A BREAST CANCER YOU MAY NOT NEED TO TREAT

Here's five years' worth of a medication given to prevent breast-cancer recurrence.
AN INCREASING NUMBER OF WOMEN ARE BEING TOLD THEY HAVE "STAGE 0" CANCER AND NEED SOME COMBINATION OF SURGERY, RADIATION AND POWERFUL DRUGS. SOME EXPERTS NOW SAY THESE TREATMENTS ARE GOING MUCH TOO FAR

BY NANCY F. SMITH

PHOTOGRAPHED BY ADRIAN GAUT
The first sign of trouble is tiny white dots on a mammogram. The dots may be scattered like filigree along one of the ducts that connect milk-producing lobules to the nipple. They may be clustered in a single clump or spread among several of the ducts, often in a branching pattern. If these tiny dots of calcium are located inside the duct, if there is more than one locus of dots or if they create an irregular shape, they may indicate the presence of a disease known as ductal carcinoma in situ, or DCIS. In these cases, cells that might later become invasive cluster inside the milk ducts, but unless they penetrate the duct walls, they are not considered life threatening.

For this reason, doctors sometimes refer to DCIS as precancer. But because the cells are abnormal, the disease is also referred to as stage 0 breast cancer or in situ breast cancer. This lack of clarity in the nomenclature is emblematic of the disagreement among doctors and researchers about how aggressively the condition needs to be treated.

Until the widespread use of mammography, the calcium dots played essentially no role in finding potential cases of breast cancer, and diagnoses of DCIS were extremely rare. "Before 1980, fewer than 1 percent of detected breast cancers were diagnosed as DCIS. Now, because of breast-imaging devices, the figure is over 25 percent," says Todd M. Tuttle, MD, chief of surgical oncology at the University of Minnesota in Minneapolis. That translates into more than 60,000 new cases of DCIS every year in the United States, a rate of growth that will yield a million American women living with this condition by 2020.

To many doctors and cancer researchers, the rise in the detection and subsequent treatment of these pre-malignant lesions is an important cause of the recent 30 percent drop in the death rate for breast cancer. (The other much-cited factor is improved medical therapies.) According to mainstream medical wisdom, these numbers are proof positive that finding and aggressively treating potential breast cancers early can keep abnormal cells from spreading beyond the duct into adjacent breast tissue and perhaps further into lymph nodes, lungs, bones and elsewhere.

But a small and growing coterie of specialists and researchers don't buy the idea that medical intervention in the majority of DCIS cases necessarily improves women's health. They say there's no evidence that treating most instances of this precancer has been especially effective in slowing the growth rate of invasive breast cancer. "Despite all the women being diagnosed with early-stage cancer and being treated aggressively to keep their DCIS from spreading, the rate of invasive cancer hasn't gone down; it's gone up 25 percent," says Laura Esserman, MD, director of the Carol Franc Buck Breast Care Center at the University of California, San Francisco, School of Medicine. The thinking of Esserman and others is that for every precancer that is found and treated early, there should be a corresponding reduction in the advanced cancer it would have become. That is exactly what happened with colon and cervical cancer: Removal of precancerous lesions has led to dramatic drops in the rates of advanced instances of the diseases. But that isn't happening with breast cancer. "Maybe, for many cases, DCIS isn't the right precursor for doctors to be looking for," Esserman says. Esserman and others believe that the high diagnosis rate of lower-risk forms of DCIS has caused an epidemic of over-treatment. Since it's possible that some women's DCIS cells will never spread outside the ducts, Esserman is concerned that certain low-risk patients have been needlessly subjected to surgery and radiation. Maybe there are patients who would be better off untreated. "We need to test if doctors should leave some DCIS cases alone," Esserman says.

That's a controversial notion. Most breast-cancer specialists, while conceding that DCIS is overtreated, say they have no choice but to proceed as if the disease could become dangerous. "There's no scientific proof that there definitely is a group of DCIS cells that won't progress to becoming invasive."

**BREAST SELF-EXAM REVISITED**

Mammography reveals only 50 percent of all breast cancers, according to a major study. The other half are found by the woman, and these so-called interval cancers are often far more aggressive than those found in regular screenings. If they didn't show up on your mammogram, they may have developed quickly—and fast-growing tumors are worrisome. This means the breast self-exam maintains a critical role in monitoring your breast health. "What we don't think is a good idea is the very detailed breast exam where you worry about every lump," says Laura Esserman, MD, of the UCSF School of Medicine. When the U.S. Preventive Services Task Force suggested in 2009 that breast self-exams weren't effective, that's the kind they were describing. "But a 30-second exam every month or every couple of months in which you simply monitor your breast for any changes, that's absolutely important," Esserman says. If you find something new, bring it to the attention of your physician, even if you recently had a mammogram that was normal. —N.F.S.
With DCIS, radiation treatments commonly follow a lumpectomy.
don't think we're there yet, though this is a hot topic of research," says Brian J. Czerniacki, MD, PhD, codirector of the Rena Rowan Breast Cancer Center at the University of Pennsylvania and surgical director of the Immuno-therapy Program for the Abramson Cancer Center. Christine Larson, MD, head of the Comprehensive Breast Program at H. Lee Moffitt Cancer Center and Research Institute in Tampa, Florida, concurs. "We have no way of figuring out which cells are the bad players," she says. But Esserman and similarly minded breast-cancer specialists disagree; they believe that current technology is adequate for some doctors to distinguish between low- and high-risk DCIS cases.

Caught in the middle of this debate are the thousands of women with a DCIS diagnosis who face life-altering decisions about their treatment.

THE PATIENT'S DILEMMA

"We found an irregularity in your left breast," the phone message from Cathy Hop's doctor said. "We need to find out what it is, and to do that, you'll need a biopsy." It was a heart-stopping moment for the 50-year-old mother of two, who lives in Rancho Santa Fe, California. She recalls, "Of course, I'm thinking, I can't have breast cancer. No one in my family has had breast cancer. I'm a healthy person. I exercise. I eat right. I'm not overweight." But still she worried. The word irregularity could not completely blot out the G-word that kept popping into her head.

It took two and a half years, eight specialists and two biopsies for Hop to decide on a course of action. The first irregularity turned out to be benign, but a mammogram to confirm its presence revealed a second lesion in the same breast. When biopsied, that lesion was diagnosed as DCIS. Even though it was not, by definition, spreading outside her ducts, the treatment options laid out for Hop weren't all that different from those offered women with invasive breast cancer: lumpectomy (surgical extraction of the abnormal tissue and its surrounding area), lumpectomy followed by a regimen of radiation, or mastectomy (surgical removal of a breast), which does not require follow-up radiation.

The choice is presented as three levels of preventing recurrence—of making sure the cancer doesn't come back, as either DCIS or invasive breast cancer. With a lumpectomy, the recurrence rate is about 25 percent in 10 years. Half of those recurrences will be DCIS, and the other half will be invasive breast cancer. Among those who choose lumpectomy and radiation, 10 percent will have a recurrence—5 percent DCIS and 5 percent invasive. With a mastectomy, about 2 percent of cancer cases will recur, and almost all of those will be invasive. Looked at another way, all these patients have at least a 70 percent chance of living out their lives without having any more brushes with DCIS or invasive breast cancer. What about the survival rate? "The 10-year survival rate of all three of the treatment options is the same: about 99 percent," Tuttle says.

Today 97 percent of women with a DCIS diagnosis undergo a lumpectomy or mastectomy. Given that this is a precancerous condition, you'd expect that most would pursue the least aggressive treatment, yet mastectomy is the choice of 33 percent of DCIS patients, and that percentage is growing. Even more surprising, the number of DCIS patients who opt to have a healthy breast removed in a prophylactic double mastectomy is also on the rise, jumping almost 150 percent from 1998 to 2005, according to the Journal of Clinical Oncology.

What are their reasons? Some women opt for mastectomy because they don't need to undergo subsequent radiation treatment. One operation, they think, and they'll be done. (The truth is that there's still a small chance of DCIS or cancer recurrence in the scar.) A diagnosed woman's first reaction often is, "Just cut off my breasts so I
can get on with my life," says Susan Love, MD, president of the Dr. Susan Love Research Foundation, a nonprofit that promotes breast-cancer research. Sometimes women ask for both breasts to be removed when only one is diseased so that their reconstructions will match. "Doctors aren't doing a great job of talking women out of the surgery," Love says. "They're not explaining the consequences of mastectomies, such as that a woman likely will not have feeling in her reconstructed breasts."

What about the opposite approach—doing nothing? DCIS lesions are typically removed, so no one has studied the results of not taking them out. "We do know that if the cells stay in the duct, DCIS has no clinical significance whatsoever. It doesn't cause symptoms, it doesn't hurt you, it doesn't kill you," says E. Shelley Hwang, MD, chief of breast surgery at the University of California, San Francisco, School of Medicine. "The only reason we treat DCIS is we're worried that if we don't, it won't stay in the duct and will become invasive. DCIS surgery is basically preventive surgery."

Hopf's DCIS diagnosis landed her in this maze of risk statistics and probabilities of recurrence. "I consulted eight specialists," she says. "All recommended surgery and radiation. One said I should have a mastectomy. One told me the DCIS wasn't really cancer, and another said it was about to explode from the duct and become invasive."

Hopf says that as she struggled with her decision about treatment, "no one mentioned that my choice would have essentially no impact on my survival rate." She chose lumpectomy with radiation. "I'm comfortable with my decision," she says.

THE ANATOMY OF ABNORMAL CELLS

The confusion surrounding DCIS begins with those tiny white dots of calcium, a by-product of biological processes that can be caused by any number of events. The vast majority of these microcalcifications—about 70 percent—are associated with some kind of benign growth in the breast. The distribution and shape of the dots on the mammogram give some clues to their cause but cannot definitively identify DCIS. That diagnosis most often comes after what is known as a core-needle biopsy, in which a hollow needle is guided to the lesion by mammography, ultrasound or MRI. The needle draws out several samples of tissue, each about the size of a grain of salt. (See sidebar, "Get a Better Biopsy".)

The samples go to a pathologist, who stains the cells and examines them with a microscope. Sometimes there's a fine line between possible diagnoses. "Carcinogenesis is a process," explains Debra Patt, MD, a breast-cancer specialist at Texas Oncology in Austin. Step one: Cells begin to grow abnormally in what is called atypical ductal hyperplasia (ADH). Those cells are not malignant, but they aren't behaving normally either; nor do they look like normal tissue when examined under the microscope. The atypical cells can become so abundant that they begin to crowd their neighbors. "But your body has great ways of regulating itself, and it may be able to destroy the cellular abnormalities that people often develop," Patt says.

Usually that is what happens. But not always. Sometimes abnormal cells don't have the courtesy to die, and they reproduce until there are thousands of sheets of cells within the duct. It's this stage that characterizes DCIS and creates the confusion about how the same cells can be labeled "preneoplastic" by one expert and "cancer" by another. "DCIS cells look for all the world like cancer cells," says Hwang. One crucial difference: At this point, they're incapable of breaking through the duct's lining and invading the surrounding breast tissue. Another mutation is required before they can become invasive breast cancer," Patt says, and not all ADH cells undergo that final transformation.

In most cases, DCIS presents in two genetically distinct groups: high-grade lesions characterized by rapid growth and early progression to an invasive cancer, and low-grade lesions that more closely resemble atypical ductal hyperplasia. If these low-grade lesions, which can be difficult for a pathologist to distinguish from ADH, progress to invasive cancer, those tumors are frequently low grade, too.

Doctors on both sides of the debate agree that the high-grade DCIS lesions should be treated in the conventional manner. The push for change is focused at the low-grade end of the continuum. "The majority of DCIS is in this form," Esserman says.

THE CASE FOR THE SURVEILLANCE OPTION

Esserman is among the most outspoken of the voices for change. She and similarly minded breast-cancer specialists such as Hwang believe that it's time to seriously look into what's known as management by active surveillance. For DCIS, any lesion that doesn't appear high grade would be left alone and not biopsied. Instead, if suspicious calcifications are discovered in mammography screening, patients would be given the option of forgoing treatment while doctors monitor them intensely to see what develops. This strategy is already used in treating low-risk prostate-cancer patients, who do not undergo surgery or radiation unless the lesion progresses to a higher risk level. "With early stages of prostate cancer, there is a lot of discussion about watchful waiting and active surveillance, about how cancers come in different types and how the patient has lots of options," says Barson Lerner, MD, internist and medical historian at Columbia University Medical Center. "For DCIS, the conversation hasn't moved so much in that direction." And, he says, "to the degree that breast-cancer specialists consider close surveillance a reasonable option, women should be made aware of this choice."

Active surveillance of DCIS would resemble the course of treatment offered to women who have other risk characteristics for invasive breast cancer—for example, a family history of breast cancer, atypical ductal hyperplasia or lobular carcinoma in situ (LCIS). LCIS, which develops in the lobules just up the duct from DCIS, is also called breast-cancer stage 0, but it usually doesn't show up on mammograms and generally isn't treated. (LCIS, recently renamed lobular neoplasia, is most often detected...
when breast tissue is biopsied for another reason.) According to Esserman, “Virtually all patients with DCIS undergo surgery, whereas the majority of women with a similar degree of risk due to other conditions do not choose surgical treatment. What makes invasive treatment of DCIS the accepted standard of care? With DCIS, the site of likely recurrence is known, and there is an opportunity for surgical removal.”

The naysayers who oppose the watch-and-wait strategy for DCIS don't recommend playing the odds. They don't want to risk seeing a low-grade case of this precursor become invasive, spreading into the breast tissue and perhaps beyond. They cite the “what if” factor: What if a doctor doesn't do everything she can and the patient develops invasive cancer and requires even more aggressive treatments? Or dies? As any doctor will attest, it is impossible to guarantee beyond a shadow of a doubt that any individual's cancer won't turn out to be deadly.

In addition, the critics say, it is not entirely clear that all low-grade DCIS is low risk. Czernecki points out that some low-grade cases contain factors that correlate with aggressive cancer, such as scoring positive for the HER2 protein (although this situation is much more common in high-grade cases). Also, many experts feel that to examine all the affected tissue, a lumpectomy—not just the samples that come with a biopsy—is necessary. “I argue that we need to treat DCIS at a minimum with lumpectomy to make sure there's no invasive cancer present,” says Tuttle. Lumpectomies aren't complicated procedures. “This surgery is far less disfiguring than a mastectomy,” says Eric P. Winer, MD, professor of medicine at Harvard Medical School and chief scientific adviser for Susan G. Komen for the Cure, a large breast-cancer research and advocacy organization. Still, a lumpectomy can have side effects, notes Esserman. These might include scarring, a loss of sensation around the area that was excised and in rare cases an accumulation of fluid in the empty space created by the surgery.

A GAME PLAN FOR PATIENTS

If you receive a diagnosis of DCIS, don't feel you need to make a quick decision on treatment. “By the time DCIS appears on a mammogram, it’s been there for several years. If you spend two weeks or three weeks or a month to find the right people to take care of it, that’s not going to make any difference in the outcome,” says Shahla Masood, MD, head of pathology at the University of Florida College of Medicine in Jacksonville.

So, there's no reason to rush into surgery. “Too often a woman gets a DCIS diagnosis on Friday, and on Monday morning she's in the operating room.”

“I held out for two years after my DCIS diagnosis before having surgery,” says Diane Valentine, an elegant 63-year-old San Francisco Bay Area resident whose bearing reflects her nearly 24 years of teaching yoga. “I consulted a second doctor, and she told me the survival rate for DCIS was 95 percent, so I decided to take those odds.” Over the next two years, her progress was tracked with mammograms at six-month intervals, and there was no change in the lesion. “But the pressure was immense,” she says. “From my doctors, who warned it would be OK to wait three months, maybe six, but no more. From the students at my yoga school. From other breast-cancer patients. Everyone kept warning that I needed to get the cancer out. Now!” Ultimately, she had a lumpectomy, no radiation.

Today the standard of care for DCIS is to surgically remove every lesion, and that’s going to be the most common recommendation for women faced with this diagnosis. “But in the end, the decision about how you treat a cancer will always remain one patient, one doctor, one room,” Patt says. Doctor and patient weigh the risk of invasive cancer (based on whether the patient has had a lot of biopsies, has a family history of breast cancer or is a BRCA-gene carrier) against the risk of surgery. What does the pathology report say? Does it explain the abnormalities found in the mammogram? Then the doctor and patient decide on a course of treatment.

The whole process could be less anxiety producing if the medical world dropped the word carcinoma in relation to DCIS. “Once you say the word cancer, the patient hears nothing else,” Patt says. “It produces a visceral reaction that demands, ‘Make it go away!’” Masood has suggested using the term borderline breast disease for cases of atypical ductal hyperplasia and low-grade DCIS. Esserman proposes changing DCIS to IDLR, short for InDolent Lesions of Epithelial origin (indolent is medical jargon for inactive; epithelial refers to the tissue lining an organ).

There isn't exactly a groundswell of support for changing the name, but researchers are making great progress in deciphering the biological markers that can distinguish between DCIS cells that are truly dangerous and those that aren't. Until we know more, many experts believe the only option is to treat them all as if they're destined to break out of the milk ducts and into the remaining breast tissue. “Sometimes, with surgery, radiation and tamoxifen, we end up treating DCIS more aggressively than we do some invasive cancers,” says Love. “It’s a crime that we don’t really know what to do.”

NANCY F. SMITH, a freelance writer who lives in Austin, Texas, frequently reports on health, personal finance and travel.