

Breast Cancer: What Every Woman Should Know
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In 2005 she was honored with the 2005 Top Doctor Award by the research firm Castle Connelly. In 2004, she received Columbia University's John Jay Award for Professional Achievement and in 2001, Columbia University's Alumna Achievement Award. Dr. Bernik is the author of numerous medical journal articles published in, among others, *The Breast Journal*, *Journal of Nuclear Medicine*, *Annals of Surgical Oncology* and *The American Surgeon*. She is a principal investigator for breast disease research at St. Vincent's Hospital and has presented her research at symposia across the country, most recently at the American Society of Breast Surgeons 2006 annual meeting and the American Society of Breast Disease 2006 annual symposium

One in eight women will develop breast cancer during the course of their lifetime, making it, after skin cancer, the most common cancer in women. Although breast cancer primarily affects women, men can also develop the disease, albeit at a much lower rate. In 2006, there were over 175,000 cases of breast cancer and over 40,000 people died of the disease. Most people tend to think it is found only in older women, but it afflicts both the old and the young. In fact, breast cancer is the leading cause of death in women ages 15-59 and one in 229 women between the ages of 30 and 39 will develop breast cancer within a 10-year period.

What is breast cancer? Most breast cancers originate in the cells that line the *lobules* and *ducts* of the breast. The *lobules* are the glands where milk is produced and the *ducts* are the tubes that carry the milk out to the nipple. Breast cancer begins when one cell *mutates*, or undergoes an alteration in its genetic framework, or DNA, and starts growing and dividing rapidly and in a disorderly fashion. Cancer cells do not respond to the normal signals the body uses to regulate cell growth. Cancer cells drain the nutrients that normal cells need to survive, overgrow their boundaries and crowd out normal cells. They often form a mass, or *tumor*, that can invade surrounding tissue and potentially spread to other parts of the body.

The majority of breast cancers arise from the cells that line the ducts and are called *ductal carcinomas*. A cancer originating from the lobules is called *lobular carcinoma*. When a cancer is contained within the ducts of the breast it is called *ductal carcinoma in situ* (DCIS). This cancer is considered *preinvasive*, insofar as it has not spread from the ducts into the surrounding breast tissue, and

the survival rate of patients with DCIS is excellent. *Lobular carcinoma in situ* (LCIS) is actually not a true cancer, but rather an abnormal mass of cells. However, the presence of LCIS in a woman's breast, if left untreated, poses a significant risk to the patient of developing into an *invasive* breast cancer. An *invasive cancer* is one that has broken through the ducts or lobules and has started growing in the surrounding tissue. Invasive cancers are most often ductal (80%) or lobular (15%). At some point in their development, some cancer cells obtain the ability to travel from the breast to other parts of the body (*metastasize*) and grow in a new area.

What Causes Breast Cancer?

While the exact cause of breast cancer is unknown, it is generally believed that many factors play a role its development. Environment, genetic predisposition, diet and activity level can all affect a person's risk of breast cancer. Most researchers feel that exposure to the hormone *estrogen* can increase the risk of breast cancer; therefore, since estrogen is naturally produced by the body, the greatest risk factor is *simply being a woman*. Women who are exposed to estrogen for a longer than average period of time (for example, a woman who gets her first menstrual cycle under the age of 12 or goes through menopause over the age of 55) can be at increased risk for breast cancer. It has now been shown that *combination hormone replacement therapy* (estrogen combined with progesterone), taken to relieve the symptoms of menopause, also increases a woman's risk of breast cancer, again due to increased exposure to estrogen. Birth control pills, another form of estrogen introduced to the body, have not consistently been shown to affect breast cancer rates, possibly because the levels of estrogen found in most of today's drug preparations are quite low. Advancing age is a risk factor that can also be partially explained by the effects of estrogen exposure: as a woman gets older, there is more time for her breasts to be exposed to the natural estrogen in her body. Almost 80% of breast cancers are diagnosed in women age 50 and older.

Family history is another significant risk factor for developing breast cancer. Having a first degree relative (mother, sister, or daughter) diagnosed with breast cancer, especially if they were diagnosed before the age of 40, almost doubles a woman's risk of being diagnosed with breast cancer during her lifetime. However, it is important to know that almost 80% of people diagnosed with breast cancer have no immediate family history of the disease.

It is estimated that almost 10% of breast cancers are caused by genetic mutations. Significant progress has been made in identifying genetic defects that are responsible for hereditary breast cancer syndromes. The most common genetic mutations occur in the genes known as *BRCA I* and *BRCA II*. Women who have a deleterious mutation in one of these two genes have a 50-80% chance of developing breast cancer in the course of their lifetime and have a higher risk of developing ovarian cancer. These genes account for a significant proportion, but not all, of inherited breast cancers. Other genes that have

not yet been identified undoubtedly exist, and therefore a negative result from genetic testing, although reducing the likelihood of a genetic predisposition, does not entirely eliminate the possibility. A woman who has a significant family history of breast and ovarian cancer must still be followed closely.

On the other hand, having a baby early in life and breastfeeding are thought to decrease a woman's exposure to cyclical estrogen because they suppress the menstrual cycle and, therefore, the risk of breast cancer is lowered. Moreover, some factors that increase a person's risk of breast cancer can be modified. Alcohol use, even only one drink per day, can increase a woman's risk of developing the disease. Obesity appears to increase risk, and some studies have shown that increasing one's activity level with a regimen of exercise can decrease the risk. It is unclear if the decreased cancer risk is due to weight loss or activity level, as these often go hand in hand. It may be that both the lost weight and the increase in activity are independently important. What seems to make sense is that a healthy lifestyle overall contributes to overall breast health.

How Is Breast Cancer Detected?

Screening for breast cancer with *mammography*, unless one has a strong family history of breast cancer or a known genetic mutation that would require an earlier start, usually begins at age 40. Mammograms are intended to find cancers that are not detectable on physical exam, and ideally before they cause symptoms. The tumors detected by mammography are likely to be small, and the smaller the tumor is at the time of detection, the better the prognosis. However, most cancers are not found by screening studies. Because the most common presentation of a breast cancer is a painless new mass in the breast, self breast exam and a clinical breast exam by a physician are important tools in detecting breast cancer at an early stage. Therefore, every woman should start breast self exams in her 20's to get familiar with the way her breasts look and feel. Breasts are inherently lumpy and it is important for a woman to report any changes that are new or different and persist through a menstrual cycle. Aside from the presence of a new mass in the breast, other symptoms of breast cancer are swelling, skin changes, nipple inversion, nipple discharge or rash, or a lump under the arm.

If a *palpable* breast mass is detected, one that can be felt by hand, it needs to be pursued further. A mass must feel benign on physical exam, look benign (noncancerous) on radiological studies and appear benign pathologically to avoid surgery to remove it. Radiological studies may include a mammogram, *ultrasound*, and in selected cases, *magnetic resonance imaging (MRI)* or *ductogram*. Each of these technologies uses a different method to determine if a mass is benign or malignant-appearing. Mammograms use X-rays to look at the breast tissue. The level of radiation used is low and newer technologies such as *digital mammography* minimize the patient's exposure to radiation. Ultrasound, or sonogram, uses sound waves and can help distinguish a cyst, or a fluid filled cavity in the breast, from a

truly solid mass. If a person has dense breast tissue, ultrasound may visualize a mass that cannot be seen by mammography. Ultrasound will pick up a few of the cancers missed by mammogram, but if a mass is as dense as the breast tissue surrounding it, the mass will be undetectable by sonogram as well. MRI's use magnetic fields to create a picture of the mass and are probably the most sensitive test we have to detect a breast cancer. However, they are very expensive and time consuming and they sometimes find lesions that look suspicious but are really benign, which can lead to unnecessary biopsies and emotional distress. They need to be used with caution and in a very select group of women.

MRI's also do not detect 100% of breast cancers, and a benign-appearing MRI study does not always mean that cancer is absent. Even if a palpable mass appears benign using these techniques, a *biopsy*, the removal of cells or tissues for examination by a pathologist, still needs to be obtained. There are several kinds of biopsy procedures, including *fine needle aspiration (FNA)*, *core biopsy*, *stereotactic biopsy*, or *surgical excision*. An FNA is the smallest and least invasive biopsy available. A thin needle is passed in and out of the breast mass and a collection of cells are pulled into the hub of the needle. These cells are then put on a slide and a pathologist looks at the sample under a microscope. When an adequate sample is obtained through this method, a trained *cytopathologist* can determine with 95% accuracy whether the mass is benign or malignant.

When a mass is large or is clearly seen on ultrasound, a *core biopsy* can be carried out. This type of biopsy requires local anesthesia and a small nick in the skin. A piece of the mass is removed through a large bore needle so that the tissue can be examined by the pathologist in its native configuration. If the lesion is only seen on mammogram, a similar biopsy, called a *stereotactic biopsy*, will be performed. With this test, the breast is placed in compression, as if a mammogram was being performed, and a needle is guided to the area in question with the aid of a computer. Samples of the mass are then extracted via the needle as the breast remains in compression. If a tissue diagnosis is not possible with the above methods or the findings from the pathology and the radiological studies are not in agreement, an *open surgical excision* is performed, removing the entire mass for further study.

Understanding the Pathology Report

We have already seen that a tumor found in the breast may be benign or malignant. We also discussed the differences between lobular carcinoma and ductal carcinoma, and what makes a cancer invasive or pre-invasive. Equally important in determining the future course of the disease is knowing the *grade* of the tumor. The grade of the tumor tells us the tumor's potential for growth. Tumor grade is determined by examining the appearance of various structures within the tumor, such as the cell nuclei, and the rate of cell division. A *low grade* or *well differentiated* tumor is slower growing and approximates normal tissue; a *high grade*, or *poorly differentiated* tumor is fast growing and the cells are very abnormal-looking; an *intermediate* or *moderately differentiated* tumor is in the middle.

Another important component of evaluating a cancer is to determine if the tumor is *estrogen receptor* (ER) or *progesterone receptor* (PR) positive or negative. A normal breast cell has *receptors* on its surface that allow estrogen and progesterone to attach to the cell, stimulating it to grow. If a tumor cell has the same receptors, it will also grow and divide more rapidly in the presence of estrogen or progesterone. These tumors can be treated with medications that block the receptors or lower the levels of the hormones in your body, often in combination with chemotherapy, slowing the tumor's growth. HER2 is a gene that helps control cell growth by increasing the production of a cell surface protein. If there are too many copies of the gene present, the cell receives signals to grow and multiply. These tumors are thought to be more aggressive than tumors that are HER2 negative. However, there are newer drugs that can target cells that are HER2 positive, slowing their growth, and these drugs have been shown to be very effective in improving survival.

Once breast cancer is diagnosed, the disease needs to be *staged* in order to determine the treatment needed and the prognosis a patient faces. The stage is based on tumor size, whether the cancer has spread to the lymph nodes under the arm, and whether the disease has spread to parts of the body beyond the breast and lymph nodes. Ductal carcinoma in situ is *Stage 0* disease: the cancer cells are contained within the duct and have not spread into the surrounding tissue. The disease cannot spread to other parts of the body and the long term survival is 99%. *Stage I* disease is a tumor smaller than two centimeters that has not spread to the lymph nodes under the arm. *Stage II* disease is one where the tumor is 2 to 5 centimeters in size and the cancer has spread to up to three lymph nodes. It also includes tumors greater than 5 centimeters in size without nodal involvement. *Stage III* tumors are less than or equal to 5 centimeters with four or more positive nodes or larger than 5 centimeters with any nodal involvement. *Stage IV* disease refers to patients who have disease outside of the breast and in the nodes found under the arm.

Treating Breast Cancer

There are many treatment options for patients with breast cancer. These include *surgery*, *chemotherapy*, *radiation*, *endocrine therapy*, and *immunotherapy*. These therapies are defined as either *local* or *systemic* treatment. Local therapies (surgery and radiation) treat the breast and *axillary* (underarm) region. Chemotherapy, endocrine therapy and immunotherapy treat cells that may have left the breast and traveled to other parts of the body.

Most women with breast cancer will need some type of surgery. Surgery is used to remove the tumor, check to see if disease has spread to the lymph nodes under the arm, and, in cases of advanced disease, remove bulky tumors to relieve discomfort. There are two main choices for surgery in the breast. One is a *mastectomy*, the removal of the entire breast, which may be performed with or without reconstruction of the breast. The other is a *lumpectomy*, the excision of the tumor along with the removal of a wide margin of normal tissue around the tumor, followed by radiation. Radiation is treatment with

high energy X-rays to shrink or kill any tumor cells that may be left behind but cannot be seen. Radiation is usually delivered as a beam of energy from a large machine. The patient lies on the table for approximately 5 minutes in the same position while the radiation is delivered to the affected area. This form of radiation is delivered five days a week for just over 6 weeks in most cases. *Internal radiation* involves administering radiation through tubes or a balloon placed in the breast. The advantage to this regimen is that it takes a much shorter period of time to complete, usually only one week. Recent studies have also shown that in some women with aggressive forms of breast cancer, radiation may be used even in the case of a mastectomy, so one cannot assume that having a mastectomy will allow the patient to avoid the need for radiation.

More and more women are opting to keep their breast if it's possible to do so with an acceptable outcome. This decision, along with the definition of "acceptable" is different for every woman. In some cases where the patient chooses a lumpectomy, the surgeon is unable to "*clear the margins*" surgically, that is, remove enough of the tissue surrounding the tumor to ensure no cancer cells are left and still provide an acceptable cosmetic result. If the surgeon is unable to clear the margins after several attempts, a mastectomy is usually needed. Some other reasons to choose a mastectomy can be the presence of tumor in more than one area of the breast, a history of previous radiation to the chest, small breast size, genetic predisposition, or a concern that the cancer may recur locally, among others. The decision needs to be discussed carefully with your surgeon.

With either procedure, the patient will need to have the lymph nodes under the arm evaluated. Most physicians feel that if there are cancerous cells in the lymph nodes under the arm, the cancer may have spread to other parts of the body. Years ago, the only way to tell if the lymph nodes were involved was for the surgeon to remove the majority of the nodes under the arm. Because the lymphatic system helps reabsorb fluid that gets pushed out into the tissues, their removal in some cases led to *lymphedema*, a permanent swelling of the arm. Over time, surgeons came to understand that the entire lymphatic drainage of the arm goes to just a few nodes first before going to the rest, much like a funneling system. With this knowledge, the *sentinel lymph node biopsy procedure* was born. In this procedure, usually two types of dye, a visible blue dye and a radioactive dye, are injected around the tumor or around the nipple. The dye takes the same path a tumor cell might take if it were to break free from the tumor. The dye gets trapped in the first few nodes, or sentinel nodes, that drain the breast. These nodes are then removed and examined for disease. If there is no disease seen in these nodes, there is no need to remove additional nodes under the arm and the risk of lymphedema is greatly reduced.

Chemotherapy

Chemotherapy for breast cancer usually involves a combination of drugs that kill tumor cells in the breast and, more importantly, cells that may have traveled elsewhere. Chemotherapy is *cytotoxic*,

meaning that the drugs will work to kill any rapidly dividing cells in the body, whether or not they are cancerous. This explains many of the side-effects experienced by patients such as hair loss, decreased red and white blood cell count and gastrointestinal symptoms (cells that line the intestines grow relatively rapidly). The drugs may be given intravenously, by mouth or by injection and usually in cycles, in order to allow the body to recover from their effects. There are many combinations and classifications of drugs available and the best course of treatment needs to be chosen in consultation with your *medical oncologist*, the doctor responsible for helping you make decisions regarding chemotherapy.

Endocrine therapy can be used by patients with cancers that have receptors for estrogen and progesterone. Therapies can include Tamoxifen, *aromatase inhibitors* in post-menopausal women, or *ovarian ablation*, drug therapy to suppress the production of estrogen. Herceptin® is a drug that works as an *antibody*. The drug attaches to the receptor created by the HER2 gene and marks the cell for destruction. There are newer drugs being developed that will target cancers that over-express the HER2 gene, offering more hope to woman with this aggressive form of disease. Again, the specific agent and length of treatment need to be discussed with your medical oncologist.

What is very important to remember when considering potential therapies is that each patient is an individual and what works with one patient may not work with the next. Also, remember that there are choices involved in treatment planning and there may be more than one path a patient can choose regarding her therapy. You need to discuss your choices carefully with your doctors and, if needed, seek more than one opinion about the treatment to be used.

Chemotherapy and Fertility

Chemotherapy can affect a woman's fertility by damaging the ovaries. The older a patient is at the time she begins chemotherapy, the more likely she is to suffer infertility. Chemotherapy can also produce an earlier menopause even if it does not make a woman completely infertile at the time of treatment, because it can reduce the number of functioning eggs. There are treatments available for women who wish to preserve their fertility and the science behind the various treatments is continuing to improve. Currently, the best method of preserving fertility is to freeze embryos. This involves in vitro fertilization, high dose hormones, and donor sperm from a husband, partner, or sperm bank. Hormones used in the treatment often include estrogen, which theoretically could be a problem if a patient has an estrogen receptor positive tumor; however, many oncologists feel one round of high dose estrogen may not pose an unacceptable risk to the patient. There are also drugs that can be used that are known to be safe in the setting of breast cancer, such as Tamoxifen or Letrozole. This should be discussed with your doctor in advance if possible.

Other possible options that are less well studied include egg freezing, where eggs are frozen without first being fertilized. Another, ovarian tissue freezing for later re-implantation, is less well studied. Still another is *Gonadotropin-releasing hormone analog treatment*, that can be given to suppress the

activity of the ovaries and put them in a dormant state while the patient receives chemotherapy. The effectiveness of this treatment is currently under study.

Choosing a Surgeon

Traditionally, surgical breast care has been provided by the general surgeon. While most or many general surgeons still treat breast patients in their practices, over the last 20 years or so breast surgery has become established as a separate subspecialty, especially in large cities. The reasons for this are many. Issues surrounding breast care are very emotional and require an abundance of time and discussion. More and more patients are sent to a breast specialist when dealing with breast cancer, as the vast amount of research in the field has led to subtle changes in management and treatment and the surgeon needs to stay informed and educated. This requires a large amount of time and effort and a true dedication to the field. You will want a surgeon who is not only knowledgeable and technically skillful, but also someone who can explain clearly the type of treatment you will need and guide you through potential pitfalls along the way. If possible, seek the recommendation of a physician you trust. Also, remember that this will be a relationship that goes on for years after your surgery, so you must actually *like* the surgeon you choose, as you will be seeing a lot of him or her in the future. Make sure your surgeon takes the time you need to answer questions and explain procedures, doesn't try to rush you into decisions, and doesn't get annoyed if you ask if a second opinion might be beneficial (whether you get one or not). In any case, take the time you require to make an informed, well thought-out decision about where to have your surgery.

Getting a Second Opinion

Because there are often many choices of treatment for breast cancer, many people get second opinions. Does everyone need a second opinion? The answer is no. If you are comfortable with your surgeon, medical oncologist, and radiation oncologist, you received your referral from a reliable source and you are completely comfortable with the treatment plan, do not feel obligated to get a second opinion. However, there are many times when it might be helpful. Breast cancer is a complicated subject and sometimes hearing the information more than once and in a slightly different way is helpful in understanding your condition. If you are told you need a mastectomy but are not convinced that this is the right course of action, seek a second—and perhaps a third—opinion. If you are given several different choices of chemotherapies to consider and you are not sure how to proceed, get another opinion. However, do not simply keep looking for the doctor who is willing to tell you what you want to hear just to get you in their door. It is most important to do lots of research before your doctor visit and when a physician gives you an opinion, make sure it is a well thought-out plan by asking questions.

Breast Reconstruction

When breast conservation is not possible or a woman prefers to have a mastectomy, she may decide to reconstruct the breast. The first phase of reconstruction is usually done at the time of the mastectomy. There are two main forms of reconstruction. *Implants* are placed under the muscle of the chest wall. *Autologous tissue transfer* is a procedure where tissue is taken from another part of the patient's body and is used to reconstruct the breast. The most common areas from which tissue is taken are the abdomen (*transverse rectus abdominus muscle (TRAM) flap*), the back (*latissimus dorsi flap*), or the buttock (*gluteal flap*). There are many reasons why a patient may be a candidate for one form of reconstruction but not another. These issues need to be discussed both with your breast surgeon and your plastic surgeon. Many women have concerns about the cost of reconstruction. It is important to remember that if a mastectomy is covered by your insurance plan, then by law the reconstruction is covered as well, as long as you seek the care by a plastic surgeon in your health care network.

Complementary and Alternative Medicine (CAM)

When someone is diagnosed with any kind of cancer they want to do whatever they can to fight the disease. Some people will turn to *complementary or alternative medicine*. Complementary and alternative medicine encompasses therapies that are outside the standard treatments of chemotherapy, hormonal and immunologic therapy, surgery, and radiation therapy and are used in conjunction with these more generally accepted therapies. Some types of CAM include herbal medications, dietary supplements, acupuncture, massage, reflexology, reiki therapy, and tai chi, to name a few. A patient must be forthcoming with her doctors about her decision to incorporate CAM as part of her treatment. Many herbs and dietary supplements may counteract the effects of the standard therapies. Be aware that, although the term "herb" sounds milder than "chemotherapy," there is some overlap between the two: some chemotherapeutic agents are derived from plants that are popular with herbalists. Herbs are also unregulated and can be administered without the approval of the FDA. Some can cause serious side effects such as liver damage and bleeding and because they are readily available, patients will often self-medicate. With proper use, CAM can have many benefits, but it needs to be carefully incorporated into the treatment plan.

Comprehensive Cancer Care

One of the greatest challenges for cancer patients, and especially the newly diagnosed patient, is managing all of their medical appointments. Dealing with appointments, treatments and tests located in different places around town is not only time consuming, but the added frustrations of scheduling, parking, traffic and potentially disjointed medical care increases the burden on the patient. It's a juggling act and it can be exhausting. In the 1980's, the idea of the comprehensive cancer center was born. In this

environment, all services are delivered under one roof. A patient can have her surgery, chemotherapy, radiation, imaging studies and lab tests in one place. Most centers often offer nutritional advice, social services, support groups and on occasion, access to complementary medicine. It can make a difficult time a little easier.

Do you have to seek care at a comprehensive cancer center? No, but if your doctors are under one roof, you can be sure that they talking to each other about your care so that everyone is on the same page. You want your care to be coordinated so that should problems arise, your doctors are informed and available to help.

Taking Charge

Women with breast cancer face many challenges. Whether a woman is young or old, this is a frightening disease. The patient must take advantage of the many resources that are available for help along the way. As hard as it may be, keeping a positive, yet realistic attitude can make all the difference. There are advances every day that lead to more hope. As strange as it may seem, one should use the disease to take charge and to focus on the things that really matter in life. It is often through hardship that we see clearly and learn more about ourselves and of what we are capable. Breast cancer survival is good and is only getting better. Not everyone will survive breast cancer, but death is not the benchmark of the victor, as everyone in this world will pass in time. The spirit of those who endure the disease with dignity and strength, and truly make the most of their time on earth, is the lasting mark of the winner.
