

# Weary of cancer's dark cloud, young woman strikes 1st

By Bonnie Miller Rubin  
Tribune staff reporter

Lindsay Avner cannot remember a time when breast cancer wasn't a part of her life. Her mother, grandmother and great-grandmother all battled the disease. So did aunts and cousins.

But the 24-year-old took charge of her fate in a way unavailable to previous generations.

After a blood test confirmed she carried an inherited genetic mutation that drastically increased her risk of breast cancer, the Chicago woman opted to have a double mastectomy.

"I took away the ticking time bomb," said Avner, one of the youngest patients at New York's Memorial Sloan-Kettering Cancer Center to elect to remove two healthy breasts.

A decade after it became possible to test for mutations in the BRCA1 and BRCA2 genes, experts remain divided on what to do with a positive result. Is mastectomy a pre-emptive strike that reduces risk and anxiety? Or a premature overreaction with permanent consequences? "There's no question that

these women are pioneers—and heroes," said Dr. Patrick Borgen, Avner's surgeon.

Growing up in Columbus, Ohio, Avner was just 11 at the time of her mother's breast cancer diagnosis. A year later, tumors invaded her mother's ovaries. Coming home from school and finding her mom throwing up in a bucket after chemotherapy left an indelible imprint.

When Avner decided to be tested, she was a recent graduate of the University of Michigan poised to start her "grown-up" life. She had moved into a Near North Side apartment and snared her first real job, as an assistant manager at Unilever.

But the positive test result seemed to make a mockery of her plans. Her mother, at least, had endured the ordeal of cancer with a husband and kids. Who would support a single woman alone in a strange city? With new urgency, Avner jumped into a relationship, wondering if she should get married and pregnant.

"I am a make-it-happen kind of person and I felt like I didn't have a moment to waste," she said softly. "Plus, I was scared." Testing negative for the



Lindsay Avner, 24, had a double mastectomy in August because her extensive family history of breast cancer left her anxious about her health. "I took away the ticking time bomb," Avner said.

Tribune photo by Candice C. Cusic

BRCA mutations is no guarantee a woman will not get breast cancer. Fewer than 10 percent of the more than 200,000 cases of breast cancer diagnosed annually in the U.S. are inherited.

Women who do carry the mutations have the power of information but face difficult decisions.

They are at much higher risk for breast cancer—between 56 and 87 percent will get the disease during their lifetime, according to the current issue of *Journal of Clinical Oncology*—and tend to develop a more lethal form at a younger age.

Migraines and insomnia—between 2 and 5 a.m., like clock-

work—dogged Avner as she wrestled with her options, which also included increased surveillance and preventive drug therapy.

During those sleepless nights, Avner sought guidance on a Web site called Facing Our Risk of Cancer Empowered. The Florida-based non-profit started in 1999 as a small message board and now gets a million hits a month. The founder, Sue Friedman, stresses that there are no right or wrong answers—just deeply personal choices.

That sentiment is echoed by Joanna Rudnick, who tested positive at 27 and is filming a documentary called "In the

Family" to be released next fall. Produced by Chicago-based Kartemquin Films, it focuses on other members of this first generation of decision-makers, who must strike a balance between acting on information and being consumed by it.

"How an individual woman experiences it is influenced by her family, her history, her place in life and her values," said Rudnick, who has taken a wait-and-see-approach to her own health.

For Avner, the epiphany came while she was at the University of Chicago's Cancer Risk Clinic. As she sat in her flimsy gown, shuttling from mammogram to ultrasound to MRI, she decided

there weren't enough weapons to battle this relentless foe.

Only a prophylactic mastectomy, which can reduce breast cancer risk by 90 percent for her group, could bring peace of mind.

So, in the early hours of Aug. 29, Borgen prepared to cut into her chest.

"If we've learned anything at all, it is that this has to be a patient's decision," Borgen said. "Lindsay took control. . . . Someone else would say, 'I'll come in every month, if you want me to, but I'm not going to have surgery.'"

Data on prophylactic (double preventive) mastectomy vary, but Dr. Steven Narod of the Centre for Research in Women's Health in Toronto studied about 7,200 women from 11 countries between 1994 and 2004 who were carriers and found that about 25 percent chose surgery.

Six weeks after the operation, which included breast reconstruction, Avner says she has no regrets—only a sense of overwhelming calm.

"With each passing week, I feel more and more convinced that this was absolutely the correct choice for me."

Fear remains a powerful deterrent to testing, and experts say only half of all carriers get screened. But Avner says that even in her darkest days she's been glad she knew her destiny. "I didn't want to stick my head in the sand," she said.

And if Mr. Right comes along? "I'll tell him that we got this thing out of the way. . . . That we can have this great life together and not put our kids through what I went through."

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## DNA: Tests may not be meaningful, critics warn

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demand further testing. After months of talks, the firm now has approval to sell the test at a discounted rate to 12,000 women as part of a study.

One of the first to be tested in the Chicago area was Charmaine Ghidara of Streamwood, who said she feared she was at increased risk for cancer and wanted to know if she should take the preventive drug tamoxifen.

"I don't want to," said Ghidara, 57. "But I'm worried I might be prone to getting breast cancer."

To take the OncoVue test, a woman swishes some mouthwash and then spits into a tube, which is sent to the company's laboratory in Oklahoma City. There, DNA from the woman's cheek cells is isolated for analysis.

The testers are looking for genetic variations called SNPs that the company identified in a study of about 8,000 women with and without breast cancer. Pronounced "snip," SNP stands for single nucleotide polymorphism.

After adding in other known risk factors, such as age and number of close relatives with the disease, a computer calculates the woman's chances of getting breast cancer. The risk is displayed as an absolute percentage and also in comparison to the average risk of women in her age group.

### Taking action after test

Craig Shimasaki, chief executive officer of InterGenetics, said women found to be at higher-than-average risk might choose to take preventive action or intensify their attempts at early detection.

"In general," said Shimasaki, "there are three types of intervention a doctor might recommend: more comprehensive surveillance, such as adding MRI or ultrasound to the usual screening mammograms; lifestyle changes, including exercise and weight control; and preventive strategies, such as tamoxifen or raloxifene."

Those two drugs have been shown to halve the odds of higher-risk women to develop the

disease, but they also have occasional dangerous side effects.

Ghidara said she has been taking estrogen since undergoing a hysterectomy in 1987, and she read recently that long-term estrogen replacement could increase her breast-cancer risk. She also had several breast biopsies, one of which turned up a precancerous condition—another risk factor.

"Fear of breast cancer was always in the background," she said. So when her doctor told her about the test, Ghidara was enthusiastic.

"He said it could help me to put my risk in the right perspective," she said. "I feel it can help me make a better decision, and I'll feel more comfortable with the decision I make."

She got her results this month. Dr. Michael Kinney of the Center for Advanced Breast Care in Arlington Heights told Ghidara she has an 18 percent chance of developing breast cancer before her 70th birthday—more than three times the average risk.

"Of course, you also have an 82 percent chance of *not* getting it," he said.

Ghidara said she was comforted by the "82 percent thing" but decided to have more frequent breast exams, to add ultrasound tests to her annual mammograms, to taper off her estrogen, and to consider taking tamoxifen or raloxifene.

Experts say the problem with the test is that the scientific literature is full of genetic markers that seem to be associated with breast cancer but don't pan out as predictors.

### 'A false sense of security'

"An individualized 'risk profile' based on common polymorphisms is extremely premature," said Dr. Kathy Albain, director of the breast research program at Loyola University Medical Center in Maywood. "It is likely that this information will either give women a false sense of security or else increase anxiety needlessly."

Dr. Wylie Burke, a medical geneticist at the University of Washington who was on the government's Advisory Council for Human Genome Research, notes there's no evidence that a woman with a high OncoVue score will benefit from tamoxifen or from imaging technologies like ultrasound or MRI.

"The data for the efficacy of tamoxifen is based on the Gail Model," a breast cancer risk assessment tool developed by the National Cancer Institute, said Burke. "If you want to take tamoxifen, get your risk assessed

in Gail."

In fact, Ghidara's OncoVue score isn't much different from her Gail Model score, which factors in information about a woman's personal and family history to produce a risk estimate. The model has been validated in large clinical trials, meaning it has been proved that women with higher scores are more likely to get breast cancer.

An interactive tool based on the Gail Model can be accessed for free at [www.cancer.gov/bcrisktool](http://www.cancer.gov/bcrisktool).

### Data not yet published

Shimasaki says OncoVue has been validated—women with higher scores are more likely to have breast cancer—but the data have not been published.

Until now, most genetic tests performed in a proprietary laboratory have not been subject to review by the FDA, which is responsible for ensuring safety and efficacy. Instead, they fell under the regulatory umbrella of the Clinical Laboratory Improvement Act. The act requires laboratories that perform medical tests to show proficiency, but it does not make manufacturers demonstrate that their tests are clinically useful.

In July the Federal Trade Commission warned there are no valid studies to support many of the genetic tests being marketed to consumers.

"Having a particular gene doesn't necessarily mean a disease will develop; not having a

particular gene doesn't necessarily mean that the disease will not," the commission said. "Genetic testing provides only one piece of information about a person's susceptibility to disease. Other factors, like family background, medical history and environment, also contribute."

Marketing of OncoVue was delayed when the FDA notified InterGenetics that it was assuming responsibility for regulating such tests and Clinical Laboratory Improvement Act oversight was no longer sufficient.

For the time being, women wishing to take the test must consent to be part of a trial. The discounted price for the test is \$397, which insurance does not

cover.

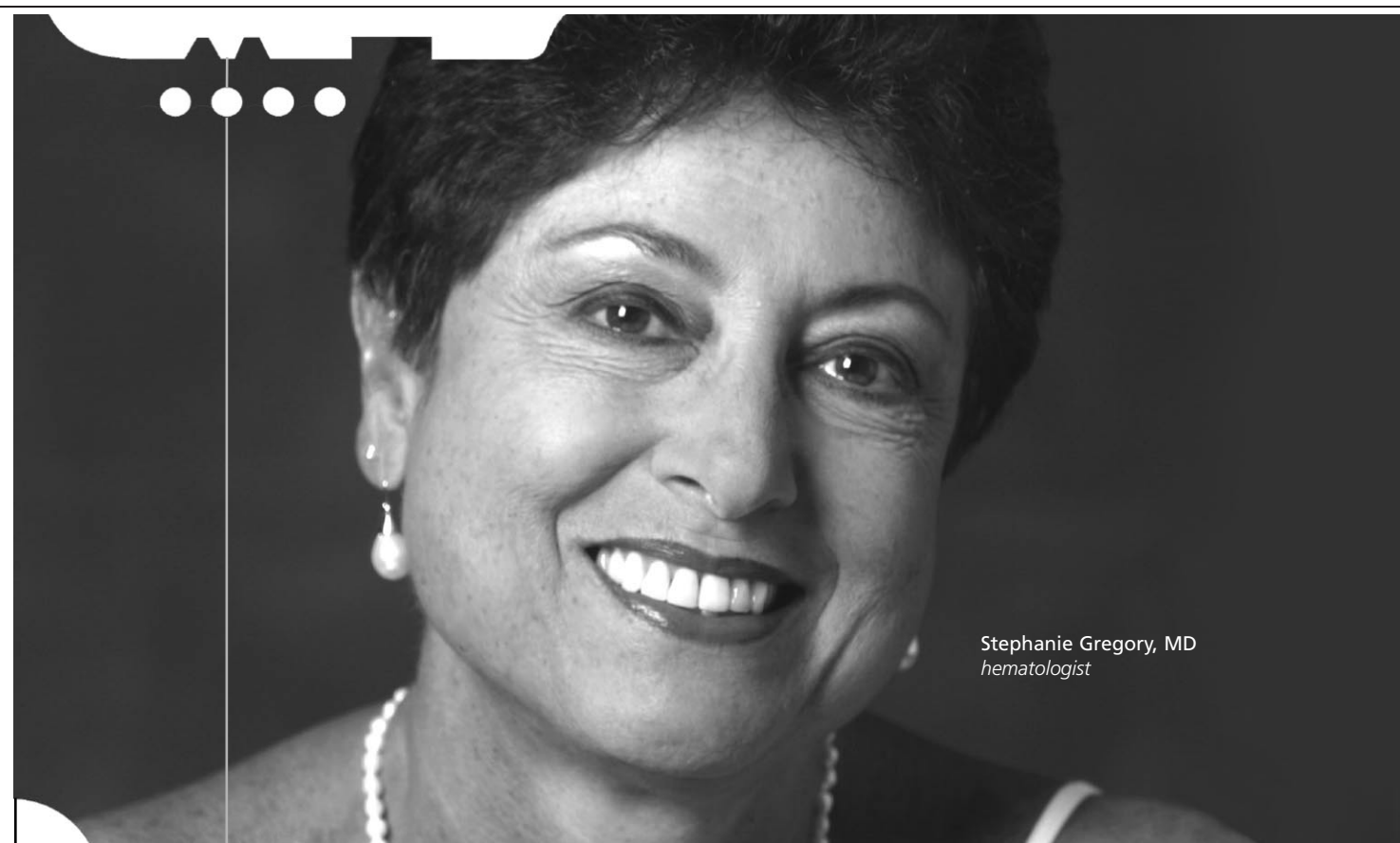
"The fact that FDA is reviewing this test reflects concern about the potential harm of making serious medical decisions based on data that no one has reviewed except those who are selling the test," said Burke.

But experts acknowledge that using genetic information to reduce medical risk is an intuitively appealing notion.

"Genetic tests are so cool," said Dr. H. Gilbert Welch of the U.S. Department of Veterans Affairs. "They have all these colors and matrices."

"There's a whole industry that's about to be launched, and you know it's going to scare a lot of people."

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