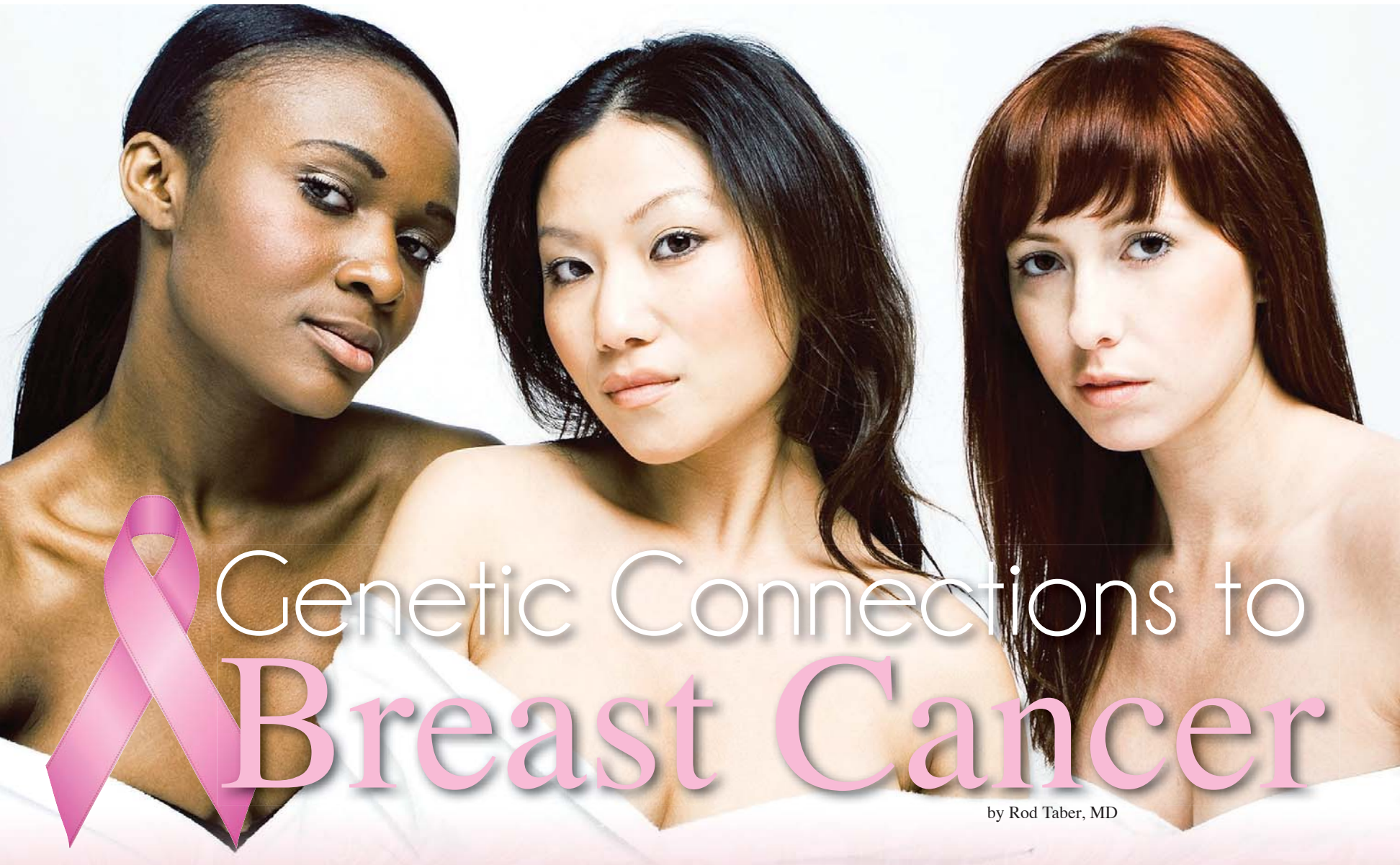

Genetic Connections to Breast Cancer

by Rod Taber, MD

A difficult question asked everyday in a doctor's office that cares for women is, "Should I be tested for the genetic link to breast cancer?" The reason we are asked this question is due to the higher rate of breast cancer we experience in this country, and the strong probability our lives will be touched by someone we know living with the diagnosis. In this article you will find who should consider genetic testing, what testing is available, and who to seek out if testing is positive.

It has been shown that women in the United States face a 10-12 percent lifetime chance of developing breast cancer by the time they reach 90. It is interesting to find that in most studies only 15-20 percent of women with that diagnosis will report a family history of breast cancer. Through gene mapping researchers have determined that only 5 to 6 percent of all breast cancers are associated with an identifiable inherited gene mutation.

Statistical models have been developed by different organizations to aid physicians and their patients to see if they are at a higher risk than the general population for developing breast cancer, and a candidate for genetic testing. One model used is the Breast Cancer Risk Assessment Tool (BCRAT) developed by the National Cancer Institute. When personal information is entered, it gives the woman her risk at her current age, and every five years after up to age 90. This is available at www.cancer.gov/bcrisktool/.

The accompanying tables are other tools developed to determine genetic counseling referral and consideration for BRCA1/2 genetic testing.

With the help from these models and your physician, you determine that genetic testing should be done because you are at high risk, we have at this time only one test that is commercially available. It is called BRCAnalysis by Myrid Genetics Laboratories in Salt Lake City, Utah. The reason this test is not routine is because of the low chance of anyone person having these gene mutations and the high cost- currently over $3000.*

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Recommendations from the United States Preventive Services Task Force on who should be offered genetic testing for BRCA mutations*

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For non-Ashkenazi Jewish women:

- Two first-degree relatives with breast cancer, one of whom was diagnosed at age 50 or younger
- A combination of three or more first or second-degree relatives with breast cancer regardless of age at diagnosis
- A combination of both breast and ovarian cancer among first and second-degree relatives
- A first-degree relative with bilateral breast cancer
- A combination of two or more first or second degree relatives with ovarian cancer, regardless of age at diagnosis
- A first or second-degree relative with both breast and ovarian cancer at any age
- History of breast cancer in a male relative

For women of Ashkenazi Jewish descent:

- Any first-degree relative (or two second degree relatives on the same side of the family) with breast or ovarian cancer

* These recommendations do not apply to women with a family history of breast or ovarian cancer that includes a relative with a known deleterious BRCA mutation.
U.S. Preventive Services Task Force. Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement. Ann Intern Med 2005; 143:355.

Risk of Breast Cancer

	Percent of Population	Percent of all Breast Cancer Cases	Average Risk of Breast Cancer to Age 70
Positive Family History Breast Cancer*	~10	15 to 20	10 to 13 percent•
Positive BRCA1 or 2 Mutation	~0.1	5 to 6	50 to 85 percentΔ
General Population without Positive Family History or BRCA Mutation	~90	80 to 85	7◊ percent

* Breast cancer in a first-degree relative.
• Data from: Colditz G, et al. JAMA 1993; 270:338.
Δ This range represents the range of lifetime risk quoted by genetic specialists.
◊ Data from: the American Cancer Society, Cancer Statistics, 2010. (CA Cancer J Clin 2010; 60:277).

This test identifies BRCA1 and BRCA2 genes that are on our chromosomes. It is currently thought that the normal forms of the BRCA1 and BRCA2 genes function in our bodies to repair DNA that has been broken and possibly help in regulating cell growth. The mutation forms of these two genes are felt to interfere with the repair of DNA in our body, allowing the accumulation of abnormal chromosomes and the loss of control on cellular growth. These two genes with their specific mutations on them that the test can identify are responsible for the majority of inherited breast cancers. They have also identified an increased lifetime risk of ovarian cancer when a women tests positive for one of these two genes.

What if the genetic BRCA blood test is positive? The first thing is to realize it does not mean that you have or will get breast cancer. The positive results for either gene mean that as you age, your risk is greater than that of the general population. Studies vary in the numbers which can be influenced by ethnic background, but in general population terms the chance of breast cancer by age 50 is estimated between 33-50 percent. As you continue to age, the risk increases to 50-87 percent by age 70. Unfortunately this also means there is an increased life time risk of developing ovarian cancer as well, with the risk increasing as you age.

With a positive test result, my recommendation is to make an appointment with a general surgeon with expertise in breast cancer surgery and a medical oncologist. Together with these professionals you can review your options of medical or surgical therapy that will reduce your risk of breast cancer from ever developing. You need to know what their experience is with women who have similar risk, regarding the long term disease free survival of their patients who chose from medical or surgical prophylactic treatment. They can also be able to refer to the latest studies involving larger groups of women with similar risk and their outcomes. After your meeting with these health care professionals, you can then see your gynecologist to review the associated risk of ovarian cancer and what options of surveillance and surgery are available to you.

Importantly, knowledge is power as the saying goes. By reviewing your family history and using a breast cancer risk assessment tool you can find out if you are possibly at an increased risk. With the addition of a blood test which helps define what that lifetime risk is for breast cancer, and then discussing these results with the right health care professionals, you will arm yourself with the important information to help you make a decision that can have a significant impact on your long term health.

ABOUT THE AUTHOR:
Dr Rod Taber is an OB/GYN at Grand Rapids Women's Health. He has been a practicing OB/GYN in the West Michigan area for almost 25 years, specializing in women's health – minimally invasive gynecologic surgery, treatment of menopause and other related issues, treatment of heavy bleeding and management of abnormal pap smears. He served as the Chairman of the Obstetrics and Gynecology Department at Spectrum Health from 2006 - 2010.

National Comprehensive Cancer Network criteria for consideration of BRCA1/2 genetic testing

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A. Individual from a family with a known deleterious BRCA1/BRCA2 mutation

B. Personal history of breast cancer plus one or more of the following:

- Diagnosed age ≤45 years
- Diagnosed age ≤50 years with ≥1 first, second, or third-degree blood relative with breast cancer ≤50 years and/or ≥1 first, second, or third-degree blood relative with epithelial ovarian/fallopian tube/primary peritoneal cancer at any age
- Two breast primaries when first breast cancer diagnosis occurred prior to age 50 years
- Diagnosed <60 years wth a triple negative breast cancer
- Diagnosed <50 years with a limited family history
- Diagnosed at any age with ≥2 first, second, or third-degree blood relatives with breast and/or epithelial ovarian/fallopian tube/primary peritoneal cancer
- First, second, or third-degree male blood relative with breast cancer
- Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer
- For an individual of ethnicity associated with higher mutation frequency (eg, Ashkenazi Jewish), no additional family history may be required

C. Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer

D. Personal history of male breast cancer

E. Personal history of breast and/or ovarian cancer at any age with ≥2 first, second, or third-degree blood relatives with pancreatic cancer at any age

F. Personal history of pancreatic cancer at any age with ≥2 first, second, or third-degree blood relatives with breast and/or ovarian and/or pancreatic cancer at any age

G. Family history only:

- First or second-degree blood relative meeting any of the above criteria
- Third-degree blood relative with breast cancer and/or ovarian/fallopian tube/primary peritoneal cancer with ≥2 first, second, or third-degree blood relatives with breast cancer (at least one breat cancer ≤50 years) and/or ovarian cancer

National Comprehensive Cancer Network, v1.2011 (www.nccn.org).