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Patient information: Genetic testing for breast and ovarian cancer (Beyond the Basics)

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INTRODUCTION

Having a strong family history of breast or ovarian cancer can increase your risk of developing these cancers. A strong family history means that:

- Multiple family members have breast or ovarian cancer, or
- A family member has both breast and ovarian cancer, or
- More than one generation of your family has breast or ovarian cancer

In many instances, women with breast or ovarian cancer were diagnosed before age 50.

Genetic testing can tell if you have inherited an abnormal gene that increases the risk of breast and ovarian cancer. If you test positive for a gene alteration (or mutation), there are things you can do to decrease your risks.

However, genetic testing is not perfect. Most women with breast cancer and/or a family history of breast cancer do **not** have an abnormal gene, and not all women who have inherited one of these genes will develop cancer.

This article will discuss who should consider genetic testing, issues to consider before you have testing, and what you can do after testing to reduce your risk. More detailed information about

genetic testing is available by subscription. (See "Genetic testing for hereditary breast and ovarian cancer syndrome".)

WHAT IS GENETIC TESTING?

Cancer develops because of mutations in one or more genes. Genes hold information about how you look and how your body works, and genes are passed from parents to children. If there is an abnormality in a gene, this is called a genetic mutation.

There are two types of genetic mutations:

- Germline mutations are inherited, passed from parent to child. Between 5 and 10 percent of breast cancers are caused by germline mutations, such as those in BRCA1 and BRCA2. These mutations increase the risk of developing breast and ovarian cancer.

  Most genetic testing for breast and ovarian cancer analyzes these two genes for mutations. The test is done on a mouthwash sample (to obtain cheek cells) or a sample of blood.
- Acquired mutations are not inherited, but instead develop during your lifetime. Acquired mutations can be caused by exposure to environmental agents such as radiation, chemicals (including those found in tobacco smoke), or viruses; they can also develop without a known cause. Most cancers, including breast cancer, are caused by acquired mutations.

WHO SHOULD CONSIDER GENETIC TESTING?

Genetic counseling and testing should be considered for women who have:

- Multiple close family members affected with breast or ovarian cancer, particularly if the relative was diagnosed with cancer at an early age (less than 50 years old). Close family members include your mother, sister, or daughter; close family members can include men with breast cancer.
- A close family member with more than one cancer, such as breast cancer involving both breasts or breast and ovarian cancer
- Multiple generations of close family with cancer (eg, grandmother, mother, sister). Family history on the father's side is as important as the mother's side. It is also important to know the cancer history of your cousins on both sides of your family.
- Other cancers in addition to breast and ovarian cancer in women can be suggestive of hereditary cancer. For example, it is important to know if there are relatives with pancreatic, prostate, colon, or male breast cancer.

BRCA testing should be initiated with an individual who has cancer, whenever possible. Usually this would mean testing a woman with ovarian cancer or breast cancer diagnosed at the youngest age within the family. If a mutation is not found, it is often not helpful to test family members without cancer.

GENETIC TESTING

Pretest counseling — Before you have genetic testing, you must think about the medical, emotional, practical, and financial effects of testing on both you and your family. You should discuss these issues with a certified genetic counselor, if possible, to understand what is involved

in genetic testing. A list of certified genetics counselors and their phone numbers is available through the National Cancer Institute (www.cancer.gov/cancertopics/genetics/directory).

Costs and insurance coverage — Because the BRCA genes are large and include hundreds of different mutations, testing can be expensive. In the United States, most health insurance companies will cover most of the costs. Your doctor or genetic counselor might need to write a letter to explain why testing is needed.

Many people are worried about how the results of genetic testing will affect the chance of getting health or life insurance in the future. In the United States, a federal law known as the Genetic Information Nondiscrimination Act (GINA) prohibits health insurers and employers from using your genetic information. This law is intended to encourage Americans to take advantage of genetic testing if needed. In general, the law means that:

- Employers cannot deny you a job or fire you because of the results of genetic testing.
- Health insurers cannot use genetic testing results to deny you coverage or set your insurance rates.
- Employers and insurers cannot require you to have genetic testing.

The law does not have provisions for disability, life insurance, or long term care insurance. In addition, GINA does not apply to individuals in the military State laws may provide additional coverage.

Posttest counseling — Most doctors and genetic counselors prefer to discuss the results of genetic testing in person. During this meeting, you can discuss your test results, ask questions about what the results mean, and ask what you can do to decrease your risk of cancer.

If you test positive for a BRCA1 or BRCA2 mutation, talk to your family about the results. Some family members will want to talk to their doctor or nurse about having genetic testing.

INTERPRETING THE RESULTS

It is not always easy to interpret the results of genetic tests. The results may be:

- Positive for a BRCA1 or BRCA2 mutation. This means that a mutation was identified that is known to be associated with increased risks for cancer.
- Negative, meaning that you do not have a BRCA mutation. This result does not rule out the possibility that you may have a hereditary risk for cancer. Not every mutation is detected by BRCA testing. In addition, there are many unknown genetic mutations that have not yet been discovered.
- A “true” negative result means that a BRCA1 or BRCA2 mutation present in one or more of your family members was ruled out in you. This result usually means that your cancer risks are about the same as other women in the general population.
- Positive for a genetic mutation with "unknown significance." This means that you have a genetic mutation, but it is not clear if the mutation increases your risk of breast or ovarian cancer.

A negative result does not mean that you will not develop cancer and a positive result does not mean that you will develop cancer.

If you test positive for a BRCA mutation:

- Your lifetime risk of breast cancer is between 55 and 85 percent for BRCA1 and 50 to 85 percent for BRCA2. This means that in a group of 100 women with BRCA1, between 55 and 85 of the women will develop breast cancer in their lifetime.
- The lifetime risk of ovarian cancer is 35 to 46 percent for BRCA1 and 13 to 23 percent for BRCA2 [1]

Test result interpretation can be complex. Sometimes "negative" results are more difficult to interpret than "positive" results. It is important to discuss what test results mean with a genetic counselor and your doctor.

REDUCING YOUR RISK OF CANCER

If you test positive for a BRCA mutation, there are several ways to screen for cancer and to reduce your risk of developing cancer:

- Have more frequent screening for breast and ovarian cancer
- Have surgery to reduce your risk
- Take a medicine to reduce your risk

The best strategy might include a combination of these methods (table 1).

If you test negative for a BRCA mutation but have a strong family history of breast or ovarian cancer, talk to your doctor or nurse about ways to reduce your risk of developing cancer. (See "Management of hereditary breast and ovarian cancer syndrome and patients with BRCA mutations".)

Breast cancer screening — Women who have inherited a BRCA mutation are usually advised to have more frequent screening for breast cancer. This includes:

- A monthly breast self-exam (BSE) beginning at age 18. You should learn how to perform BSE; instructions are provided in the table (table 2).
- A breast exam, performed by your doctor or nurse, every six months beginning at age 25.
- A mammogram once per year, beginning at age 25 (or individualized based on family history).
- A breast MRI, which is typically done alternating with a mammogram every six months, beginning at age 25 or individualized based on family history.

Ovarian cancer screening — Women who have inherited a BRCA mutation have an increased risk of developing ovarian cancer. However, screening tests for ovarian cancer are not very accurate in detecting the disease. (See "Patient information: Ovarian cancer screening (Beyond the Basics)".)

However, ovarian cancer screening is an option if you have a BRCA mutation. Screening includes a combination of a blood test and a pelvic ultrasound. Some experts recommend this combination of tests every six months, beginning at age 35 or 5 to 10 years before the youngest relative was diagnosed with breast or ovarian cancer. (See "Patient information: Ovarian cancer screening (Beyond the Basics)".)

Surgery — An alternative to frequent cancer screening is surgery to reduce the risk of developing cancer. This is called preventive surgery, and it can significantly decrease your risk

of cancer and may help you to feel less anxious. Talk to your doctor about the potential risks and benefits of preventive surgery.

Mastectomy — Women who have both breasts removed (called prophylactic bilateral mastectomy) reduce their chance of developing breast cancer by at least 90 percent.

Removal of the ovaries — Having the ovaries and fallopian tubes removed (termed a prophylactic bilateral salpingo-oophorectomy, or BSO) has been shown to reduce the risk of ovarian and fallopian tube cancer by 80 to 90 percent and breast cancer by 50 to 60 percent (for premenopausal women). The benefits of this surgery are greatest in women who have surgery before menopause, particularly before age 40, after you finish having children. (See "Risk-reducing bilateral salpingo-oophorectomy in women at high risk of epithelial ovarian and fallopian tubal cancer".)

Medicines to reduce the risk of cancer — A medicine called tamoxifen can reduce the risk of breast cancer in women who have BRCA mutations, although the degree of reduction is not clear for women without a history of breast cancer (see "Patient information: Medications for the prevention of breast cancer (Beyond the Basics)"). However, the amount of risk reduction is unclear for women without a history of breast cancer.

Hormonal birth control (pill, skin patch, vaginal ring, shot, implant) can decrease the risk of ovarian cancer. Data suggest that this is also true for women with a BRCA mutation. In addition, there is a concern that hormonal birth control may increase the risk of breast cancer, particularly in BRCA1 mutation carriers. If you have a BRCA mutation, talk to your doctor or nurse about the risks and benefits of hormonal birth control.

WHERE TO GET MORE INFORMATION

Your healthcare provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our web site (www.uptodate.com/patients). Related topics for patients, as well as selected articles written for healthcare professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient information: Genetic testing for breast and ovarian cancer (The Basics)
Patient information: Ovarian cancer (The Basics)
Patient information: Ovarian cancer screening (The Basics)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Patient information: Ovarian cancer screening (Beyond the Basics)
Patient information: Medications for the prevention of breast cancer (Beyond the Basics)

Professional level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

BRCA1 and BRCA2: Prevalence and cancer risks for breast and ovarian cancer
Management of hereditary breast and ovarian cancer syndrome and patients with BRCA mutations
Genetic risk assessment for individuals at risk for hereditary breast and ovarian cancer syndromes

The following organizations also provide reliable health information.

- National Cancer Institute

  (cancer.gov/cancertopics/pdq/genetics/breast-and-ovarian/HealthProfessional)
- American Society of Clinical Oncology

  (www.cancer.net/patient/All+About+Cancer/Genetics/Genetic+Testing)
- Facing Our Risk of Cancer Empowered (FORCE)

  (www.facingourrisk.com)

Literature review current through: Oct 2013. | This topic last updated: Mar 13, 2012.