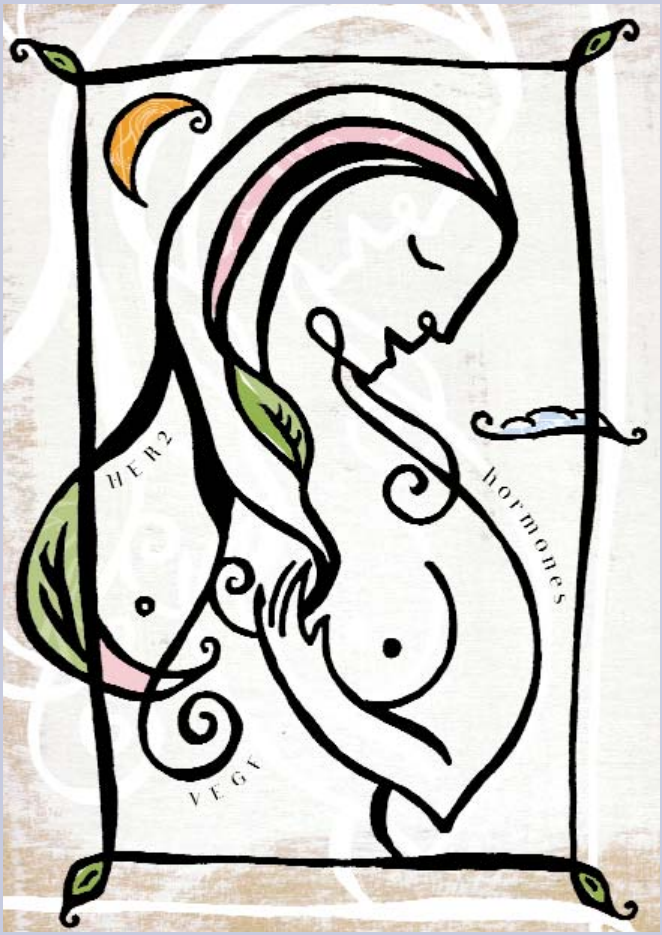
A Patient's Guide to Breast Cancer



Genetic Risk Factors ■ Breast **MRI** ■ **Prevention** Trials ■ **Targeted** Therapies
■ **New Treatments** ■ **Exercise & Nutrition** ■ **Survivorship** ■ **and More**

cure
CANCER UPDATES, RESEARCH & EDUCATION

Based on science, but filled with humanity, *CURE* makes cancer understandable.

A Patient's Guide to Breast Cancer

MORE THAN 200,000 women and 1,500 men will be diagnosed with invasive breast cancer in the United States in 2005, with another 58,000 receiving a diagnosis of early-stage breast cancer. With a lifetime breast cancer risk of one in eight for American women, the good news is that although more women are being diagnosed with the disease, more are surviving due to early detection and advancing treatment options. **This guide includes information for women who are newly diagnosed with breast cancer and those who want to know more about this disease for themselves or their family.**

Detection & Prevention

Q&A on Inherited Breast Cancer with Joanne Blum, MD, PhD

Of women born today in the United States, 13.2 percent will develop breast cancer at some point in life.

But for the 5 to 10 percent of women who carry an abnormal BRCA1 or BRCA2 gene, the risk jumps to 85 percent by age 70. In addition, these women have an increased lifetime risk of ovarian cancer.

Joanne Blum, MD, PhD, is director of the Hereditary Cancer Risk Program at Baylor Charles A. Sammons Cancer Center in Dallas.

Q When should a woman be concerned about an inherited component in her cancer?

Women with early onset breast cancer diagnosed prior to age 50 should be concerned, as well as women with a history of bilateral breast cancer, women with a family or personal history of ovarian cancer and males diagnosed with breast cancer. Women of Ashkenazi Jewish heritage with a personal or family history of breast or ovarian cancer also have a one in 40 chance

of having a mutation in BRCA1 or BRCA2 compared with the general population, which has a one in 1,000 chance of carrying a mutation. All of these criteria do not have to be met. Young age at onset of breast cancer alone is associated with a 10 percent chance of an inherited form of breast cancer.

Q If a woman decides to be tested, what is the next step?

We have counseled more than 800 women since the inception of our program in 1997. Of the patients we have tested, we've counseled approximately 100 carriers. If a woman or man carries a BRCA1 or BRCA2 mutation, we discuss increased surveillance, which includes monthly breast self-exams, yearly exams, mammography and MRI. Other options include prophylactic mastectomy and prophylactic salpingo-oophorectomy, which removes the fallopian tubes, because these women are also predisposed to developing cancers of the fallopian tubes. Some have also argued that there might be some role in removing the uterus. We know that for premenopausal women, undergoing salpingo-oophorectomy reduces the risk of developing ovarian cancer by 96 percent and breast cancer by 50 percent among mutation carriers. Undergoing prophylactic mastectomy reduces the risk of developing breast cancer by over 90 percent. There aren't too many things in medicine that have such high preventive power. Other strategies include chemoprevention options like tamoxifen.

Q What about family members?

We recommend genetic testing for family members of mutation carriers once they are over 18.

For more information, visit www.cancer.gov/search/geneticsservices or contact the National Society of Genetic Counselors at www.nsgc.org or 610-872-7608.

Preventing Breast Cancer

Recently, results from several large randomized clinical trials demonstrated that incorporating aromatase inhibitors, such as Arimidex® (anastrozole), Femara® (letrozole) and Aromasin® (exemestane), into therapy regimens following surgery significantly reduced the risk of breast cancer recurrence in postmenopausal women.

This benefit was seen whether the aromatase inhibitor (AI) was used initially or sequentially following **Nolvadex®** (tamoxifen, www.tamoxifen.com). What may be equally important is that researchers observed a substantial decrease in the number of new primary cancers in the opposite breast, suggesting these drugs may act as preventive agents and could possibly be used to reduce risk in healthy women.

Estrogen plays a key role in stimulating the growth of certain forms of breast cancer, and thus, it seems reasonable to think that blocking the action of estrogen might interrupt the development of new cancers. AIs (www.arimidex.com, www.aromasin.com, www.femara.com) are a new class of hormonal agents approved for breast cancer. This approach has been

tested with promising results.

Women at increased risk of developing breast cancer were randomized to treatment with either tamoxifen or a placebo in the International Breast Cancer Intervention Study 1 (IBIS1). In this study, tamoxifen reduced the number of new breast cancers when compared with a placebo. However, tamoxifen is associated with an increased risk of potentially serious side effects, such as blood clots. Researchers are trying to identify agents with comparable activity but fewer risks.

The International Breast Cancer Intervention Study 2 (IBIS2) will compare Arimidex with placebo in postmenopausal women. This study began in 2003 and will follow 6,000 high-risk women. Entry requirements include risk factors such as family history of breast cancer, late menopause or increased mammographic density. Women on the study will receive either Arimidex or placebo for five years.

Another study, named ExCel, will examine the potential preventive benefit of Aromasin. The ExCel study will enroll approximately 4,500 postmenopausal women 35 and older. Women must have an elevated risk of developing breast cancer, measured by risk factors including age and family history. Researchers are hopeful that they could see as much as a two-thirds reduction in cancer incidence with Aromasin and expect to have preliminary results within four years.

Women who wish to participate in the ExCel study, which is currently recruiting patients in North America, can visit www.excelstudy.com or call 800-4-CANCER in the United States or 888-939-3333 in Canada.

Diagnosing Breast Cancer

Mammograms, which have been a staple in breast cancer detection, have reduced the fatality rate for breast cancer by nearly 25 percent. But in a small population of women, mammograms may not be enough.

Almost half of all screening mammograms fail to detect early breast cancer in women with an inherited genetic mutation due to either dense breast tissue or certain pathological features of their tumors. This genetic mutation of BRCA genes causes an aggressive type of breast cancer that can grow and spread to lymph nodes in under a year, just below the radar for annual mammogram screens.

Magnetic resonance imaging (MRI) shows the tissue vascularity in the breast that mammograms cannot by using a large magnet and contrast dye instead of radiation to build two- and three-dimensional pictures of the breasts. MRIs can also better detect tumors in dense breast tissue, common in young women, than a mammogram. MRI screening is highly sensitive and identifies cancer not seen on mammography films in approximately 4 percent of cases.

MRI technology, in widespread use for about 20 years, has been used fewer than 15 years for breast cancer detection. As the technology advances, MRI machines are getting smaller, more compact and less expensive. Open MRI machines are available for claustrophobic patients or those who cannot fit into the hole in the middle of the MRI machine.

The downsides are that MRIs are very costly, reading the MRI scans can differ based on radiologists' interpretations and women with pacemakers or other metallic objects in their body are not able to use MRIs. Survival advantage with MRI over mammography has not been proven in a clinical study, and in some rare instances, mammography scans detected cancer while the MRI failed.

While annual mammograms are a key diagnostic tool, it is either too little or too late for some women, most notably those with fast-growing, aggressive cancers. Women with a family history of breast cancer, dense breast tissue or breast implants may consider MRIs in addition to an annual mammogram if they are over 40 or at high risk for breast cancer.

To find an MRI-accredited facility in your area, visit www.acr.org.

Gene Analysis

Gene profiling may be the future for classifying cancers and deciding the best treatment for individual patients.

In the past, breast cancer patients were treated based on simple guidelines, such as tumor size, if and where the cancer had spread and if cancer cells were hormone receptor positive. Today, with a sample of the patient's tumor cells, doctors can look at the cancer's gene expression profile using a microarray, where thousands of genes can be viewed at once to determine the degree to which they are being expressed in certain cancers.

Oncotype DX™, an assay that determines the likelihood of recurrence in certain breast cancer patients, analyzes 21 genes in early-stage estrogen receptor–positive disease in women taking tamoxifen. Recurrence scores can predict the likelihood of recurrence, which may help the physician and patient make a decision on whether to take adjuvant chemotherapy (chemotherapy after surgery and radiation). Interestingly, the recurrence score given by the Oncotype DX assay (www.genomichealth.com/oncotype) can predict response to chemotherapy in patients with advanced breast cancer.

MammaPrint®, a 70-gene profiling microarray assay used in young women with primary invasive breast cancer, helps determine the risk of recurrence after surgery and radiation. If this 70-gene profile signature shows that a woman has a high risk of recurrence, chemotherapy is recommended. If a woman tests negative for this signature, she could be spared chemotherapy and its side effects. MammaPrint (www.molecularprofiling.com) became available in the United States in January.

The **Breast Cancer ProfileChip** (BCPC), the first analytical tool based on microarray technology created for a hospital-based program, looks at nearly 1,000 genes. Assays are usually sent to outside laboratories to be analyzed, but BCPC (www.ipsogen.com) will allow patients to have the test analyzed at the clinic or hospital, speeding up the process.

With gene profiling, doctors can be better equipped to know what treatments will work best and if the cancer will return.

Treatment Options

New Adjuvant Treatment for Breast Cancer

Herceptin® (trastuzumab) was approved in 1998 for the treatment of women with metastatic breast cancer whose tumors have increased amounts of HER2 protein.

Presence of HER2 protein on the surface of breast cancer cells is associated with a poorer outcome. In the tumors of up to 25 percent of breast cancer patients, the gene responsible for production of HER2 is increased from the usual two copies to over 30 copies (called gene amplification). Breast cancer patients that have HER2 gene amplification in their tumors are candidates for treatment with Herceptin (www.herceptin.com).

There are over 160,000 women who are diagnosed with early-stage breast cancer each year that is treated with surgery and radiation. About 20 percent of them (about 30,000) have HER2 gene amplification in their tumors.

Three recent studies presented at the 2005 meeting of the American Society of Clinical Oncology examined the addition of Herceptin to traditional chemotherapy after surgery and/or radiation in women with HER2-positive early-stage breast cancer. Each one of these studies showed a marked decline in the risk of recurrence in women who received Herceptin with chemotherapy.

Two adjuvant trials of Herceptin have been conducted that involve the treatment of HER2-positive breast cancer patients, most of whom had cancer cells in their lymph nodes, with standard chemotherapy followed by Taxol® (paclitaxel) with or without weekly Herceptin for one year. Both studies demonstrated a significant improvement in disease-free and overall survival. The addition of Herceptin to Taxol in both trials reduced the frequency of breast cancer recurrence by more than 50 percent compared with Taxol alone. Herceptin was associated with a slight increase in cardiac damage (weakening of the heart).

The third trial, called HERA (HERceptin Adjuvant), is being conducted in 39 countries and began enrolling women with breast cancer in December 2001. In the HERA study, which has enrolled nearly 5,100 patients to date, patients are treated with standard chemotherapy after surgery with or without Herceptin for either one or two years. This trial showed that the addition of Herceptin to chemotherapy dramatically increased the disease-free survival of breast cancer patients after surgery.

These preliminary results are very exciting for doctors and patients alike as they provide a good option for patients with this aggressive form of breast cancer. Longer follow-up is needed to see if this decline in recurrence improves the long-term survival of these patients.

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If you have been diagnosed with HER2-positive breast cancer, ask your doctor if you should be considered for treatment with Herceptin. For more information about clinical trials with Herceptin, go to www.clinicaltrials.gov.

Avastin in Breast Cancer

Avastin™ (bevacizumab) may soon revolutionize treatment options for women with newly diagnosed advanced breast cancer.

A recent study (referred to as the E2100 trial) involving a large number of women with previously untreated metastatic breast cancer found that adding Avastin to standard Taxol chemotherapy increased the period of time their cancer remained under control by four months. This was a significant advantage, and it is important to note that Avastin did not work alone, but allowed the chemotherapy to work better. It is recommended that both drugs, which are delivered intravenously, be taken together.

Avastin, a novel targeted drug developed by Genentech, was originally approved by the FDA in February 2004 for use in combination with chemotherapy to treat patients with colorectal cancer. Recent findings have shown that Avastin also works with chemotherapy in treating certain types of lung cancer.

Avastin is a humanized monoclonal antibody that binds to an important protein called vascular endothelial growth factor (VEGF), which is responsible for new blood vessel growth in normal cells as well as cancerous tumors. Avastin works by blocking the growth of these new blood vessels, which carry food and oxygen to the tumor, essentially choking the blood supply to the tumor and causing it to die. By doing this, Avastin helps chemotherapy drugs kill more cancer cells.

In the near future, it is anticipated that physicians will begin to incorporate Avastin into chemotherapy treatments in order to starve the patient's tumor and extend the length of disease-free survival.

Overall, Avastin is very well tolerated with minimal side effects that include high blood pressure and an increased risk of blood clots, which can, in rare instances, cause stroke. A rare complication seen with Avastin was perforation of the intestinal wall.

Studies combining Herceptin with Avastin in women with HER2-overexpressing breast cancer are now ongoing.

For more information about Avastin, visit www.avastin.com.

New Drugs in Breast Cancer

ABRAXANE® (NAB PACLITAXEL)

Because Taxol does not dissolve well in water, it is formulated in an oil-like substance called Cremophor that may cause severe allergic reactions. **Abraxane**, which is injected by 30-minute intravenous infusion, is made with a normal human protein called albumin. By taking advantage of a tumor's increased need for nutrients, particularly albumin, drug delivery is made easier. The FDA approved Abraxane in January 2005 for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy. The most common side effects are hair loss and numbness in the hands and feet. For more information, visit www.abraxane.com.

LAPATINIB (GW572016)

Lapatinib is a small-molecule tyrosine kinase inhibitor of the epidermal growth factor receptor (EGFR) and HER2, which may become overactive and cause uncontrolled growth in a number of solid tumors. Blockage of both receptors simultaneously might avoid potential drug resistance and has been shown to be effective in treating patients whose tumors have failed to respond to Herceptin therapy. The most frequent side effects were rash, fatigue and diarrhea. Large phase III trials with lapatinib, which is taken orally once a day, in breast cancer are ongoing. For information about clinical trials with lapatinib, call 800-563-7137 or visit www.4BreastCancerTrials.com.

RAD001 (EVEROLIMUS)

RAD001 is an inhibitor of the mammalian target of rapamycin (mTOR), a key protein involved in regulating cell survival and growth. The FDA has not yet approved this oral drug for any cancer. New trials will soon be recruiting breast cancer patients for RAD001 treatment in combination with Femara. For more about RAD001, visit www.novartisoncology.com.

IXABEPILONE (BMS-247550)

Ixabepilone, a new investigational anti-cancer agent, binds to tubulin and prevents cells from dividing. But it continues to work in Taxol-resistant tumors. Typically, Ixabepilone is given daily by one-hour intravenous infusion. The most common side effects are fatigue, neutropenia and numbness in the hands and feet. The drug is being evaluated as a treatment for various cancers, including breast cancer, and has not yet been approved by the FDA. For information about clinical trials with Ixabepilone, call the Bristol-Myers Squibb Call Center at 866-892-1BMS.

ZARNESTRA™ (TIPIFARNIB)

Zarnestra, a farnesyl transferase inhibitor, stops proteins that promote the growth of breast cancer cells. Lowered blood level count is the most common side effect associated with this drug. Zarnestra, which is taken orally, is being investigated as a treatment for breast cancer in combination with other agents, including tamoxifen, but it has not been approved for this use. To find clinical trials in breast cancer using Zarnestra, visit www.clinicaltrials.gov.

Supportive Care Issues

Exercise & Nutrition

While both exercise and a healthy diet are recommended for preventing cancer, research suggests exercise and nutrition may also be effective during and after treatment for breast cancer.

Most previous studies have not been able to link total fat intake to recurrence risk or survival, but a new study provides some answers. The Women's Intervention Nutrition Study (WINS) tested whether a low-fat diet after drug therapy could reduce breast cancer recurrence and improve survival in localized breast cancer patients.

The more than 2,400 women involved in the study were split into two groups. The first group was counseled to reduce their fat intake to 15 percent of calories during a rigorous four-month intervention period followed by monthly group sessions. The other group received no dietary counseling. A decade after the study began, investigators concluded that decreasing dietary fat intake may significantly reduce the risk of recurrence among postmenopausal breast cancer patients.

Another study expected to create excitement looks at whether a diet low in fat and rich in vegetables, fruit and fiber is associated with longer breast cancer survival. The Women's Healthy Eating and Living Study (WHEL) randomly assigned more than 3,000 early-stage invasive breast cancer survivors to an intensive diet intervention or to a comparison group. Investigators plan to follow participants through 2006.

When it comes to exercise after cancer treatment, numerous studies report a reduction in symptoms of depression and anxiety and a boost in self-esteem. Patients who stay active by cardiovascular walking or cycling have less fatigue, lower emotional distress and fewer hospital stays. Exercise has also shown to lessen nausea associated with chemotherapy in breast cancer patients. Stretching and flexibility exercises performed in the weeks following breast surgery can reduce stiffness and swelling.

Lymphedema, a condition characterized by irreversible swelling, is caused by build-up of lymph fluid after the removal of lymph nodes. Although overexertion of affected limbs is a risk factor for lymphedema, regular exercise is one of the best ways to prevent the problem. (Gentle exercises such as yoga may actually improve lymph flow.) Just be sure to wear a properly fitting compression garment while exercising. Swimming or water aerobics are particularly good options, as the water provides natural, even pressure on the body.

Many facilities have physical therapists on hand to develop a program specifically for breast cancer patients, which can include cardiovascular, toning and stretching exercises.

In a Women's Health Initiative study, investigators looked at postmenopausal women ages 50 to 79 and saw that strenuous or even moderate physical activity reduced the risk of breast cancer, especially when started at a younger age. Researchers saw an 18 percent drop in risk in women who walked just 1.5 to 2.5 hours per week.

For more, visit the American Institute for Cancer Research at www.aicr.org.

Understanding the Journey: A Message from a Survivor

By Kathy LaTour

When I was diagnosed with stage 2 breast cancer in 1986, there were no pink ribbons, magazine cover stories or celebrities who had gone public with their varied experiences.

Women were only just beginning to talk about breast cancer and form the organizations that educate and advocate for women with breast cancer today.

You reading this says you have joined my sorority, the one where the dues are too high. And yet, because there are now so many breast cancer survivors, it's a time when a breast cancer diagnosis brings with it a wealth of information gathered by the sisterhood of survivors.

You don't have to do this alone—in your local community, in hospitals, churches and social centers, women are there to support you. Online, you will find a wealth of information and an ongoing 24-hour conversation no matter where you live.

Each woman must make her own way on this journey, but below are suggestions gleaned not only from my experience, but also from hundreds of survivors across the country who I have met during my travels.

CURE AND HEAL

Breast cancer, you will quickly find, requires a dual journey. The medical journey means seeking elimination of the disease, or cure, and this will consume the early days after your diagnosis. This is what I call the "head" time, when empowering yourself means gathering the best information and the best practitioners.

The other journey is one of spirit and soul, as we try to integrate the reality of what has happened in our life, or healing. This part of the journey addresses the person you will be after treatment—no matter the outcome.

To treat your body, find the best medical practitioners available. Gather information, understand your options and become an active participant in your care.

While physicians treat your body, do not forget your soul and spirit and those practitioners whose gentle touch, soft words or beautiful skills bring peace and understanding.

To be well is to be cured; to be whole is to be healed.

ASK FOR HELP

As women, we aren't very good at asking for help. We are the caretakers and find it hard to give up that role even for a short time to be on the receiving end.

To care for yourself is to love yourself and to let others care for you is to love them. People want to help, so when they ask, take them up on it. If trying to organize their help is too confusing or overwhelming, then ask the most organized friend to become the organizer of the caregivers. Remember, there will be days when cooking, parenting, shopping or going to work may be too much. You can handle some things but not everything.

So, here's what you need to do. First, say yes when people offer. Second, tell them what you need. Third, let them do it.

RECOGNIZE GIFTS

A cancer diagnosis brings with it a sixth sense. Along with smell, touch, sight, hearing and taste comes presence. It has become a cliché that cancer helps us understand the importance of the little things, but it's true. Never were flowers so beautiful or children so huggable.

Be present in each emotion. If it's possible, don't worry about the future. You are alive today. Probably the most important piece of advice I ever got was from a friend dying of metastatic breast cancer. "Kathy," she said, "there are worse things than dying. Not living until you die is worse." As I look back on the past 19 years, one of cancer's gifts to me was my child and being present for her every step of the way. When other parents comment on how quickly the time has gone and how they wish they had enjoyed each stage more, I smile.

My daughter was only a year old when I was diagnosed and today she is a sophomore in college. I can't relate to other parents lamenting a loss at not being present. I can close my eyes and see her in the little flowered overalls with the purple T-shirt, gingerly lifting the brightly colored egg from the grass and putting it in her Easter basket at age 3 just as easily as I can recall her sleepily wandering into the kitchen half awake as a teenager. I knew that getting to raise her was a gift and I wasn't going to miss a minute of it.

Where is your joy and passion? If you have let it fall by the wayside, go back to it. One of cancer's gifts is that we get to make decisions and act in ways that as healthy people, we never would.

FEELINGS

As I watched scenes of the tsunami last year, I could easily see an analogy to being diagnosed with cancer. One minute, the world is one way and a second later, we are washed away in a wave of feelings: fear, anxiety, pain, grief, loss. The best way to survive is to ride the feelings, feel them and let them have their place in this journey.

When friends and family reassure you that everything is going to be fine and you shouldn't feel afraid, they are trying to quell their own panic. Remind them that you need to feel what you are feeling.

I learned this the hard way, spending the first three years of my diagnosis trying to suppress the fear of recurrence, the pain of loss, the anxiety of the unknown. It didn't help that everyone kept saying, "Aren't you glad that's over," when for me cancer was a daily companion.

When I joined a support group, I finally met the real experts in this disease, the other women who had been there. I learned that it's healthy to express fears and that the only way to cope is to feel.

Feelings are not right or wrong, and if you're having them, they are valid. **As the wise therapist in our group said: To feel is to heal.**

"You don't have to do this alone." —KATHY LaTOUR