

# Anticipating family issues associated with cancer risk assessment and genetic testing

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Family history assessment and genetic testing are worth the effort and can help to decrease the cancer burden in some families when increased risk is recognized and addressed by heightened surveillance and/or risk-reduction measures. However, genetic testing is associated with psychosocial issues that are important to address during the genetic counseling process prior to sample collection. Skipping this process and moving directly to DNA testing may be detrimental for some families and may impair the patient's ability to cope with the genetic test result and use the information in a beneficial manner. Some individuals may not realize how this information affects their family members and may not understand the importance of sharing this information. Because of the predictive nature of genetic testing, it is different from other diagnostic tests—the emotional needs of the patient must be anticipated. Conversely, personal biases that dissuade the patient from proceeding with genetic consultation or testing may also lead to detrimental effects.

**M**ore patients are raising the issue of genetic testing for inherited cancer susceptibility with their healthcare providers to help determine their level of risk. It may be difficult for the healthcare provider to remove his/her personal biases about these issues when formulating answers to the patient's questions. Studies show that patients rely heavily on the opinion of their healthcare provider when deciding on medical options and that reliance may extend to deciding whether or not to undergo genetic testing. Therefore, understanding the experiences of some families who have been through the genetic consultation and testing process may help formulate a more objective response and anticipate the patient's questions and emotional burden.<sup>1-7</sup> The following story describes an increasingly common situation faced by families and their medical providers.

An elderly woman receives a telephone call from her niece who says that she tested positive for a *BRCA2* mutation (Figure 1). Her niece was recently diagnosed with breast cancer at age 37. Her sister, the young woman's mother, had died from cancer years ago at the age of 36. Both parents of the elderly woman had immigrated to the United States, leaving their biologic families behind. When the parents died of sudden illnesses at young ages, the family history was lost.

Although this elderly woman had never devel-

oped breast cancer, she is worried about her two daughters and desperately wants to know that they are not at increased risk of developing cancer. She has spent a significant amount of time on the Internet educating herself about *BRCA2* mutations and the implications of testing. Her niece's recent

## KEY POINTS

During genetic counseling, it's crucial to address psychosocial issues in the family.

Some patients may choose not to be tested.

Test results should always be interpreted in the context of family history.

Regardless of the results, genetic testing can change family dynamics.

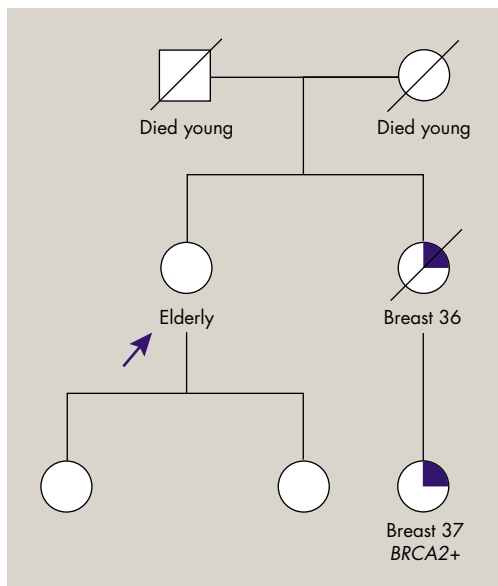
Survivor guilt can strike those who test negative for a genetic mutation.

In families at risk for breast and ovarian cancers, don't overlook testing the men.

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**FIGURE 1** Pedigree of a family with a *BRCA2* mutation in the niece of the elderly woman described in the text (arrow).

breast cancer diagnosis has caused her to relive the loss of her sister and has forced her to focus her concern on her children. She states that she is not worried about her own health, as she has lived a long life and can deal with the disease. But she does not wish for her children to face a lifelong concern about cancer. DNA testing for hereditary breast cancer susceptibility would provide the desired information and might help answer this question.

Although this woman is elderly and so far cancer-free, it is not safe to assume that she has not inherited the *BRCA2* mutation detected in her niece. Both pre- and postmenopausal breast cancer and ovarian cancer have been associated with *BRCA2* mutations.<sup>8</sup> Given that the woman is at 50% risk of having inherited the mutation—and that a relatively inexpensive and accurate test exists—DNA testing would be an appropriate and cost-effective option. However, she has revealed several points that must be addressed to help her cope with the test results (either positive or negative) and her concerns for her niece and her own children and to grieve again the loss of her sister. These is-

ssues will be discussed in the subsequent sections below.

### The waiting process

Patients can feel anxious about being referred to a genetics specialist if their healthcare provider has not explained the purpose of the consultation, the information that can be gained, and how the provider might use the information to develop a plan for early detection and surveillance. Because patients and family members often must wait several weeks to several months for an appointment at a cancer counseling service, a few minutes of discussion can add a level of comfort before the date of the consultation. The waiting period does provide the family with an opportunity to collect detailed information on the family history and the appropriate medical records.

For some patients, afraid of what they might learn, the consultation itself may be anxiety provoking. Others will find the consultation beneficial because an explanation may be available for their personal and/or family histories of cancer. Often, patients recognize that they are at increased risk of developing cancer, but they usually have not determined a specific risk number or risk level (high, moderate, or average).<sup>9</sup>

Waiting for the test results is another anxiety-provoking time. Genetic test results often take 3–4 weeks to become available. Most patients report that they are able to displace their thoughts about the test results until a day or two before the results disclosure appointment. On the day of the results disclosure, patients are often surprised as to how much they had been thinking about the test results without allowing themselves to acknowledge these thoughts. Some patients report more distress during the waiting time; they may be more concerned about the decisions they will make following the results disclosure and/or the impact the results

may have on their loved ones.<sup>10–12</sup>

### The positive test result

Each test result is met with a different reaction, depending on the patient’s personal or family cancer experience. For example, some patients whose relatives with cancer have survived may be more likely to choose increased surveillance for cancer, as their experience is that cancer is a beatable disease. In contrast, some patients whose relatives have not survived cancer may choose risk-reducing surgeries or treatments, as their experience has only been that cancer takes lives. The patient’s age may also affect his or her medical management decisions.<sup>13</sup>

There are some families who clearly meet the definition of a hereditary predisposition to cancer but are still surprised when a family member receives a positive test result. It can be difficult to understand the family’s shock over the test result, but understanding their anxiety is imperative to help them cope with the information. Some patients will have a difficult time adjusting to the fact that they are at increased risk of developing certain types of cancer. In some cases, they feel that they have a “glimpse into the crystal ball,” but more questions arise that remain unanswered.

Test results can confirm that an increased risk of cancer exists, but they cannot tell the patient which type of cancer, if any, will develop, nor can they predict the age of onset. This can

#### Topics for discussion

The typical cancer genetics consultation covers a wide range of topics, including:

- family history assessment
- cancer risk estimates
- potential risk-reduction strategies
- genetic testing options
- issues specific to genetic testing
- cost of testing
- meaning of test results
- implications for insurance

be met with frustration, as it may be difficult to comprehend an increased ovarian cancer risk if the disease has not been seen in previous generations. As more data become available with regard to genotype-phenotype risks, it may become clear that some women with a specific *BRCA1* or *BRCA2* mutation will not be at increased risk for developing ovarian cancer. For now, women will need to make their decisions on risk-reduction options based on information gleaned from other families with a mutation in the same gene, as the data are not yet available for mutation-specific predictions.

Some patients cope better with knowing the cancer risks than not knowing them and find the information from genetic testing empowering. Others find relief, because they have an explanation for the cancers that have occurred in their family, and some of the causal myths can be dispelled. Still others find the information beneficial, as they can use it to begin surveillance at a younger age than the general population or to assist with timing of risk-reduction procedures. For example, some women are grateful for the knowledge that an oophorectomy is indicated at a young age and are willing to enter into early menopause and deal with the associated side effects. Other families see positive test results as providing an opportunity to reach out to distant relatives that they may not have spoken to in years. How well the patient copes with positive test results depends upon the support system within the family and among friends and how well prepared the patient is prior to the sample collection.<sup>12,14</sup>

### The negative test result

Some patients are overjoyed with a negative test result, even in the absence of a known family mutation. Others are frustrated, as they still do not have an answer for their breast cancer or that of their relatives nor can they answer their next set of

questions: What is the risk of additional cancers? Is an oophorectomy indicated? What do I tell my children about their risk?

Interpreting a negative test result must be done in the context of the family history. In the setting of a large family in which one woman is diagnosed with early-onset breast cancer and the other women are cancer-free in their postmenopausal years, the negative test result can provide reassuring information to the patient and her relatives. In the setting of a small, uninformative family (predominantly male), the negative test result may represent a limitation of the test; a mutation may still be present that was not identifiable by the current assay or perhaps because the mutation lies in a gene that has either not been studied or not yet identified. Therefore, a negative test result can have very different meanings, depending on the initial degree of suspicion of a hereditary predisposition.

Some women will have a difficult time adjusting to negative test results, even when a known mutation exists within the family. They may struggle with the notion that they are not at increased risk when they have spent many years operating under the notion that it was not a matter of "if" they got breast cancer but "when." They may choose to undergo risk-reduction options or heightened surveillance regardless of the test results because they do not feel they can trust a negative test result.

### The uncertain test result

The uncertain test result can be frustrating for all involved: this result means that a change has been identified in one of the genes, but there are not enough data to confirm whether the change is associated with increased cancer risk or whether it is a normal variation that does not alter cancer risk. In this setting, the patient often needs to involve other family members in the testing process to

help determine whether the variant tracks with the cancer in the family.

If family members are unwilling to participate, it may cause discord within the family, as the individual must wait for more data to be gleaned from other families participating in the testing process. These data may take years to gather. In the meantime, the patient must make decisions based upon the possibility that he/she may have an increased cancer risk, even though, in a few years' time, the patient may learn that he/she was truly not at risk. In this setting, the test should not be offered to relatives on a presymptomatic basis, as it is unclear how this test result will affect medical management.

### Delaying or declining testing

Some patients are ready to proceed with testing in the hopes that the test result will be negative; they are not prepared to hear that a mutation has been identified. Confirming an increased cancer risk in a person who is not prepared emotionally to deal with the test results can also have negative consequences. In this setting, delaying DNA testing and continuing with heightened surveillance may be an appropriate option to give the patient more time to determine how he/she will use the information and mentally prepare for the test result. Even though the technology is available, for patients who are not ready to cope with and utilize the information that technology provides, DNA testing may not be useful. Identifying this issue prior to sample collection is one way the genetic counseling process can help patients, as well as the family, adjust to and prepare for the testing outcome.

### Us versus them

Survivor guilt is a powerful phenomenon that is often under recognized and under discussed by families during and after the testing process. All siblings start the testing process at

the same level of risk. Theoretically, half of them are not at increased risk of developing cancer. The other half will learn that their risk of developing cancer is significantly increased. Some siblings will choose not to be tested, as they do not wish to know their mutation status; they will either choose heightened surveillance or avoidance. Some family members may not agree with the decisions of their relatives and will try to persuade them to make alternative decisions. Some individuals, who may feel better prepared to deal with the results than others in their family or who do not have children who would be affected by their mutation status, prefer that they be the ones to have inherited a mutation rather than a relative in a more vulnerable position.

Some families who have completed the testing process have reported feeling that relatives who tested negative no longer understand the level of risk, straining relationships within the family. Some family members turn to

those who have had positive test results, looking for advice on whether or not to test and wanting to discuss the results and how they led to decisions on surveillance versus risk-reduction procedures. Other individuals will turn to organizations for emotional support (see the box, "Resources"). Whereas some families will face short-term strains in their relationships, others may face more lasting changes.<sup>15</sup> It can be a challenge to predict which families will experience these difficulties. It is helpful to have counselors available with experience in cancer and family therapy to refer families for professional ongoing consultations.

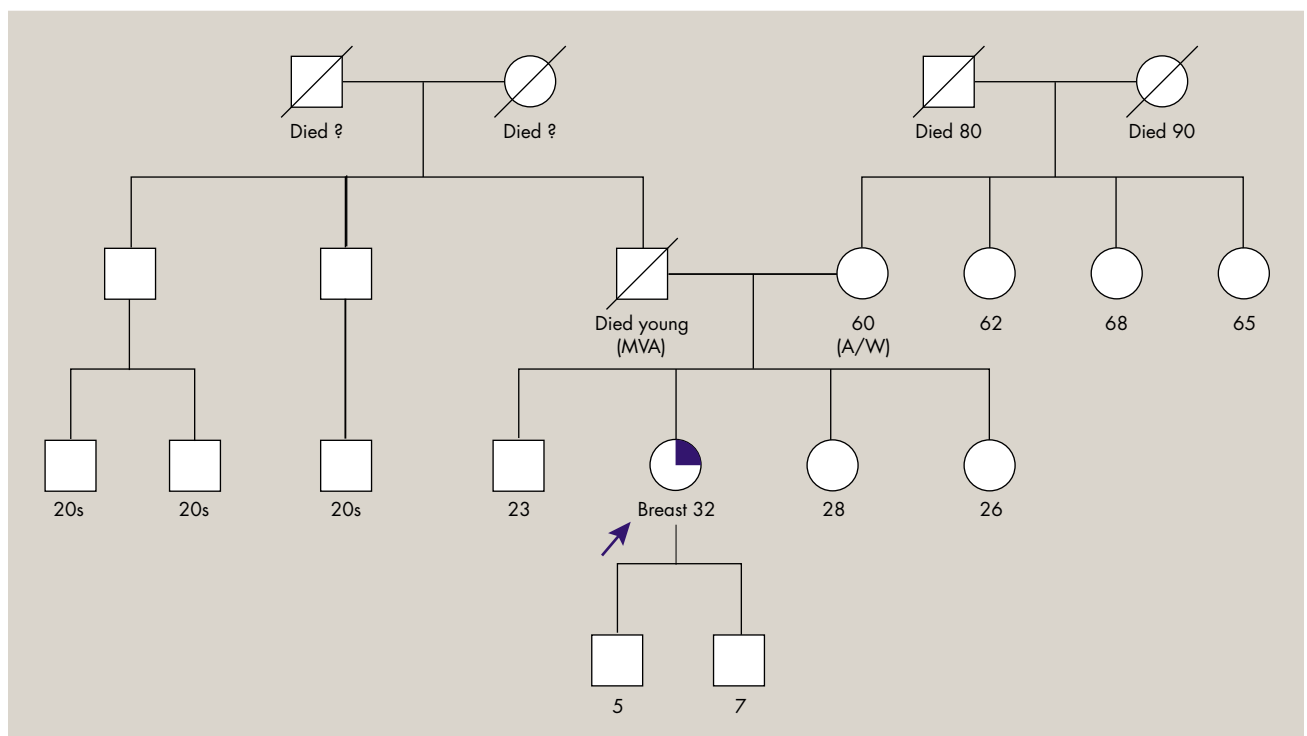
### Don't forget the men

Once a mutation is identified, families and medical providers often focus on the female relatives. However, men in the family also have a risk of inheriting the mutation and may also have an increased cancer risk, specifically of developing prostate cancer (20% risk by age 70) and breast can-

cer (6% lifetime risk).<sup>16</sup>

The following case history illustrates this point.

A 32-year-old woman was diagnosed with high-grade invasive breast cancer. As part of the treatment for her original cancer, she chose a bilateral mastectomy and an oophorectomy, rather than taking hormone injections to suppress ovarian function. Three years later, she presents with distant metastases and will likely not survive the recurrent cancer. There is no other family history of cancer. However, her father died at a young age; she only has paternal uncles, no paternal first cousins who are female, two younger sisters, and two sons (Figure 2). Although she is a candidate for genetic testing due to her young age and pathology characteristics, her physicians are reluctant to recommend testing as it will not change her medical management, there is no family history of cancer, and she only has sons. However, she has an uninformative family history in the generations above, and



**FIGURE 2** Pedigree of a family in which one of its members (arrow) was diagnosed with early-onset breast cancer. MVA = motor vehicle accident; A/W = alive and well.

her sisters are young enough that even if they carried a mutation, they likely would not have developed cancer yet.

Although it is true that DNA testing will likely not affect her outcome, the decision not to test does affect her sisters and will someday affect her young sons. She becomes the family history for her sisters. She is the best person in the family to undergo the DNA test and her result would provide information to the family as a whole unit. If DNA testing is not done on the young woman or if a sample of DNA is not banked, the relatives may not have a fully informative DNA test to guide their medical management decisions or determine their level of cancer risk. In this case, an emphasis is placed on the patient's immediate medical situation, but the psychosocial needs have not been fully addressed. Although she is dealing with her own prognosis, she will need to make plans to care for her sons and may likely be concerned about her siblings. If DNA testing and/or DNA banking is not offered, has she been given the full opportunity to complete this task?

Would the decision not to offer DNA testing or DNA banking have been different if she had a daughter? If her younger sisters are given the task of caring for the boys, was the sisters' health protected so the boys did not lose a second "mother" to cancer? Although these situations can be emotionally challenging, personal biases of the medical providers and family members should be minimized to facilitate the patient's wishes.

This story illustrates that the gender of at-risk relatives plays a large role in the decision process to offer DNA testing and/or DNA banking. Half of the at-risk relatives should not be excluded based on gender alone, as this information may affect their future management or that of their descendants. Although men have a lower breast cancer risk than their female relatives, men may still

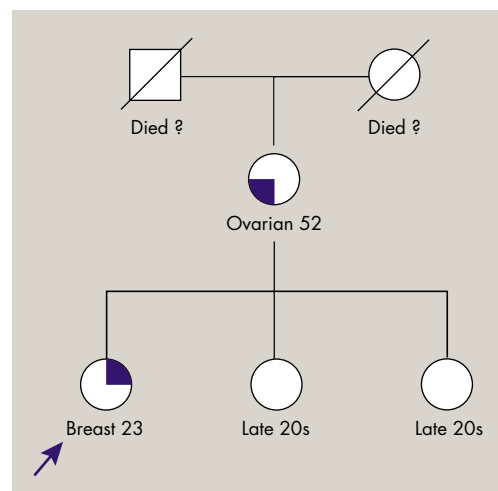
benefit from increased surveillance.<sup>16</sup> Men may also have daughters who are at increased risk of developing breast or ovarian cancer, but the cancer may appear to skip a generation, as the male relative may not develop cancer. In either case, families should be encouraged to include male relatives in deciding whether to proceed with DNA testing.

### Sharing the news

Many patients struggle with how to share the news with relatives or with understanding how distantly related people can be affected by the results. Often, parents struggle with when and how to tell their children about the test results, the implications of those results, and the guilt of potentially passing a cancer risk onto their offspring.

During the genetic consultation, many genetic counselors will review options of how to share the information with relatives. Role playing is one possibility, as is writing a letter to relatives that includes the test result and names and phone numbers of genetic counselors in their community. Some patients are willing to share the information with their immediate family and do not consider that cousins or more distant relatives will also benefit from the information. Using the pedigree to show the expanding circle of impact as each person tests positive is helpful to demonstrate this point.

Some patients do not wish to share the results with their relatives. Although sharing the information with relatives is encouraged, concerns about patient privacy and difficulty adjusting to test results can delay the disclosure of test results to relatives. This situation can put the healthcare provider in an uncomfortable situation, as at-risk family members may not be aware of their cancer risk or appropriate surveillance guidelines.<sup>17</sup> (*The issue of duty to warn will be addressed in a subsequent article—Editor.*) Other patients will either decline the



**FIGURE 3** Pedigree of a family with apparent hereditary breast and ovarian cancer syndrome.

consultation and/or testing or will not disclose the information to relatives out of their fear of insurance discrimination or other negative insurance implications.

### Fear of insurance discrimination

A woman is diagnosed with ovarian cancer at age 52 years. Four years later, her daughter is diagnosed with breast cancer at age 23. Her two remaining daughters are in their late 20s and are concerned about their breast cancer risks. The mother is an only child, and no other family history is known (Figure 3). The young breast cancer survivor is willing to proceed with DNA testing to help protect her sisters. However, their mother is opposed to the testing, as she fears insurance ramifications for herself and her daughters based on the results of the testing.

This process has opened avenues of discussion for the women: What is their level of anxiety over a potential cancer diagnosis? How will they deal with this risk? What coping mechanisms for their relatives with cancer can they offer? Insurance concerns are frequently raised by patients prior to accepting an appointment for consultation and/or DNA

## Resources

American Board of Genetic Counseling  
Web site: [www.abgc.net](http://www.abgc.net)

American Board of Medical Genetics  
Web site: [www.genetics.faseb.org/genetics/abmg/abmgmenu.htm](http://www.genetics.faseb.org/genetics/abmg/abmgmenu.htm)

American College of Medical Genetics  
Web site: [www.acmg.net](http://www.acmg.net)

American Society of Human Genetics  
Web site: [www.genetics.faseb.org](http://www.genetics.faseb.org)

Facing Our Risk of Cancer Empowered (FORCE)  
Web site: [www.facingourrisk.org](http://www.facingourrisk.org)

GeneTests  
Web site: [www.genetests.org](http://www.genetests.org)

National Cancer Institute  
Web site: [www.nci.nih.gov/search/geneticsservices/](http://www.nci.nih.gov/search/geneticsservices/)

National Society of Genetic Counselors  
Web site: [www.nsgc.org](http://www.nsgc.org)

testing. Federal legislation exists in addition to legislation in some states to protect against genetic discrimination. Although better legislation is needed to help ease fears of the general public, few cases of genetic discrimination have been documented to date.<sup>18</sup> Genetic discrimination will be addressed further in a subsequent article in this series.

## Conclusion

Although this article used *BRCA2* as an example, there are many other known genes that cause an increased risk for cancer. The points raised in this article are applicable to the vast majority of genetic tests for inherited cancer risk.

Every person deals with the risk, testing process, test results, and post-test decisions in a different way. The goal of the genetic consultation is to provide the information necessary to give informed consent and to explore the psychosocial components, so that the patient is better able to cope with

the test results.

Although some individuals may choose not to pursue genetic testing for various reasons, the families that choose to pursue the testing have benefited. Families that choose not to test have also benefited, as they have made an informed choice that is right for them. In either case, the psychosocial needs of the patient must be anticipated to maximize the benefit and allow patients to have the opportunity to deal with their own inherited susceptibility to cancer.

Patients will be more apt to proceed with the genetic consultation, risk assessment, DNA testing, and appropriate surveillance measures with reinforcement of their physician. Shared decision-making between the individual and his/her medical provider will have increasing importance as the usage of genetic information becomes a greater part of routine medical care.

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*In a future issue, Ms. Larsen Haidle and Rebecca Anderson, JD, MS, CGC, will address genetic discrimination concerns: the duty to recognize, duty to warn, and duty to act.*

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