

FEATURE STORY

Family Ties

BY LAURA BEIL

The individual & family decisions behind testing for genetic cancer risk.

Of the 25,000 or so genes Patty Mendez inherited from her parents, her life turned on just one.

She grew up the youngest of five children in Waterloo, Iowa, in a household where each member seemed to bask in the company of the other. She married, assumed an enviable corporate job, and doted on her two dogs. Then came the day in 2002, when her doctor found a lump in her breast. The malignancy had reached the diameter of a quarter, and overtaken four lymph nodes. She was 37.

A fluke, her oncologist said about the tumor. Sure, she was awfully young, but no other woman in her family ever had a trace of breast cancer. “I thought I should have eaten my vegetables,” says Mendez. Her surgeon slid a pamphlet about genetic testing across the desk, but as she took her six rounds of chemotherapy, her genes didn’t occupy another thought.

Until the phone call, more than three years later, from big sister Ruth. A mammogram had spied a tumor. Ruth’s doctor advised genetic testing. The problem seemed greater than broccoli.



Patty Mendez and her twin sisters, Rita (left) and Ruth, all carry the BRCA2 mutation. Photo by David Gresham.

Cancer is often the conspiracy of misguided genes and their surroundings, but some people live disproportionately at the mercy of their DNA. Genes for cancer susceptibility—regular genes transformed into outlaws—wind their way through some family trees, with a 50-50 chance of striking each new member. Of the known genes, BRCA1 and BRCA2 carry the strongest risk of hereditary breast and ovarian cancer.

These damaged genes can’t be repaired, but they can be found. A decade ago, gene-mapping research scientists assumed that everyone at risk would embrace testing, freely sharing results with their kin, says Kenneth Offit, MD, chief of the clinical genetics service at Memorial Sloan-Kettering Cancer Center in New York. They envisioned genetic testing as empowering and enlightening, and for the most part, it has been.

But the geneticists forgot something their psychology colleagues knew well:

Nothing hinging on family interaction is ever predictable. A genetic test can be an emotional glimpse into the past and future, and results occur amid love, resentment, remorse, pride and other currencies of family relations. Some members feel guilty for carrying or not carrying a gene. Some families are brought together over a shared risk. Others are fractured by it.

Annette Patterson, a genetic counselor at the University of Texas Southwestern Medical Center at Dallas, says just about anything can happen among families. Sometimes people are loathe to contact their relatives at all, while others are relieved to understand why they and so many relatives keep ending up in the care of oncologists. The most important thing for families to appreciate, Patterson and others say, is the need for good counseling, before and after, about what the results mean and don't mean. Good decisions are born only of good information.

Perhaps the biggest burden falls on the first person affected—the one who introduces testing into the family. Doctors for Mendez's sister Ruth, who was 43 at diagnosis, advised testing immediately when they saw a hallmark of hereditary cancer: two affected sisters. "Now you don't have to think you had cancer because you didn't eat your vegetables," Ruth tells her sister.

☒ You're being told you have up to an 85 percent lifetime risk of breast cancer. How do women deal with accepting that information? ☒

—Sheila Prindiville, MD

But not everyone suspected to have a genetic mutation should necessarily have a test. If the results wouldn't alter a person's medical course—for example, if the gene raises risk of a disease with no reliable screening method or effective treatment—then the knowledge is of little benefit. In 2003, the American Society of Clinical Oncology laid out three terms to be met before health providers offer genetic testing. They are a personal or family history suggestive of a genetic susceptibility, a test that can be adequately interpreted and a result that will aid in diagnosis or medical decisions.

Scientists have now identified an alphabet soup of genes, in addition to the known BRCA genes, that raise the risk of a handful of cancers. Experts advise testing for many of these, but not all. "Just because there's a genetic test doesn't mean we should be doing it," says Sheila Prindiville, MD, director of the clinical cancer genetics program at the National Cancer Institute. In that regard, she and others are concerned about some commercial Internet sites offering genetic testing services.

Even if they fall into the criteria, some people will reject testing. One of the most common reasons is the fear of genetic discrimination against people who test positive—that employers, insurers and even curious onlookers might see a walking bull's-eye for cancer. Yet among the approximately 5,000 people tested at Sloan-Kettering, no one has yet complained of any social or financial consequences based on their genetic status, says Dr. Offit.

Sue Friedman of Tampa, who gave up a veterinary practice to found FORCE: Facing Our Risk of Cancer Empowered, says that she, too, has not encountered a case of genetic discrimination. The website for her organization (www.facingourrisk.org) maintains a vast national database of women with a genetic cancer risk. “What we see are people who don’t even want their family members to test because they are so afraid of it,” she says.

That anxiety, experts say, illustrates that some of the deepest and most complex psychological reactions to a positive test occur among the family members known as “unaffected carriers.” Affected carriers have already known cancer. Healthy carriers, on the other hand, have to navigate in a kind of demilitarized zone between having cancer and not having cancer—separated from bonafide survivors, but hardly unaffected. So Friedman’s group invented another term for unaffected carriers: previvors.

When she first heard the term, Ilana DeBare of San Francisco thought she had finally found kindred souls. She chose testing two years ago, after her mother died of ovarian cancer at age 56. Being Ashkenazi Jewish, she wanted reassurance that she had little chance of facing her mother’s killer. Instead, she got a BRCA2 positive test result.

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“You start feeling like you’re walking down the street with this little black cloud over your head, and it’s just over you—like in a cartoon,” DeBare says. In and out of a mental fog for weeks, she told no one except her husband. She would alert her family, but first the news had to crystallize in her own mind.

The main idea behind genetic testing is to reduce the risk of cancer in carriers, and save non-carriers from unnecessary stress and medical procedures. Some means of risk reduction are straightforward, such as heightened screening through mammography or colorectal exams. Other measures are more complicated and go beyond simple medical risk. Some women at increased risk of breast cancer because of a BRCA mutation will have their ovaries and breasts removed. This was DeBare’s ultimate choice. But decisions are rooted in each woman’s emotional, mental and social context.

“You’re being told you have up to an 85 percent lifetime risk of breast cancer. How do women deal with accepting that information?” says Dr. Prindiville. “Some women want to do absolutely everything they can and have their breasts removed. Other women can’t imagine undergoing a procedure that’s going to alter their appearance.” A 2004 study in the journal *Cancer Epidemiology Biomarkers and Prevention* demonstrated the variability among healthy carriers with BRCA1 or BRCA2 mutations. Consider prophylactic mastectomy: No members of a mostly Mormon group chose the option, compared with more than half of women in a Dutch study population.

Genetic counselors help people understand that a gene doesn't mean certain doom, but it does bring a certain level of risk. And not carrying a gene doesn't mean that a person will never get cancer. Even major surgery won't completely wipe out the risk since remnants of tissue can be left behind, but the odds are drastically cut.

Counselors also help families communicate, and though test results are delivered on an individual basis, seeing members together for the initial counseling can be helpful. Some family members break the news only after they have results. And they can do it in creative ways. Patterson says one lawyer drew up a memorandum to his family and another person printed fliers for a family reunion. But since most families today are separated by geography, they are left to confer over the telephone.

Patty Mendez's sister Ruth consulted her family before her blood was drawn last summer. The evening Ruth's twin sister Rita hung up the phone, she instinctively lay across the bed and gave herself a breast exam. A chill set over her as her fingers touched a lump. Rita would soon learn she had advanced cancer in both breasts. Not a month after her first-ever mammogram, she lay on an operating table, undergoing a double mastectomy.

Genetic tests on the sisters would find BRCA2 mutations. The gene was probably passed silently through the fathers in the family, until it reached a generation of women. Though she didn't know about the gene soon enough to spare herself chemotherapy, Rita is nonetheless grateful to know. "Knowledge is power," she says. It may yet save her young daughter.

Now, the carriers of one generation must address the next. When and how to break the news to children is as individual as each boy and girl. Ilana DeBare has already told her daughter, who is 12, of the errant family gene. She has faith that by the time her daughter reaches adulthood, medical science will have more to offer.

As the era of genetic testing matures, and more cancer genes revealed, experts will continue to grapple with new issues that few, if anyone, ever anticipated. Among them: Do health care providers have a duty to warn family members if the initial patient can't or won't share results? What are the ethical considerations when couples undergoing in vitro fertilization want embryos screened for adult hereditary cancer genes? These dilemmas are, in some ways, the welcome cost of progress. A decade ago, gene hunters imagined genetic testing would save lives, offer reassurance, and spare unnecessary harm. It is doing just that.