Breast Cancer and Genetic Testing

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Cancer and the Maiden

FIVE months ago, I took a test for something called the BRCA genetic mutation, which is often referred to as the breast cancer gene. My mother had fought off breast cancer and she waged a ferocious battle against a second cancer, ovarian, when it ambushed her body seven years later. The cancer won.

After my mother's death, doctors and other cancer-savvy friends suggested that my sister and I should, at some point, be genetically tested for the faulty BRCA gene. I was 34 when I took it. I tested positive.

BRCA mutations are known to cause early-onset cancer, and statistics show that having the mutation means it's almost certain that I will develop breast cancer at some point in my life. It also means that I have a greatly increased chance of developing ovarian cancer. I share this gene with my mother, but I now have something my mother did not: the warning that, in all likelihood, cancer will be coming for me.

With tests like these, modern science acts as a crystal ball - warning us of dark events that may come. We seek such knowledge so we can take measures to protect against illness. Unfortunately the test for the BRCA gene is just a decade old, and doctors can offer no definitive guidance to women diagnosed with a genetic predisposition to cancer. In the case of BRCA mutations, science has outpaced our understanding of what to do with the data. Because the test is unaccompanied by any clear medical recommendations, it doesn't provide solace so much as open a Pandora's box.

Although I'm currently cancer-free, the knowledge of my genetic predisposition requires me to squarely face excruciating life choices - yet with inexact information. Breast cancer genetic screening is so new that doctors don't really know what to tell women with BRCA mutations except to be vigilant about increased surveillance. Preventative chemotherapy has proven effective for women who carry the BRCA2 mutation, but it does not work for carriers of the BRCA1 mutation (the one I have.) The surest way to prevent breast and ovarian cancers is to have your breasts and ovaries removed. Recent studies show that undergoing these radical surgeries will reduce the risk of inherited breast and ovarian cancers by 90 percent.

However, I'm single, dating, and I want to have a family. I won't consider having my ovaries removed until after I've had children (thankfully the risk of ovarian cancer is slighter than that of breast cancer). But what about a double mastectomy? Having witnessed the death-grip of cancer, I'm not inclined to wait around for it to strike, especially since inexact surveillance machines do not always catch it at an early stage. Aside from drastically interrupting my life, how might a double mastectomy adversely affect issues of sexuality? My romantic future? How early in the dating process do I reveal the information about my faulty gene, with all its ramifications?

My sister is 31. She's not certain whether she will take the test. She remarked recently on the diametrically opposed approaches we have taken: knowing that cancer is often a genetic legacy, I sought out the knowledge that would permit me to make informed decisions. Knowing that there is a 50 percent chance she did not inherit the gene, my sister is not yet willing to give up the luxury that our mother had - to live her life freely, unaffected by the shadow of illness.

I empathize with my sister's point of view but in spite of the burden, I believe that women like me are fortunate to have the knowledge, imperfect as it is, of the likelihood of cancer - to know what our mothers did not.

I can say without question that my mother would have traded those 51 years of innocence for the dark knowledge that could have potentially saved her life. My mother would have done anything to live.

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Breast cancer affects a significant percentage of the female population across all socioeconomic, age, race, and ethnic classes. There are over 192,000 new cases of breast cancer each year. Statistically, the National Cancer Institute estimates that 13.4 percent of women will be diagnosed with breast cancer – which is about 1 in every 7 women. This disease affects males as well; 1,300 men are affected annually. However, breast cancer treatment for males comes mainly from work done with women's breast cancer because of its relative rarity. For its greater prevalence, research emphasis has continuously been placed on women's breast cancer.

Over the years, female breast cancer has risen in incidence. This can be attributed to a number of factors such as better detection tools, new statistical methods, longer female life spans, and changing lifestyles of American women. In particular, increased risks for breast cancer stem from women choosing to have their first pregnancy when they are older and the use of hormonal replacement therapy to treat symptoms of menopause.

Morbidity and mortality from breast cancer depends on the stage of the disease a patient is diagnosed in as well as the area of the breast affected. While the causal

relationships aren't fully understood yet, it has been shown that basal cell tumors are associated with shorter patient survival times than are luminal cell tumors. Having breast cancer has different implications, all depending on the particular cells affected.

While at the turn of the century and into the late 1970s, treating breast cancer involved radical mastectomy, treatment for breast cancer today involves several options. The most common treatment is either through simple mastectomy or lumpectomy with radiation. The former refers to removing the breasts surgically while the latter involves removing the affected breast tissue and following through with chemotherapy. Preventative measures (before any breast cancer tumors manifest) include removing at-risk tissue or the entire removal of healthy breasts. In addition, drugs such as tamoxifen have shown promise in preventing breast cancer.

Breast cancer detection is through mammograms and clinical breast exams. Members of families with histories of breast cancer and people of Ashkenazi Jewish descent are at a higher risk of breast cancer. The scientific knowledge on breast cancer is still lagging behind the considerable improvements in the treatment of breast cancer that have been made in the past century. Progress has been made however; scientific work has discovered two genes that lead to an increased risk of breast cancer when mutated.

In the early 1990s, BRCA1 and BRCA2 were discovered to be proto-oncogenes – cancer causing genes when mutated, for both breast and ovarian cancers. A negative regulator in cell growth, the BRCA genes normally would protect against cancer. Mutations in these protective regions lead on to breast and ovarian cancer. It is estimated that inherited mutations in BRCA genes lead to a 3 to 7 fold increase in the risk for breast cancer. There are difficulties assessing the correlation between a BRCA mutation and

breast cancer because there are numerous sites of mutation – not just one like in diseases such as phenylketonuria.

While genetic tests are available to screen for BRCA1 and BRCA2 mutations, many people are ambivalent about pursuing this. Because genetic testing would only be able to give a probability of getting breast cancer and is not a definite indicator of when and whether a patient will get the disease, some people choose not to get tested. Concerns about changing the subjective quality of life if the test is positive for BRCA mutation(s) and the uncertainty on when or whether breast cancer will onset are some of the reasons why people forgo testing.

With the technological breakthroughs in genetic screening, widespread genetic testing is becoming more and more a reality. Considering these circumstances, the Stanford Program in Genomics, Ethics, and Society drew together a Working Group which concluded that BRCA1 and BRCA2 mutation testing would only be beneficial for use in families with multiple cases of cancer – not for the entire population at large.

The recommendation to gear genetic screening for breast cancer to certain individuals stem from concerns over the quality of life should the test be positive, even though a BRCA mutation isn't destined to always lead to breast cancer. Negative consequences aren't limited to the individual either. Family disruption and social consequences leading to loss of insurability or employability are some possibilities a positive test result for BRCA1 or BRCA2 mutations may bring about.

The Working Group recommended targeting genetic testing for BRCA1 or BRCA2 for men and women from "high-risk families" – families with cases of breast cancer, because of the predictive significance of a combination of family history and

genetic testing. Furthermore, they argue the suitability of genetic testing for high-risk individuals considering prophylactic surgery (removal of at-risk tissue). Population-wide testing was not advocated because of potential inadequacies in maintaining patient privacy, training the professionals administering the test, and patient reaction to the test.

With the limited knowledge about breast cancer stemming from BRCA1 or BRCA2 mutations we have today and the uncertainty in actual breast cancer onset even with mutations in these sensitive areas, generalized population-wide testing is indeed not a prudent policy decision. However, generalized population-wide testing or increasing the feasibility for testing with respect to age should be considered. "High-risk" individuals for BRCA1 or BRCA2 mutations only involve 5-9% of the population. According to the Working Group, non-inherited mutations are not indicative of whether an individual's offspring and relatives will also develop breast cancer. Given that surveillance treatments such as clinical breast exams are recommended and accepted by women above a certain age already – regardless of BRCA1 or BRCA2 mutations, incorporating genetic testing into surveillance treatment for middle-aged women would effectively identify individuals at an increased risk and increase the chances of early breast cancer detection.

Promoting genetic testing for the middle-aged population already at an increased risk for breast cancer already can be beneficial to society. Given that there are socioeconomic and racial/ethnic disparities in access to healthcare and thus, early and treatable detection of breast cancer for many women in underprivileged situations, public policies promoting genetic testing after a certain age may help to identify increased risk individuals.

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