

# Risks, Benefits of BRCA Genetic Testing Weighed

BY ROBERT FINN

EXPERT ANALYSIS FROM A MEETING ON  
WOMEN'S HEALTH

SAN FRANCISCO — The era of personalized genetic medicine has arrived, but this is not an unalloyed blessing, especially in the area of breast cancer, according to Dr. Mary S. Beattie.

More women are asking their physicians about whether they should undergo genetic testing for mutations in one of the two BRCA genes, and some physicians are approaching such questions with trepidation. But Dr. Beattie, director of clinical research in the cancer risk program at the University of California, San Francisco, said that there's not that much difference between genetic testing and standard lab tests.

"I envision genomics and genetics as a tool in our armamentarium. We can be intimidated by it, or we can practice medicine using the same principles we've always used, personalizing test results and helping patients to improve their general health and lower their risk of disease," she said at the meeting sponsored by UCSF.

Still, it's important to understand not only the benefits of BRCA testing, but also the risks and limitations, she said at

the meeting. For example, although BRCA testing can detect certain known mutations and certain high-risk individuals, not every dangerous mutation is known. And of course, breast cancer often arises sporadically, even in women with no BRCA mutations.

Dr. Beattie offered the following suggestions to help respond to questions about BRCA testing:

► **Don't just order a test.** Ask the patient about her family history, and be especially alert for a pedigree that includes deaths from breast cancer in premenopausal women. If the patient has only a vague notion of her family history, send her home with an assignment to learn as much as she can.

This is where it can be valuable to enlist the aid of a genetics counselor. "They do a better job and they have more time" than physicians do, Dr. Beattie said at the meeting. "They're trained to take very thorough three-generation pedigrees, sometimes even four or five generations." Genetics counselors will typically verify the causes of death and the age and diagnosis at death, and they will collect documents to make sure they're all correct.

Let's say that the patient has a paternal aunt who died of breast cancer at 40 years of age, as well as a father who was diag-

nosed with prostate cancer (whose risk can also be increased by BRCA mutations) at 55 years, Dr. Beattie posited. And let's add that the aunt's daughter has just been diagnosed with breast cancer at 33 years of age. This is a fairly concerning family history, and it seems clear that testing the patient for BRCA is indicated.

But don't jump to this conclusion, she advised. "It might seem a little counterintuitive, but in the genetics world, we typically think about testing the person who has the highest probability of testing positive," Dr. Beattie said. "So the next step, if we were going to go ahead and test, would not be to test [the patient]; it would be to test someone in her family who's had cancer, the person who has the highest probability and who's still alive and available for testing."

► **Make sure testing is informed by ethnic history.** Hundreds of different BRCA mutations are now known, and a comprehensive analysis can cost \$3,800. But these mutations are not evenly distributed in populations.

In the Ashkenazi Jewish population, for example, three BRCA alterations account for 90% of the mutations; testing for those three specific alterations costs only about \$400.

Such founder mutations are not

unique to Ashkenazi Jews. French Canadians, for example, typically have one of four mutations in each of the two BRCA genes, and Icelanders typically have one of two mutations in each of the genes.

Once a family's specific BRCA alteration has been identified, the patient will need only single-site testing, reducing the cost even further.

► **Consider a patient's psychosocial situation before ordering genetic testing.** A positive test can have far-reaching consequences, both psychologically and economically. Dr. Beattie advised. For example, "never do BRCA testing with someone who's going through an episode of depression or anxiety."

Fortunately, the economic consequences of a positive BRCA test are not as dire as they once were. In 2008, Congress passed—and President George W. Bush signed—the Genetic Information Nondiscrimination Act (GINA). The section of the law that prohibits health insurance plans from increasing premiums or dropping coverage based on the results of genetic testing went into effect on May 22, 2009, for individual health insurers, and must be in effect by May 21, 2010, for group plans. ■

**Disclosures:** None was reported.

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Vitamin D <sub>3</sub>	200 IU	50%	50%
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Vitamin B <sub>6</sub>	25 mg	1250%	1000%
Folate (L-methylfolate as Metafolin 600 mcg) (folic acid, USP 400mcg)	1 mg	250%	125%
Vitamin B <sub>12</sub>	12 mcg	200%	150%
Biotin	250 mcg	83%	83%
Calcium (calcium carbonate)	140 mg	14%	11%
Iron (ferrous fumarate)	28 mg	156%	156%
Iodine (potassium iodide)	150 mcg	100%	100%
Magnesium (magnesium oxide)	45 mg	11%	10%
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**References:** 1. Hollowell JG, Staehling NW, Hannon WH, et al. Iodine nutrition in the United States. Trends and public health implications: iodine excretion data from National Health and Nutrition Examination Surveys I and III (1971-1974 and 1988-1994). *J Clin Endocrinol Metab.* 1998;83(10):3401-3408. 2. Zimmermann MB. Iodine deficiency. *Endocr Rev.* 2009;30(4):376-408. 3. Mock DM. Marginal biotin deficiency is common in normal human pregnancy and is highly teratogenic in mice. *J Nutr.* 2009;139(1):154-157. 4. Horrocks LA, Yeo YK. Health benefits of docosahexaenoic acid (DHA). *Pharmacol Res.* 1999;40(3):211-225. 5. Uauy R, Hoffman DR, Mena P, Llanos A, Birch EE. Term infant studies of DHA and ARA supplementation on neurodevelopment: results of randomized controlled trials. *J Pediatr.* 2003;143(suppl 4):S17-S25. 6. Birch EE, Garfield S, Hoffman DR, Uauy R, Birch DG. A randomized controlled trial of early dietary supply of long-chain polyunsaturated fatty acids and mental development in term infants. *Dev Med Child Neurol.* 2000;42(3):174-181. 7. Agostoni C, Trojan S, Bellù R, Riva E, Giovannini M. Neurodevelopmental quotient of healthy term infants at 4 months and feeding practice: the role of long-chain polyunsaturated fatty acids. *Pediatr Res.* 1995;38(2):262-266. 8. Dietary supplement fact sheet: folate. National Institutes of Health Web site. <http://ods.od.nih.gov/factsheets/folate.asp>. Accessed March 15, 2010. 9. March of Dimes<sup>®</sup> Quick Reference. Folic acid. March of Dimes<sup>®</sup> Web site. [http://www.marchofdimes.com/professionals/14332\\_1151.asp](http://www.marchofdimes.com/professionals/14332_1151.asp). Accessed March 15, 2010. 10. Metafolin<sup>®</sup>: about Metafolin<sup>®</sup>. Merck KGaA Web site. <http://www.metafolin.com/servlet/PB/menu/1784410/index.html>. Accessed March 15, 2010.

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