infoaging guides

DISEASES OF AGING

BREAST CANCER

An introduction to aging science brought to you by the American Federation for Aging Research

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WHAT IS BREAST CANCER?

Breast cancer is a malignancy that starts in the breast but can spread throughout the body. Some of the sites to which breast cancer can spread are the lymph nodes, particularly those under the arm next to the affected breast, the brain, the liver, the lungs, and the bones. Breast cancer is a major cause of illness and death in older women. There are approximately 200,000 new cases and 40,000 deaths from breast cancer each year.

Breast cancer is categorized by its cell type (histology), tumor size, and degree of spread.

TYPES OF BREAST CANCER

Ductal carcinoma in situ originates in and is confined to the milk duct of the breast. It has the potential to become an invasive breast cancer, but has not yet done so. The abnormal cells are still confined to the milk ducts. When these cells break out of the walls of the milk duct, this is considered an "invasive breast cancer." When cells do that, they have demonstrated that they have the ability to spread to places they are not meant to be— the hallmark of true cancer. Although rare, one particular form of ductal carcinoma that increases in frequency with age is Paget's disease of the nipple. Symptoms include crusting, scaling, and redness of the nipple or aureola, with areas of bleeding or oozing. When caught early, prognosis for this cancer is excellent.

The two major forms of invasive breast cancer are infiltrating ductal carcinoma (80 percent of invasive cancers), which begins in the milk ducts, and infiltrating lobular carcinoma (20 percent), which begins in the milk glands. Unusual cell types include tubular carcinoma and medullary carcinoma, which tend to have more favorable prognoses. Another rare type, inflammatory breast cancer, is especially aggressive and generally carries a poor prognosis. It accounts for about three percent of all breast cancers diagnosed each year.

BREAST CANCER AND MEN

Less than one out of every hundred cases of diagnosed breast cancer occurs in a man. Males are born with primitive breast tissue, and this tissue is susceptible to tumor formation. Unfortunately, these tumors are often advanced by the time of diagnosis. However, the prognosis for a man diagnosed with breast cancer is the same as that of a woman diagnosed at the same stage.

DIAGNOSING BREAST CANCER

Most breast cancer starts without symptoms. Only 10 percent of breast cancers are found by physical examination first; 90 percent are first diagnosed by mammography. But many women do not undergo mammograms as often as they should. In these women, the diagnosis can be delayed until there are clear signs of local spread, such as skin ulcers and nipple discharge, or distant spread. Breast cancer can spread to bone, causing fractures and high blood calcium levels; to the brain, causing seizures or other neurologic changes; and to the liver, causing liver failure or ascites, a collection of fluid in the abdomen. All of these physiological events may be the signs or symptoms that lead to the diagnosis.

Several different imaging studies exist that can identify breast lesions, although only regular mammograms for women 40 or older have so far been shown to be an effective screen for the general population. These tests, some of which are still experimental, include:

Mammograms

These remain the "gold standard" for the diagnosis of breast cancer. A small dose of radiation produces clear images of most breast tumors in women of at least 40 years of age. The presence of very small particles of calcium (called microcalcifications) is also suggestive of cancer. Controversy has arisen over the appropriate frequency for mammograms. All authorities agree that women over age 50 should receive annual mammograms, but for women between 40 and 50, recommendations vary.

The American Cancer Society suggests they be done annually; the National Cancer Institute suggests every one to two years, and the American College of Physicians does not recommend them for women age 40 to 50 due to some uncertainty as to their benefits. When to stop performing mammograms is also controversial, with the American Geriatrics Society suggesting cessation at age 85, unless the patient is in excellent health (life expectancy greater than five years) and functions well in day-to-day activities. The American Cancer Society suggests continued screening for any woman with a life expectancy of more than five years. The U.S. Preventive Services Task Force, while not specifying a cutoff, notes that the benefit of mammograms is unclear in women over 70. Although not definitive, there is a growing body of literature on the impact of screening mammograms in women who are 70 or older.

A Swedish study published in the May 2001 issue of *Cancer* found that regular screening mammo-

While mammograms remain the "gold standard" for the diagnosis of breast cancer, mammography is under-utilized in the United States, with only about half of the women who could benefit from it receiving it.

grams among women ages 40 through 69 resulted in a 63 percent decrease in the death rate from cancer. Access to mammography services and insurance coverage for the procedure are two obstacles that many women in the U.S. must overcome in obtaining regular screening mammograms.

Ultrasound
Standard ultrasound is not a first line diagnostic test for breast cancer. Rather, it is usually reserved to further study lesions that have been found on mammograms or to investigate a palpable lump that is not seen on mammogram. Ultrasound can best determine if those lesions are fluid-filled cysts, which are far less likely to be cancerous than solid lesions. Studies are currently underway to determine whether high-resolution ultrasounds can be as effective as mammograms in screening for breast cancer.

Galactography
Galactography involves the insertion of a fine probe into the milk ducts of the breast and the injection of methylene blue or some other dye to define pathologic lesions in those ducts. Galactography is considered the state-of-the-art approach to investigating nipple discharge when there is no lump or other change.

Magnetic Resonance Imaging (MRI)
A number of studies have looked at the value of MRI studies in making an accurate diagnosis of breast cancer. MRI may be of particular value in screening of women who are at high risk of hereditary breast cancer. It has also been found to improve the accuracy of breast cancer staging before surgery, notably in looking for disease that has spread to the bone marrow. However, the test remains expensive.

Positron Emission Tomography
Commonly called a PET scan, this has the possibility of detecting cancers when CT and MRI scans are normal. No large-scale studies have been completed yet to demonstrate the effectiveness or possible greater usefulness of PET scanning in diagnosing breast cancer localized to the breast.

Ductal lavage
A new experimental technique was described by researchers at Johns Hopkins University School of Medicine in the April 2001 issue of *Obstetrics and Gynecology* for the early detection of breast cancer. This procedure, called ductal lavage, involves the insertion of a micro catheter into the milk ducts and then flushing the milk ducts with saline. The fluid is collected and the washed out cells examined under a microscope. This technique might prove to be

of value in women who are at high risk, such as those with a previous history of breast cancer or those who carry genes that predispose them to the disease, in detecting very early stage cancer before mammography could. Recently, however, a small study published in *Cancer* found that the test was ineffective at detecting malignancy in women with invasive breast cancer. The procedure is still experimental.

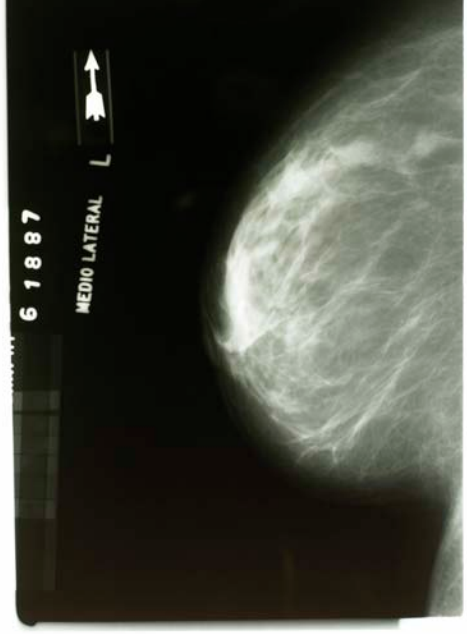
Optical probes

Several probing techniques are currently in the experimental stage. In collaborative studies involving the University of Pennsylvania, Harvard, and Washington University, a technique has been developed that involves the injection of fluorescent molecules into the bloodstream. These molecules then migrate to the breast. When the molecules penetrate cancer cells, the cancer cells use enzymes to expose the molecules, which can then be detected by external sensors.

Another new optical device under study is being developed at Lawrence Livermore National Laboratory. Dubbed the "Smart Probe," this device is inserted into the breast and guided to the suspicious area. It has the capability of detecting electrical and chemical characteristics that are unique to cancer cells.

BREAST CANCER PROGNOSIS AND AGING

Breast cancer is a major cause of illness and death in women. Women under the age of 40 often have the worst prognosis. Older women generally have a slightly better one. This is because breast cancer in older women more often comprises mature or well-differentiated cells, while younger women often have immature cell forms, called poorly differentiated cells. Also, older women are far more likely to have breast tumors that are "hormone-receptor-rich." A hormone-receptor-rich tumor has proteins on its surface that attract and bind hormones like estrogen. This estrogen encourages the growth of those tumors. The presence of hormone-binding proteins also allows the use of endocrine therapy [anti-estrogens (aromatase inhibitors) or selective estrogen receptor modulators (tamoxifen) to treat the cancer.



Population studies have shown that older women receive mammograms and doctor-performed breast examinations less often than they should.

The prognosis of breast cancer depends mainly on the stage of the disease when it is found (that is, how big the tumor is and whether it has spread or not). Several factors contribute to the fact that too often, breast cancer has spread by the time it is diagnosed in older women. Population studies have shown that older women receive mammograms and doctor-performed breast examinations less often than they should. This is due in part to the fact that post-menopausal women are less likely to have routine gynecological or general physical examinations. Other factors may contribute to this, including increased difficulties in accessing health care and the presence of multiple other health problems (called comorbidities) which may mask the presence of cancer or attract attention away from it.

The stage at which a cancer is discovered typically guides treatment recommendations. Treatment can involve lumpectomy, mastectomy, post-operative radiation, chemotherapy, endocrine treatment, or a combination of those. Studies have shown that older women sometimes receive less aggressive treatment than younger women. This may be because of the decline in kidney, heart, lung and immune function seen with aging, which can make the more potent chemotherapeutic drugs more risky. There also appears to be some physician bias toward under-treating older women (over 70), and in some cases, the patient does not desire therapy.

Recent studies underscore the tendency toward undertreatment of older women. A study published in the October 1, 2003, issue of the *Journal of Clinical Oncology* found that only 47 percent of women over age 80 receive standard treatment, as compared to 90 percent of women aged 50 to 79. This greatly affected outcome of the disease, as five-year survival was greater than 80 percent for women who received surgical treatment and only about 50 percent for women who received tamoxifen alone. Another study

published in the September 15, 2003, issue of *Cancer* found that women over 50 are less likely to receive chemotherapy than younger women, with the discrepancy in care particularly acute in women over 65. These findings were independent of health status and cancer severity.

An article published in the *Journal of the American Geriatrics Society* offers a possible solution to this problem: nurse case managers. Breast cancer patients who were 65 years and older and who received calls, visits, and/or accompaniment to medical appointments from nurse care managers were 64 percent more likely than controls to receive lumpectomy, and 60 percent more likely than controls to receive adjuvant radiation after breast-conserving surgery.

THE RISK FACTORS FOR BREAST CANCER

The major risk factors that research has identified as important in the development of breast cancer include:

Age

Breast cancer risk increases steadily with age, peaks at about age 80, and drops off again at 85.

Personal or family history of breast cancer

Breast cancer in one breast increases the risk of developing another new breast cancer in the opposite breast.

A family history of breast cancer in a first-degree relative (a parent, sister or child) increases a woman's risk of developing breast cancer by two to three folds. Some studies suggest that the risk is even higher for those women whose relatives had cancer in both breasts or in those in whom it was diagnosed before menopause.

About 5 percent of women with breast cancer have been found to carry mutations in one of the two recognized breast cancer genes, called BRCA1 and BRCA2. Those with one of these defective genes have been found in some studies to carry a risk as high as 50 to 85 percent of developing breast cancer by age 80. Carrying BRCA1 also causes a ten-fold increase in a woman's risk of developing ovarian cancer. Men with BRCA2 are at increased risk of breast cancer as well.

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Race

Although white women are more likely than black women to develop breast cancer, black women seem to have a worse prognosis for breast cancer when compared, stage-for-stage, with their white counterparts. Researchers have initially attributed this disparity to inequalities in health care access. However, a study published in the September 1, 2003, issue of *Cancer* that studied women with breast cancer in the U.S. Department of Defense health care system, an equal-access system, still found black women to be at a greater risk of dying from breast cancer than white. This may be partially due, say researchers at New York-Presbyterian hospital, to a racial difference in white blood cell count. Blacks tend to have a lower white blood cell count than whites, a condition called neutropenia. Because doctors base chemotherapy scheduling and dosing on the patient's white blood cell count, racial differences in cell count could be affecting the inten-

sity of chemotherapy administered to black women, thereby also affecting their prognosis. Whether race truly imparts a worse prognosis for breast cancer patients still remains a controversial subject, and additional confirmatory studies are required.

Estrogen exposure
Prolonged exposure to estrogen, whether it be one's own native estrogen or synthetic estrogen administered for therapeutic reasons, increases the risk of breast cancer. Lengthy exposure to high native or natural estrogen levels occurs in those with a history of an early onset of menstruation, a late menopause, and a first pregnancy after the age of 31 (or no pregnancies).

Therapeutic estrogens are found in oral contraceptives, but the increased risk of breast cancer, if real, is very small (about 5 more per 100,000 women than expected), and the risk seems to be related to how recently a woman used oral contraceptives, rather than the length of time she took them.

Research published in the *Journal of the American Medical Association* in October 2000 revealed that having a first degree relative with breast cancer and having ever used the earliest formulations of oral contraceptive pills approximately tripled a woman's risk of developing breast cancer. The earliest versions of the pill contained significantly more estrogen than more modern forms.

Estrogens are also administered to women to ease symptoms of menopause, such as hot flashes, vaginal dryness and osteoporosis. Estrogen has also been used to reduce the risk of heart disease in postmenopausal women. However, recent studies have shown that estrogens do not offer the protection against heart disease once thought. In July 2002, one of the largest and best-designed studies of hormone replacement therapy was halted because of the risks to the participants. Researchers reported that if 10,000 postmenopausal women take a combination of estrogen and progesterone (Prempro®) for a year, eight more would develop invasive breast cancer compared with a similar group of 10,000 women not taking these hormones.

The same trial also showed that women taking combined hormone replacement therapy were more likely to have abnormal mammograms and more likely to have a larger breast cancer and/or a more advanced stage at diagnosis. Other studies have also found that women on hormone replacement therapy are more likely to develop a less common type of breast cancer called infiltrating lobular carcinoma, which is more difficult to detect on a mammogram than infiltrating ductal carcinoma, the more common form of breast cancer.

Obesity and diet
Regular consumption of alcohol has been shown in some studies to increase the risk of breast cancer. A high fat diet has been claimed as a possible risk as well, but study results are inconsistent.

Exposure to radiation and other environmental toxins
Radiation exposure to the chest area, particularly before the age of 30, can increase the risk of breast cancer in later life. The risk from the radiation of regular mammograms, however, is negligible, and the benefits of proper diagnosis far outweigh any miniscule increase in breast cancer risk that may possibly be associated with mammography.

The role of environmental toxins in breast cancer is quite controversial. Certain pesticides and other synthetic chemicals have been associated with an increased risk. At least 50 percent of all breast cancers arise in women who have no obvious risks for breast cancer, and some scientists believe that many of those cancers are related to as yet unidentified environmental toxins. Recent results from the Long Island Breast Cancer Study Project show that organochlorine compounds, primarily found in pesticides, have no association with breast cancer risk, and that polycyclic aromatic hydrocarbons, found in auto exhaust, cigarette smoke, and grilled foods, have only a small association with breast cancer risk. Studies are underway through the National Cancer Institute and the National Institute of Environmental Health Sciences to further explore the role environmental toxins play in the development of breast cancer.

REDUCING THE RISK OF BREAST CANCER

More than 212,000 women will be diagnosed with breast cancer in the United States this year, and more than 30,000 will die of the disease. The occurrence of breast cancer rises until about the age of 80, and then falls off after 85. The oft-quoted statistic that 1 in 8 American women will develop breast cancer is theoretical and based on a lifetime risk. Nevertheless, until the last part of the 20th century, breast cancer was the leading cancer killer in women (it is now surpassed by lung cancer).

Women can take steps that may reduce the risk of breast cancer.

Evidence for some is more established than for others. These include:

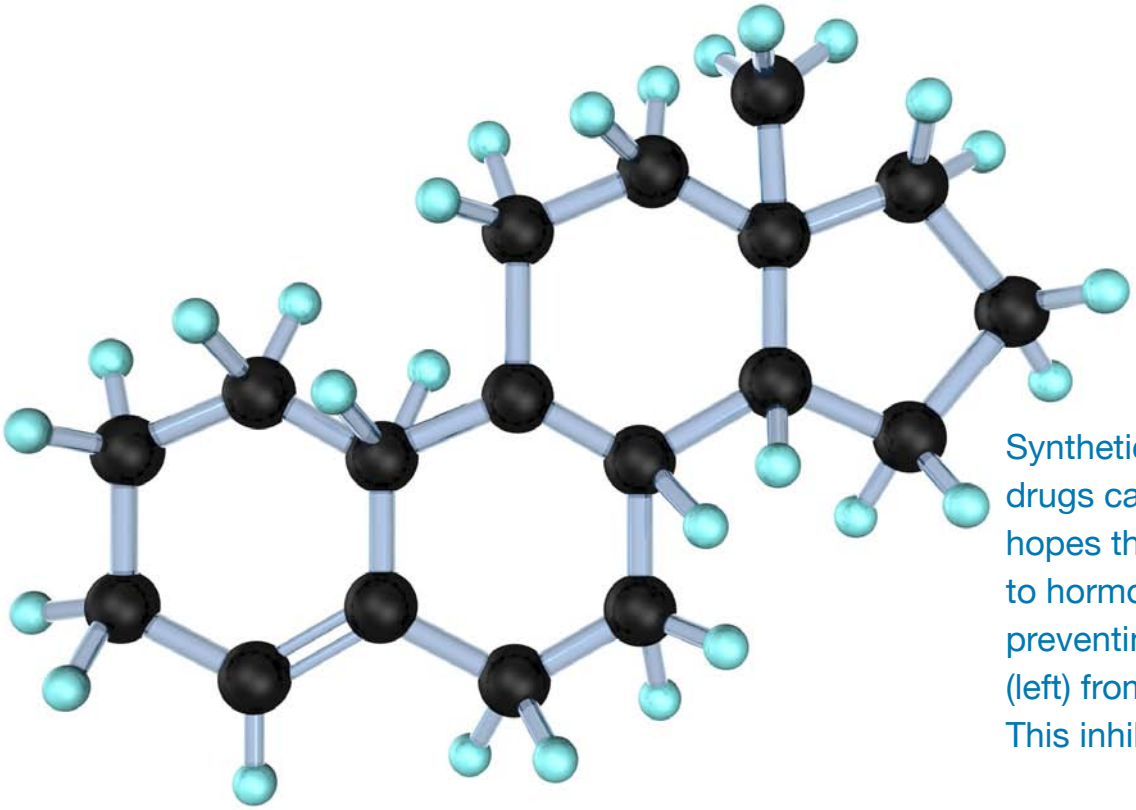
Diet
While the precise role that a high fat diet can play in causing breast cancer is controversial, several studies have shown an association between central obesity—fat that is concentrated around the waist (rather then the hips)—and breast cancer. So a low-fat diet and regular exercise to prevent the accumulation of central obesity is at least prudent, if not proven. Avoidance of excess alcohol consumption may also be wise for women at high risk, since a few studies have linked regular alcohol use to an increased risk of breast cancer. Several studies suggest that drinking green tea may reduce the risk of developing breast cancer, but these results are controversial.

Physical Activity
A study by researchers at the University of California Los Angeles, has shown that women who engage in moderate to strenuous activity for five or more hours each week are less likely to develop several forms of breast cancer.

Mastectomy
Women who have inherited one of the genes associated with breast cancer, called BRCA1 and BRCA2, sometimes opt for prophylactic mastectomy, the surgical removal of both breasts before any cancer might occur. Though this seems drastic, the risk of breast cancer (and ovarian cancer, in those with BRCA1) is so high that some women strongly wish to reduce their risk. Although this surgery does seem to reduce the incidence of breast cancer substantially for women who are at high risk, it does not completely eliminate the risk. Getting tested for BRCA1 and 2 and acting on the results are very personal decisions and should be undertaken in conjunction with specially trained genetic counselors and physicians, so that a woman would be well informed and could do what is right for her.

Women who engage in moderate to strenuous activity for five or more hours each week are less likely to develop several forms of breast cancer.

Tamoxifen
Tamoxifen is a drug that has estrogen-like effects and belongs to a class of drugs known as Selective Estrogen Receptor Modulators, or SERMs. Because tamoxifen reduces the risk of recurrence of breast cancer in women whose cancers have been shown to have estrogen receptors, researchers decided to test whether it might also prevent breast cancer in women at high risk. The National Surgical Adjuvant Breast and Bowel Project enrolled over 13,000 women at high risk for breast cancer, giving them either tamoxifen or placebo. The study was terminated early because the results were so con-



Synthetic estrogen-like drugs can be given in hopes that they will bind to hormone receptor sites, preventing native estrogen (left) from attaching itself. This inhibits tumor growth.

clusive. There were nearly twice as many cases of breast cancer in the placebo group as in the tamoxifen group (175 versus 89). Tamoxifen does carry a small, but definite risk of uterine cancer, and giving it to women at risk of breast cancer who have not had a hysterectomy poses a quandary. The large majority of uterine cancer cases after tamoxifen therapy were early stage cases and curable with hysterectomy, and the risk seems to be primarily in postmenopausal women with a uterus still in place. Another risk of tamoxifen is the development of blood clots, presenting either as clots in the blood vessels of the lower extremities, or more dangerously, in the lungs or brain. These events are rare. Women with personal or family history of blood clots should report these to their physicians before deciding whether tamoxifen is safe for them.

Raloxifene

Newer SERMs such as raloxifene are estrogen-like drugs that have fewer of the toxic effects of estrogen. They have been approved for the prevention and treatment of osteoporosis, and to date, have not been associated with any increased risk of uterine cancer. A large trial called the Study of Tamoxifen and Raloxifene (STAR) compared these two drugs for the prevention of breast cancer. Begun in 1999, the study enrolled 19,747 post-menopausal women at high risk for breast cancer and assigned them to take either tamoxifen or raloxifene. Both drugs reduced the occurrence of breast cancer by about 50 percent, but raloxifene also reduced the incidence of uterine cancer, a known side effect of tamoxifen, by 36 percent. Both drugs also increase the incidence of blood clots, but there were 29 percent fewer occurrences among the raloxifene patients.

A similar study called MORE (the Multiple Outcomes of Raloxifene Evaluation) involved 7,700 older women with known osteoporosis who were prescribed either raloxifene or a placebo. About one third of women received 60 mg of raloxifene; another third received 120 mg and the last third were given a placebo. At the end of four years, there were 22 cases of breast cancer among the approximately 5,000 women who received some dose of raloxifene and 39 cases among the 2,500 who took the placebo. This translates into a 72 percent reduction of breast cancer risk. The reduction in risk of developing breast cancer that is estrogen-receptor positive was 84 percent.

Aromatase Inhibitors

A recent Canadian study of a drug called exemestane (compared to placebo) showed a 65 percent reduction in the incidence of

invasive breast cancer among the women who took the medication, all of whom were post-menopausal. Exemestane is an aromatase inhibitor, which means it causes the body to produce less estrogen. This type of drug works by blocking aromatase, an enzyme that converts the hormone androgen into small amounts of estrogen in the body. Because it can't stop the ovaries from creating estrogen, however, it's effective only in post-menopausal women.

Both tamoxifen and raloxifene have significant side effects, but exemestane seems to have a much better safety profile. A three-year follow up after the study showed no significant differences between the placebo group and the exestane group in terms of skeletal fractures, cardiovascular events, other cancers, or treatment-related deaths.

Exemestane and two other aromatase inhibitors, letrozole and anastrozole, are replacing tamoxifen as the first-choice therapy for postmenopausal women with early breast cancer of a type called hormone receptor positive (HR+). The tumors have estrogen receptors on their surfaces. If estrogen binds to those sites, it encourages the tumor to grow. Both national and international guidelines now recommend aromatase inhibitors as the preferred therapy for early HR+ cancer.

REDUCING THE RISK OF BREAST CANCER RECURRENCE

Once breast cancer has been diagnosed and surgically removed, some steps can be taken to reduce the risk of a recurrence. These include:

Hormonal Therapy
Hormonal therapy is an adjuvant (that is, given after surgery) treatment for HR+ breast cancer. Synthetic estrogen-like drugs can be given in hopes that they will bind to hormone receptor sites, preventing native estrogen from attaching itself. This inhibits tumor growth. The most commonly used of these drugs is tamoxifen.

Older women are more likely to have HR+ cancers, and all women with this type of tumor might benefit from tamoxifen. Tamoxifen has another benefit, as well: it might help prevent osteoporosis. However, it can also increase the risk of uterine cancer. Studies have documented that the substantially reduced risk of death from breast cancer with tamoxifen is greater than the slightly increased risk of death from cancer of the uterus or possible complications of developing a blood clot.

Tamoxifen can be taken for five years after the diagnosis of breast cancer, but a study published in the *New England Journal of Medicine* demonstrated that treatment with letrozole, another hormone used in the treatment of breast cancer, after the completion of five years of adjuvant tamoxifen, further improved disease-free survival (that is, the chances of living longer without breast cancer recurrence).

And yet another study has shown that switching to exemestane after two-to-three years of tamoxifen therapy can significantly increase disease-free survival and reduce side effects among post-menopausal early breast cancer patients.

Chemotherapy
Chemotherapeutic drugs are given orally or intravenously. Some patients are given chemotherapy before removal of the breast cancer; more receive it afterwards. A number of different combinations of drugs are used for the treatment of breast cancer. The combinations are often named using the first initials of the drugs administered.

Post-operative radiation treatment
Post-operative radiation treatment is often given after more limited or breast-conserving surgery, commonly called lumpectomy. Radiation is delivered to the breast from which the lump has been removed and sometimes to the lymph tissue under the arm and near the collarbone on that side, typically using "external-beam radiation," delivered five days a week for several weeks. Post operative radiation is also given after a mastectomy in patients with large tumors or many positive lymph nodes to decrease the risk of a local recurrence.

Brachytherapy (also called limited-field radiation therapy) is another way to deliver post-operative radiation to the breast cancer patient. It involves the insertion of radioactive "seeds" in the area where the tumor was removed. This method is currently being tested. A paper published in the *Journal of the National Cancer Institute* studied nearly 400 women with breast cancer, comparing rates of recurrence among those treated with lumpectomy plus traditional whole-breast radiation to those treated with lumpectomy plus brachytherapy. Over a five-year period, rates of breast cancer recurrence were comparable between the two groups.

Other trials involve the delivery of radiation therapy during the same surgery in which the breast tumor is removed. The potential advantages of this technique include avoiding radiating the breast skin (which sometimes leaves a disfiguring trace) and saving the patients from coming to the radiation sessions for several weeks after surgery.

Experimental treatments
A cancer vaccine is being studied for women who have already had the disease in the hopes that it will prevent a recurrence. These trials are still preliminary. The vaccines that are under study are targeted at particular proteins called antigens on the surfaces of breast cancer cells and are intended to incite the immune system to attack those antigens. Other researchers are working to create other types of vaccines that could help prevent breast cancer in high-risk women.

WHEN THE CANCER HAS SPREAD

In a small percentage of individuals newly diagnosed with breast cancer, the disease has already metastasized (spread) to other organs in the body—most commonly the bones, lungs, and liver. At this point in the cancer's progress, it is no longer considered curable. However, current treatments have helped an increasing number of patients survive for a much longer time than they might have just a few years ago. Treatment may include systemic chemotherapy, hormone therapy, surgery, and/or radiotherapy.

One study from M.D. Anderson Cancer Center that compared length of survival of metastatic breast cancer patients treated at their institution in five-year increments, found that median survival had doubled to 51 months (range 33-69 months) in 1995-2000 from a median survival of 27 months (range 21-33 months) only five years earlier, 1990-1994. Five years after diagnosis, 40 percent of these patients were still alive, as compared with 29 percent during 1990 to 1994. During the first period of the study, (1974 to 1979), only 10 percent of patients were still alive at five years and the median survival was only 15 months (range 11-19 months).

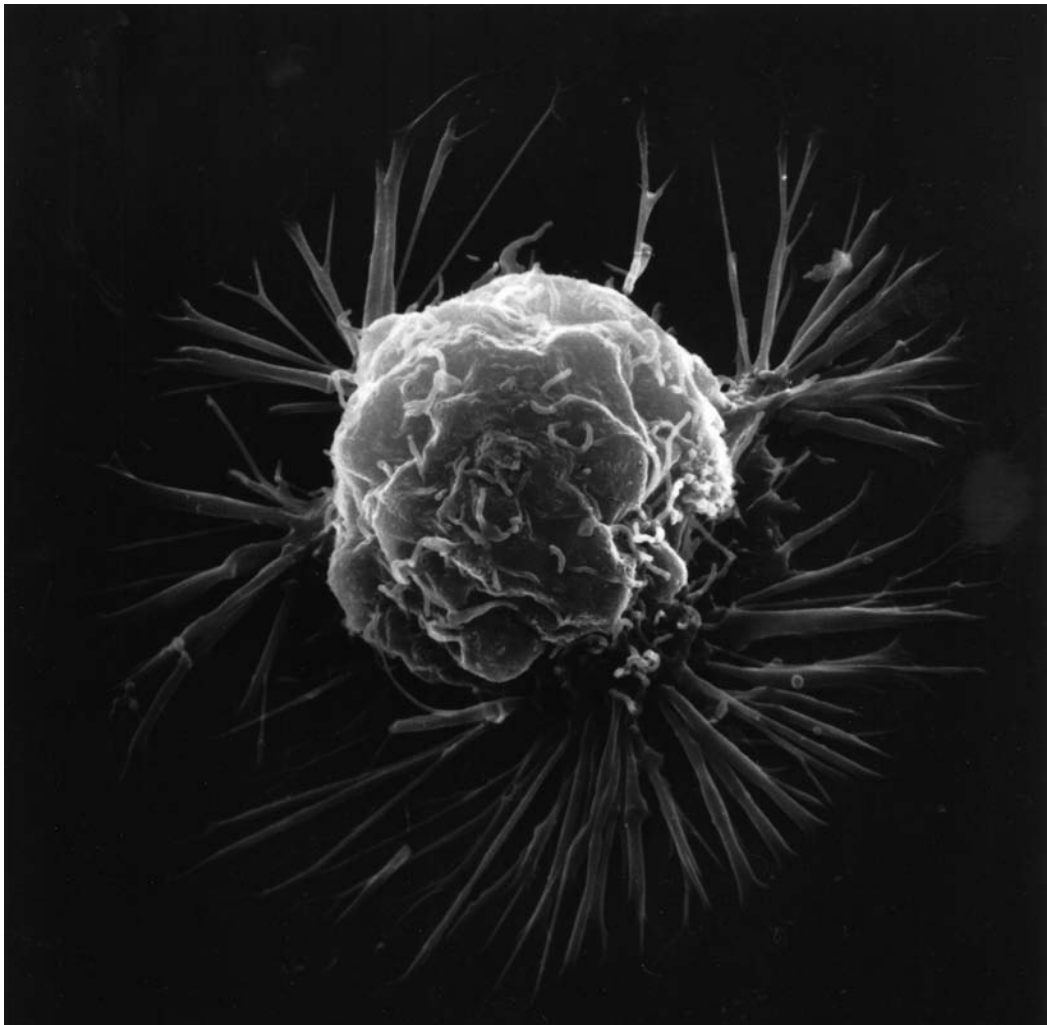
In addition to cancer treatment, patients with advanced breast cancer will eventually need medical support to help control pain and other symptoms of their disease; hospital stays to deal with cancer-related crises are not uncommon; and during the final stages of the patient's life, he or she may need hospice care. However, in general, the outlook for patients with advanced cancer is brighter, both in terms of survival time and quality of life, than ever before.

THE FUTURE OF BREAST CANCER RESEARCH

What is the future of breast cancer research likely to tell us?

Some of the most promising breast cancer research is investigating new treatments. New

New therapies are being explored that target very specific properties of breast cancer cells, such as the cell shown here, photographed by a scanning electron microscope. Photo courtesy of the National Cancer Institute.



therapies are being explored that target very specific properties of breast cancer cells.

Trastuzumab (Herceptin®) is the first drug in its class approved for use in breast cancer. It binds to a protein on the surface of breast cancer cells and prevents a circulating factor from binding to those cells and promoting cancer growth. Other drugs that will also thwart a substance called epidermal growth factor are in the early phases of clinical testing.

Drugs that inhibit angiogenesis (the growth of new blood vessels) are also under investigation. Included in these studies are some that give these new drugs continuously, rather than intermittently, as is more commonly the case with chemotherapy, and at lower than the maximally tolerated doses to reduce side effects and prolong exposure to the medications.

Exploration in the area of hormonal therapy will continue, looking at new selective estrogen-receptor modulators or SERMs, and the new aromatase inhibitors, which prevent the body from producing certain hormones.

Further work in identifying the proteins and genes associated with breast tumors and whether the presence of those substances is a good or poor prognostic sign will continue. CEA, p53 oncogene, and LEA.135 are only a few of these substances whose levels can be measured.

Another exciting area of breast cancer research involves developing better diagnostic techniques. Cancer of the breast sometimes presents with nothing but a nipple discharge. In galactography, tiny fiberoptic filaments with camera capabilities can be threaded into the milk ducts and the interior of those ducts viewed on a monitor. Benign and malignant intraductal tumors far too small to be seen on standard mammography can be seen by this technique, and carefully directed surgery to remove them can be performed. Digital mammography may eventually offer an improvement over conventional film mammography as a primary screening tool.

Studies have demonstrated the lack of utility of bone marrow transplant or autologous stem cell transplant in breast cancer. Autologous transplant is the removal of native young blood cells, treatment of those cells with high dose chemotherapy to kill any cancerous cells among them, and re-implantation of those cells back into the patient, who has also received very high dose chemotherapy.

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