help you get tested and make decisions about what to do if you have a positive test result. **JAAPA**

