BREAST CANCER

What Is Cancer?

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries.

Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person’s DNA becomes damaged by exposure to something in the environment, like smoking.

Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Often, cancer cells travel to other parts of the body, where they begin to grow and replace normal tissue. This process is called metastasis. Regardless of where a cancer may spread, however, it is always named for the place it began. For instance, breast cancer that spreads to the liver is still called breast cancer, not liver cancer.

Not all tumors are cancerous. Benign (non-cancerous) tumors do not spread (metastasize) to other parts of the body and, with very rare exceptions, are not life threatening.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

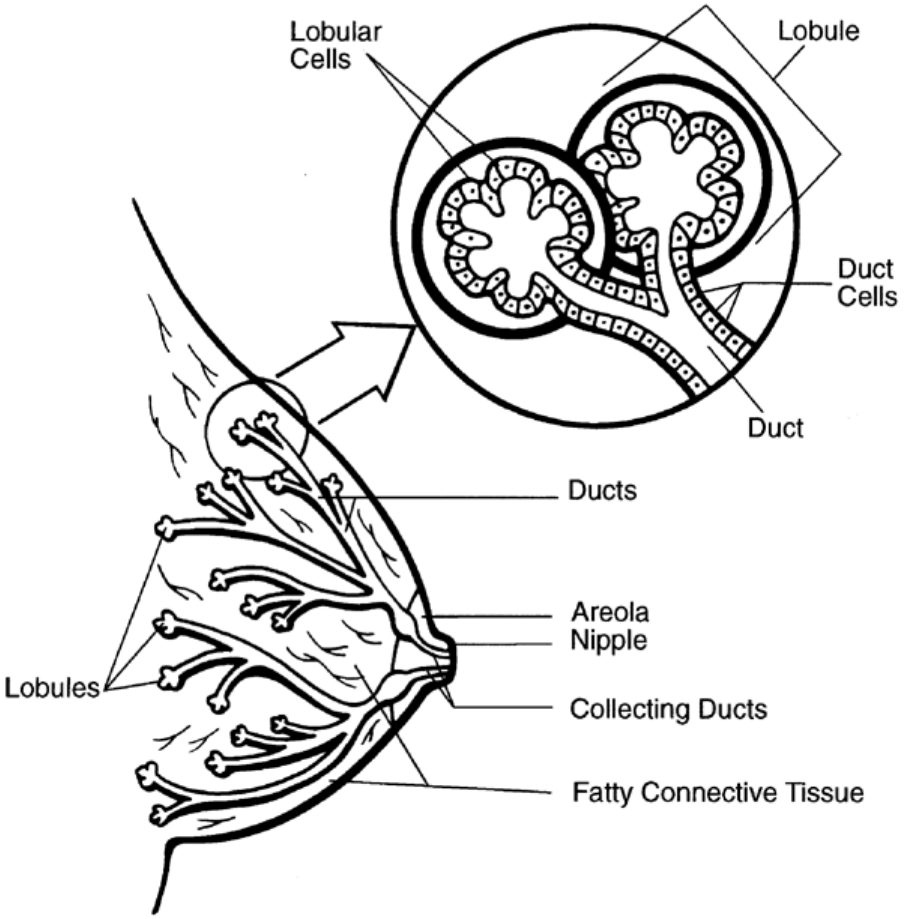
Cancer is the second leading cause of death in the United States. Nearly half of all men and a little over one third of all women in the United States will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. The sooner a cancer is found and treatment begins, the better are the chances for living for many years.

What Is Breast Cancer?

Breast cancer is a malignant tumor that has developed from cells of the breast. A *malignant tumor* is a group of cancer cells that may invade surrounding tissues or spread (metastasize) to distant areas of the body. The disease occurs almost entirely in women, but men can get it, too. The remainder of this document refers only to breast cancer in women. For information on breast cancer in men, see the American Cancer Society's document, "Breast Cancer in Men."

Normal Breast Structure

The female breast is made up mainly of *lobules* (milk-producing glands), *ducts* (tiny tubes that carry the milk from the lobules to the nipple), and *stroma* (fatty tissue and connective tissue surrounding the ducts and lobules, blood vessels, and lymphatic vessels).



Most breast cancers begin in the cells that line the ducts (*ductal* cancers), some begin in the cells that line the lobules (*lobular* cancers), and the rest in other tissues.

Blood vessels (arteries and veins) carry plasma, red blood cells, white blood cells, and platelets to and from the breast. *Lymphatic vessels* are like veins, except that they carry lymph away from the breast, instead of blood. *Lymph* is a clear fluid that contains tissue fluid and waste products and immune system cells (cells that are important in fighting infections). *Lymph nodes* are small bean-shaped collections of immune system cells that are found along lymphatic vessels. Cancer cells can enter lymphatic vessels and begin to grow in lymph nodes. This becomes important when we talk about staging (see below).

Most lymphatic vessels in the breast connect to lymph nodes under the arm (*axillary lymph nodes*). Some lymphatic vessels connect to lymph nodes inside the chest (*internal mammary nodes*) and those either above or below the collarbone (*supra-* or *infraclavicular nodes*).

Knowing if the cancer cells have spread to lymph nodes is important because if it has, we know that there is a higher chance that the cells could have also gotten into the bloodstream and spread to other sites in the body. This spread is called *metastasis*. The more lymph nodes that are involved with the breast cancer, the more likely it is that the cancer will eventually be found in other organs as well. It is important to know if you have metastatic cancer when you are choosing a treatment plan. Not all women with lymph node involvement develop metastases, and it is not unusual for a woman to have negative lymph nodes and later develop metastases.

Benign Breast Lumps

Most breast lumps are not cancerous, that is, they are benign. Still, many need to be biopsied (see below) to prove they are not cancer. Most lumps turn out to be fibrocystic changes. The term "fibrocystic" refers to fibrosis and cysts. Fibrosis is the formation of fibrous (or scar-like) tissue, and cysts are fluid-filled sacs. Fibrocystic changes can cause breast swelling and pain. This often happens just before a period is about to begin. Your breasts may feel nodular, or lumpy, and, sometimes, you may notice a clear or slightly cloudy nipple discharge.

Benign breast tumors such as *fibroadenomas* or *intraductal papillomas* are abnormal growths, but they are not cancer and cannot spread outside of the breast to other organs. They are not life threatening. Still, some benign breast conditions such as papillomas and *atypical*

hyperplasia are important because women with these conditions have a higher risk of developing breast cancer. For more information see the section, "What Are the Risk Factors for Breast Cancer?" and the American Cancer Society document, "Non-Cancerous Breast Conditions."

Types of Breast Cancers

It is important to understand some of the key words used to describe different types of breast cancer. It is not unusual for a single breast tumor to be a combination of these types and to have a mixture of invasive and in situ cancer.

Adenocarcinoma: Nearly all breast cancers start in the ducts or lobules of the breast. Because this is glandular tissue, they are called adenocarcinomas, a term applied to cancers of glandular tissue anywhere in the body. The 2 main types of breast adenocarcinomas are *ductal carcinomas* and *lobular carcinomas*.

In situ: This term is used for the early stage of cancer, when it is confined to the immediate area where it began. Specifically in breast cancer, in situ means that the cancer remains confined to ducts (ductal carcinoma in situ) or lobules (lobular carcinoma in situ). It has not invaded surrounding tissues in the breast nor spread to other organs in the body.

Ductal carcinoma in situ (DCIS): Ductal carcinoma in situ (also known as *intraductal carcinoma*) is the most common type of noninvasive breast cancer. DCIS means that the cancer cells are inside the ducts but have not spread through the walls of the ducts into the surrounding breast tissue.

About 20% of new breast cancer cases will be DCIS. Nearly all women diagnosed at this early stage of breast cancer can be cured. A mammogram is the best way to find DCIS early

When DCIS is diagnosed, the pathologist (a doctor specializing in diagnosing disease from tissue samples) will look for an area of dead or degenerating cancer cells, called *tumor necrosis*, within the tissue sample. If necrosis is present, the tumor is considered more aggressive. The term *comedocarcinoma* is often used to describe DCIS with necrosis.

Lobular carcinoma in situ (LCIS): Although not a true cancer, LCIS (also called *lobular neoplasia*) is sometimes classified as a type of noninvasive breast cancer, and this is why it is included here. It begins in the milk-producing glands but does not grow through the wall of the lobules.

Most breast cancer specialists think that LCIS itself does not become an invasive cancer very often, but women with this condition do have a higher risk of developing an invasive breast cancer in the same breast or in the opposite breast. For this reason, women with LCIS, in particular, should pay close attention to having regular mammograms (see below for guidelines).

Invasive (or infiltrating) ductal carcinoma (IDC): This is the most common breast cancer. It starts in a milk passage, or duct, of the breast, has broken through the wall of the duct, and invaded the fatty tissue of the breast. At this point, it can metastasize, or spread to other parts of the body through the lymphatic system and bloodstream. About 80% of invasive breast cancers are infiltrating ductal carcinomas.

Invasive (or infiltrating) lobular carcinoma (ILC): Invasive lobular carcinoma starts in the milk-producing glands, or lobules. Similar to IDC, it also can spread (metastasize) to other parts of the body. About 10% of invasive breast cancers are ILCs. Invasive lobular carcinoma may be harder to detect by a mammogram than invasive ductal carcinoma.

Inflammatory breast cancer: This uncommon type of invasive breast cancer accounts for about 1% to 3% of all breast cancers. Usually there is no single lump or tumor. Instead, inflammatory breast cancer (IBC) makes the skin of the breast look red and feel warm and gives the skin a thick, pitted appearance that looks a lot like an orange peel. Doctors now know that these changes are not caused by inflammation or infection, but by cancer cells blocking lymph vessels or channels in the skin. The affected breast may become larger or firmer, tender, or itchy. Inflammatory breast cancer is often mistaken for infection in its early stages.

Inflammatory breast cancer has a higher chance of spreading and a worse outlook than typical invasive ductal or lobular cancer. Inflammatory breast cancer is always staged as stage IIIB unless it has already spread to other organs at the time of diagnosis which would then make it a stage IV (see the section, "How Is Breast Cancer Staged?").

Mixed tumors: Mixed tumors describe those that contain a variety of cell types, such as invasive ductal combined with invasive lobular breast cancer. In this situation, the tumor is treated as if it were an invasive ductal cancer.

Medullary cancer: This special type of infiltrating breast cancer has a rather well-defined, distinct boundary between tumor tissue and normal tissue. It also has some other special

features, including the large size of the cancer cells and the presence of immune system cells at the edges of the tumor. Medullary carcinoma accounts for about 5% of breast cancers. The outlook, or *prognosis*, for this kind of breast cancer is better than for other types of invasive breast cancer. These are often hard to distinguish from invasive ductal carcinoma and are treated the same way. Most cancer specialists think that medullary cancer is very rare, and that cancers that are called medullary cancer should be treated as the usual invasive ductal breast cancer.

Metaplastic tumors: Metaplastic tumors are a very rare variant of invasive ductal cancer. These tumors include cells that are normally not found in the breast, such as cells that look like skin cells (squamous cells) or cells that make bone. These tumors are treated similarly to invasive ductal cancer.

Mucinous carcinoma: This rare type of invasive breast cancer is formed by mucus-producing cancer cells. The prognosis for mucinous carcinoma is better than for the more common types of invasive breast cancer. *Colloid carcinoma* is another name for this type of breast cancer.

Paget disease of the nipple: This type of breast cancer starts in the breast ducts and spreads to the skin of the nipple and then to the areola, the dark circle around the nipple. It is rare, accounting for only 1% of all cases of breast cancer. The skin of the nipple and areola often appears crusted, scaly, and red, with areas of bleeding or oozing. The woman may notice burning or itching. Paget disease may be associated with in situ carcinoma or with infiltrating breast carcinoma. If no lump can be felt in the breast tissue and the biopsy shows DCIS but no invasive cancer, the prognosis is excellent.

Phyllodes tumor: This very rare breast tumor develops in the stroma (connective tissue) of the breast, in contrast to carcinomas, which develop in the ducts or lobules. Phyllodes (also spelled *phylloides*) tumors are usually benign but on rare occasions may be malignant.

Benign phyllodes tumors are treated by removing the mass and a narrow margin of normal breast tissue. A malignant phyllodes tumor is treated by removing it along with a wider margin of normal tissue, or by mastectomy. These cancers do not respond to the usual treatments for invasive ductal or lobular breast cancer. In the past, both benign and malignant phyllodes tumors were referred to as cystosarcoma phyllodes.

Tubular carcinoma: Tubular carcinomas are another special type of invasive ductal breast carcinoma. It was named tubular because of the way the cells look under the microscope. Tubular carcinomas account for about 2% of all breast cancers and have a better prognosis than infiltrating ductal or lobular carcinomas. The majority of tubular cancers are hormone receptor positive but HER-2 negative (see discussion of tumor tests in the section, "Laboratory Examination of Breast Cancer Tissue").

Angiosarcoma: This cancer rarely occurs in the breasts. When it does, it is usually seen as a complication of radiation to the breast. It tends to develop about 5 to 7 years after radiation treatment. However, this is an extremely rare complication of breast radiation therapy. Treatment is the same as for other sarcomas (see the American Cancer Society document, "Soft Tissue Sarcomas"). Angiosarcoma can also occur in the arm of women who develop lymphedema as a result of lymph node surgery or radiation therapy to treat breast cancer. For information on lymphedema, see the section, "How Is Breast Cancer Treated?"

What Are the Key Statistics About Breast Cancer?

Breast cancer is the most common cancer among women, except for nonmelanoma skin cancers. The chance of developing invasive breast cancer at some time in a woman's life is about 1 in 8 (13% of women). It is estimated that in 2007 about 178,480 new cases of invasive breast cancer will be diagnosed among women in the United States. At this time there are slightly over 2 million breast cancer survivors in the United States. Women living in North America have the highest rate of breast cancer in the world.

In addition to invasive breast cancer, carcinoma in situ (CIS) will account for about 62,030 new cases in 2007. CIS is noninvasive and is the earliest form of breast cancer. Breast cancer also occurs in men. An estimated 2,030 cases of invasive breast cancer will be diagnosed in men in 2007.

Breast cancer incidence rates showed a rapid increase in the 1980s, although the rate of increase slowed in the 1990s, compared to the 1980s. In the years from 2001 to 2003, incidence rates decreased.

Breast cancer is the second leading cause of cancer death in women, exceeded only by lung cancer. The chance that breast cancer will be responsible for a woman’s death is about 1 in 33 (3%). In 2007, about 40,460 women and 450 men will die from breast cancer in the United States. Death rates from breast cancer continue to decline, with larger decreases in women younger than 50. These decreases are believed to be the result of earlier detection through screening and increased awareness, as well as improved treatment.

What Are the Risk Factors for Breast Cancer?

A risk factor is anything that increases your chance of getting a disease, such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lung, mouth, larynx, bladder, kidney, and several other organs.

But having a risk factor, or even several, does not mean that you will get the disease. Most women who have one or more breast cancer risk factors never develop the disease, while many women with breast cancer have no apparent risk factors (other than being a woman and growing older). Even when a woman with breast cancer has a risk factor, there is no way to prove that it actually caused her cancer.

There are different kinds of risk factors. Some factors, like a person's age or race, can't be changed. Others are linked to cancer-causing factors in the environment. Still others are related to personal choices such as smoking, drinking, and diet. Some factors influence risk more than others, and your risk for breast cancer can change over time, due to factors such as aging or lifestyle.

Risk Factors You Cannot Change

Gender: Simply being a woman is the main risk factor for developing breast cancer. Although women have many more breast cells than men, the main reason they develop more breast cancer is because their breast cells are constantly exposed to the growth-promoting effects of the female hormones estrogen and progesterone, thus making breast cancer much

more common in women than men. Men can develop breast cancer, but this disease is about 100 times more common among women than men.

Aging: Your risk of developing breast cancer increases as you get older. About 17% of invasive breast cancer diagnoses are among women in their 40s, while about 78% of women with invasive breast cancer are age 50 or older when they are diagnosed.

Genetic risk factors: Recent studies have shown that about 5% to 10% of breast cancer cases are hereditary as a result of gene changes (called mutations). The most common mutations are those of the BRCA1 and BRCA2 genes. Normally, these genes help to prevent cancer by making proteins that keep cells from growing abnormally. However, if you have inherited either mutated gene from a parent, you are at increased risk for breast cancer.

See the section, "Do We Know What Causes Breast Cancer?" for more information about genes and DNA. Women with an inherited BRCA1 or BRCA2 mutation have up to an 80% chance of developing breast cancer during their lifetime and at a younger age than those women who are not born with one of these gene mutations in their cells. Women with these inherited mutations also have an increased risk for developing ovarian cancer. Although BRCA mutations are found most often in Jewish women of Ashkenazi (Eastern Europe) origin, they are also seen in African-American women and Hispanic women, many of whom have the kind of mutation seen in Ashkenazi Jewish women.

Other genes have been discovered that might also lead to inherited breast cancers. One of these is the ATM gene. ATM stands for ataxia-telangiectasia mutation. The gene is responsible for repairing damaged DNA. Certain families with a high rate of breast cancer

have been found to have mutations of this gene. Another gene, the CHEK-2 gene, also increases breast cancer risk about twofold when it is mutated. Neither one of these genes, however, is a frequent cause of familial breast cancer. But in women who carry the CHEK-2 mutation and have a strong family history of breast cancer, the risk is greatly increased.

Inherited mutations of the p53 tumor suppressor gene can also increase your risk of developing breast cancer, as well as leukemia, brain tumors, and/or sarcomas (cancer of bones or connective tissue). The *Li-Fraumeni syndrome*, named after the 2 researchers who described this inherited cancer syndrome, is a rare cause of breast cancer.

If you are considering genetic testing, it is strongly recommended that first you talk to a genetic counselor, nurse, or doctor qualified to interpret and explain these tests. It is very important to understand and carefully weigh the benefits and risks of genetic testing before these tests are done. Testing is expensive and is not covered by some health insurance plans. There is concern that people with abnormal genetic test results will not be able to get life insurance or that coverage may only be available at a much higher cost, but many states have passed laws that prevent insurance companies from denying insurance on the basis of genetic testing. To learn about the laws in your state, you can go to this internet site -- http://www.ncsl.org/programs/health/genetics/ndishlth.htm.

For more information, see the American Cancer Society's position statement on genetic testing or go to the National Cancer Institute site on genetic testing for breast cancer at http://www.cancer.gov/cancertopics/genetic-testing-breast/.

Family history of breast cancer: Breast cancer risk is higher among women whose close blood relatives have this disease. Your risk of developing breast cancer is increased if:

- You have 2 or more relatives with breast or ovarian cancer.
- Breast cancer occurs before age 50 in a relative (mother, sister, grandmother or aunt) on either side of the family. The risk is higher if your mother or sister has a history of breast cancer.
- You have relatives with both breast and ovarian cancer.
- You have 1 or more relatives with two cancers (breast and ovarian, or 2 different breast cancers).
- You have a male relative (or relatives) with breast cancer.
- You have a family history of breast or ovarian cancer and Ashkenazi Jewish heritage.
- Your family history includes a history of diseases associated with hereditary breast cancer such as Li-Fraumeni or Cowden Syndrome.

Having 1 first-degree relative (mother, sister, or daughter) with breast cancer approximately doubles a woman's risk. Having 2, first-degree relatives increases her risk 5-fold. Although the exact risk is not known, women with a family history of breast cancer in a father or brother also have an increased risk of breast cancer. Altogether, about 20% to 30% of women with breast cancer have a family member with this disease.

Personal history of breast cancer: A woman with cancer in one breast has a 3- to 4-fold increased risk of developing a new cancer in the other breast or in another part of the same breast. This is different from a *recurrence* (return) of the first cancer.

Race: White women are slightly more likely to develop breast cancer than are African-American women. African-American women are more likely to die of this cancer. Many experts now feel that the main reason for this is because African-American women have

more aggressive tumors (see basal-like breast cancer, below). The reasons for this are not known. Asian, Hispanic, and Native-American women have a lower risk of developing and dying from breast cancer.

Abnormal breast biopsy: Some types of benign breast conditions are more closely linked to breast cancer risk than others. Doctors often divide benign breast conditions into 3 general groups, depending on how they affect this risk: non-proliferative lesions, proliferative lesions without atypia, and proliferative lesions with atypia.

The non-proliferative lesions (those not associated with any overgrowth of breast tissue) do not seem to affect breast cancer risk, or if they do at all it is to a very small extent. They include:

- fibrosis
- cysts
- mild hyperplasia
- adenosis (non-sclerosing)
- simple fibroadenoma
- phyllodes tumor (benign)
- a single papilloma
- fat necrosis
- mastitis
- duct ectasia
- benign tumors (lipoma, hamartoma, hemangioma, neurofibroma)

The proliferative lesions without atypia (those with excessive growth of cells in the ducts or lobules of the breast tissue) seem to raise a woman's risk of breast cancer slightly (1 ½ to 2 times normal). They include:

- usual ductal hyperplasia (without atypia)
- complex fibroadenoma
- sclerosing adenosis
- several papillomas or papillomatosis
- radial scar

The proliferative lesions with atypia (those with excessive growth of cells in the ducts or lobules of the breast tissue and the cells no longer appear normal) have a stronger effect on breast cancer risk, raising it 4 to 5 times higher than normal. They include:

- atypical ductal hyperplasia (ADH)
- atypical lobular hyperplasia (ALH)

Women with a family history of breast cancer and either hyperplasia or atypical hyperplasia have an even higher risk of developing a breast cancer.

Previous chest radiation: Women who as children or young adults had radiation therapy to the chest area as treatment for another cancer (such as Hodgkin disease or non-Hodgkin lymphoma) are at significantly increased risk for breast cancer. Some reports found the risk to be 12 times normal risk. This varies with the age of the patient at the time of radiation. Younger patients have a higher risk. If chemotherapy was also given, the risk may be lowered if the chemotherapy stopped ovarian hormone production. The risk of developing breast cancer appears to be highest if the breast was still in development (during adolescence) when the radiation was given.

Menstrual periods: Women who started menstruating at an early age (before age 12) or who went through menopause at a late age (after age 55) have a slightly higher risk of breast cancer.

Diethylstilbestrol (DES): In the 1940s through the 1960s some pregnant women were given diethylstilbestrol because it was thought to lower their chances of losing the baby (miscarriage). Recent studies have shown that these women have a slightly increased risk of developing breast cancer. Recent findings have also suggested that women whose mothers

took DES during pregnancy may have a higher risk for breast cancer than women not exposed to the drug in utero. For more information on DES see the American Cancer Society document, “DES Exposure: Questions and Answers.”

Lifestyle-Related Factors and Breast Cancer Risk

Not having children: Women who have had no children or who had their first child after age 30 have a slightly higher breast cancer risk. Having multiple pregnancies and becoming pregnant at an early age reduces breast cancer risk.

Oral contraceptive use: It is still not certain what part oral contraceptives (birth control pills) might play in breast cancer risk. Studies have suggested that women now using oral contraceptives have a slightly greater risk of breast cancer than women who have never used them. Women who stopped using oral contraceptives more than 10 years ago do not appear to have any increased breast cancer risk. When considering using oral contraceptives, women should discuss their other risk factors for breast cancer with their health care team.

Postmenopausal hormone therapy (also known as hormone replacement therapy, or HRT): It has become clear that long-term use (several years or more) of postmenopausal hormone therapy (PHT), particularly estrogen and progesterone combined, increases your risk of breast cancer. Long-term PHT use may also increase your chances of dying of breast cancer.

If you still have your uterus (womb), doctors generally prescribe estrogen and progesterone (known as combined PHT). Estrogen relieves menopausal symptoms and delays *osteoporosis*

(thinning of the bones that can lead to fractures). But estrogen can increase the risk of developing cancer of the uterus. Progesterone is added to help prevent this.

If you no longer have your uterus, estrogen alone can be prescribed. This is commonly known as estrogen replacement therapy (ERT). This probably does not increase the risk of breast cancer very much, if at all, especially if used for a relatively short period of time.

Several large studies, including the Women's Health Initiative (WHI), have found that there is an increased risk of breast cancer related to the use of combined PHT. The most recent results from the WHI found that not only did combined PHT increase breast cancer risk, but it also increased the likelihood that the cancer would be found at a more advanced stage. This is because it appeared to reduce the effectiveness of mammograms, as more abnormal findings on mammograms were noted. A large study from the United Kingdom has now found that women who took the combined therapy were also more likely to die of breast cancer than women who didn't.

The risk of PHT appears to apply only to current and recent users, and a woman's breast cancer risk seems to return to that of the general population within 5 years of stopping PHT.

Estrogen alone (ERT) does not appear to increase the risk of developing breast cancer. But when used long term (for more than 10 years), ERT has been found to increase the risk of ovarian and breast cancer in some studies.

At this time there appear to be few strong reasons to use postmenopausal hormone therapy (combined PHT or ERT), other than possibly for the temporary relief of menopausal

symptoms. In addition to the increased risk of breast cancer, the WHI found that combined PHT also increased the risk of heart disease, blood clots, and strokes, and did not have a beneficial effect on mental function or preventing Alzheimer's disease. It did lower the risk of colorectal cancer and osteoporosis, but this must be weighed against the possible harms, and it should be considered that there are other effective ways to prevent osteoporosis. And, as noted above, while ERT did not seem to have much effect on the risk of breast cancer, it did increase the risk of stroke.

The decision to use PHT should be made by the woman and her doctor after weighing the possible risks (including increased risk of heart disease, breast cancer, strokes, and blood clots) and benefits (relief of menopausal symptoms, reduced risk of osteoporosis), and considering each woman’s other risk factors for heart disease, breast cancer, osteoporosis, and the severity of her menopausal symptoms.

Breast-feeding and pregnancy: Some studies suggest that breast-feeding may slightly lower breast cancer risk, especially if breast-feeding is continued for 1.5 to 2 years. Other studies found no impact on breast cancer risk.

The explanation of this may be that both pregnancy and breast-feeding reduce a woman's total number of lifetime menstrual cycles. This may be similar to the reduction of risk due to late menarche (start of menstrual periods) or early menopause, which also decrease the total number of menstrual cycles. One study concluded that having more children and breast-feeding longer could reduce the risk of breast cancer by half.

Alcohol: Use of alcohol is clearly linked to an increased risk of developing breast cancer. The risk increases with the amount of alcohol consumed. Compared with nondrinkers, women who consume 1 alcoholic drink a day have a very small increase in risk. Those who have 2 to 5 drinks daily have about 1½ times the risk of women who drink no alcohol. Alcohol is also known to increase the risk of developing cancers of the mouth, throat, and esophagus. The American Cancer Society recommends limiting your consumption of alcohol.

Obesity and high-fat diets: Obesity (being overweight) has been found to be a breast cancer risk in all studies, especially for women after menopause. Although your ovaries produce most of your estrogen, fat tissue produces a small amount of estrogen. Having more fat tissue after menopause can increase your estrogen levels and, thereby, increase your likelihood of developing breast cancer.

The connection between weight and breast cancer risk is complex, however. For example, risk appears to be increased for women who gained weight as an adult but is not increased among those who have been overweight since childhood. Also, excess fat in the waist area may affect risk more than the same amount of fat in the hips and thighs. Researchers believe that fat cells in various parts of the body have subtle differences in their metabolism that may explain this observation.

Studies of fat in the diet have not clearly shown that this is a breast cancer risk factor. Most studies found that breast cancer is less common in countries where the typical diet is low in total fat, low in polyunsaturated fat, and low in saturated fat.

On the other hand, many studies of women in the United States have not found breast cancer risk to be related to dietary fat intake. Researchers are still not sure how to explain this apparent disagreement. Many scientists note that studies comparing diet and breast cancer risk in different countries are complicated by other differences (such as activity level, intake of other nutrients, and genetic factors) that might also alter breast cancer risk.

More research is needed to better understand the effect of the types of fat eaten and body weight on breast cancer risk. But it is clear that calories do count and fat is a major source of these. A diet high in fat has also been shown to influence the risk of developing several other types of cancer, and intake of certain types of fat is clearly related to heart disease risk. The American Cancer Society recommends you maintain a healthy weight throughout your life and limit your intake of processed and red meats.

Physical activity: Evidence is growing that physical activity in the form of exercise reduces breast cancer risk. The only question is how much exercise is needed. In one study from the Women's Health Initiative (WHI) as little as 1.25 to 2.5 hours per week of brisk walking reduced a woman's risk by 18%. Walking 10 hours a week reduced the risk a little more. The American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention recommend that you engage in 45 to 60 minutes of intentional physical activity 5 or more days a week.

Factors With Uncertain, Controversial, or Unproven Effect on Breast Cancer Risk

Antiperspirants: Internet e-mail rumors have suggested that chemicals in underarm antiperspirants are absorbed through the skin, interfere with lymph circulation, cause toxins

to build up in the breast, and eventually lead to breast cancer. There is very little experimental or epidemiological evidence to support this rumor. Chemicals in products such as antiperspirants are tested thoroughly to ensure their safety. One small study recently found trace levels of parabens (used as preservatives in antiperspirants), which have weak estrogen-like properties, in a small sample of breast cancer tumors. However, the study did not look at whether parabens caused the tumors. This was a preliminary finding, and more research is needed to determine what effect, if any, parabens may have on breast cancer risk. On the other hand, a recent large study of breast cancer causes found no increase in breast cancer in women who used underarm antiperspirants or shaved their underarms.

Underwire bras: Internet e-mail rumors and at least one book have suggested that bras cause breast cancer by obstructing lymph flow. There is no scientific or clinical basis for this claim.

Induced abortion: Several studies have provided very strong data that induced abortions have no overall effect on the risk of breast cancer. Also, there is no evidence of a direct relationship between breast cancer and spontaneous abortion (miscarriage) in most of the studies that have been published. Scientists invited to participate in a conference on abortion and breast cancer by the National Cancer Institute (February 2003) concluded that there was no relationship. A recent report of 83,000 women with breast cancer found no link to a previous abortion, either spontaneous (stillbirth) or induced.

Breast implants: Several studies have found that breast implants do not increase breast cancer risk although silicone breast implants can cause scar tissue to form in the breast. Implants make it harder to see breast tissue on standard mammograms, but additional x-ray

pictures called implant displacement views can be used to more completely examine the breast tissue.

Environmental pollution: A great deal of research has been reported and more is being done to understand environmental influences on breast cancer risk. The goal is to determine their possible relationships to breast cancer. Currently, research does not show a clear link between breast cancer risk and exposure to environmental pollutants, such as the pesticide DDE (chemically related to DDT), and PCBs (polychlorinated biphenyls).

Tobacco smoke: Most studies have found no link between active cigarette smoking and breast cancer. Though active smoking has been suggested to increase the risk of breast cancer in some studies, the issue remains controversial.

An issue that continues to be an active focus of scientific research is whether secondhand smoke may increase the risk of breast cancer. Both mainstream and secondhand smoke contain about 20 chemicals that, in high concentrations, cause breast cancer in rodents. Chemicals in tobacco smoke reach breast tissue and are found in breast milk.

The evidence regarding secondhand smoke and breast cancer risk in human studies is controversial, at least in part because the risk has not been shown to be increased in active smokers. One possible explanation for this is that tobacco smoke may have different effects on breast cancer risk in smokers and in those who are just exposed to smoke.

A report from the California Environmental Protection Agency in 2005 concluded that the evidence regarding secondhand smoke and breast cancer is "consistent with a causal

association" in younger, mainly premenopausal women. The 2006 US Surgeon General's report, *The Health Consequences of Involuntary Exposure to Tobacco Smoke*, concluded that there is "suggestive but not sufficient" evidence of a link at this point. In any case, women should be told that this possible link to breast cancer is yet another reason to avoid contact with secondhand smoke.

Night work: Several studies have suggested that women who work at night, for example, nurses on a night shift, may have an increased risk of developing breast cancer. However, this increased risk has not yet been proven and more studies are in progress. According to some researchers, the effect may be due to disruption in melatonin, a hormone that is affected by light, but other hormones are also being studied.

Do We Know What Causes Breast Cancer?

Although many risk factors may increase your chance of developing breast cancer, it is not yet known exactly how some of these risk factors cause cells to become cancerous. A woman's hormones somehow stimulate breast cancer growth. Just how this comes about has not yet been figured out.

Researchers are beginning to understand how certain changes in DNA can cause normal breast cells to become cancerous. DNA is the chemical that carries the instructions for nearly everything our cells do. We usually resemble our parents because they are the source of our DNA. However, DNA affects more than our outward appearance.

Some *genes* (parts of DNA) contain instructions for controlling when our cells grow, divide, and die. Certain genes that promote cell division are called *oncogene*s. Others that slow down

cell division, or cause cells to die at the right time, are called *tumor suppressor genes*. It is known that cancers can be caused by DNA *mutations* (changes) that "turn on" oncogenes or "turn off" tumor suppressor genes.

The BRCA genes (BRCA1 and BRCA2) are tumor suppressor genes. When they are mutated, they no longer function to suppress abnormal growth and cancer is more likely to develop. Certain inherited DNA changes (you are born with these) can cause an increased risk for developing cancer in people who carry these changes and are responsible for the cancers that run in some families.

Most DNA mutations related to breast cancer, however, occur in single breast cells during a woman's life rather than having been inherited. These acquired mutations of oncogenes and/or tumor suppressor genes may result from radiation or cancer-causing chemicals. So far, studies have not been able to identify any chemical in the environment or in our diets that is likely to cause these mutations, or a subsequent breast cancer. The cause of most acquired mutations remains unknown.

Women have already begun to benefit in several ways from recent advances in understanding the genetic basis of breast cancer. The section, "What Are the Risk Factors for Breast Cancer?" explains how genetic testing can identify some women who have inherited abnormal BRCA1, BRCA2, CHEK-2, or p53 tumor suppressor genes. These women can then take steps to reduce their risk of developing breast cancers and to monitor changes in their breasts carefully to find cancer at an earlier, more treatable stage. (For more information see the American Cancer Society documents, “Medicines to Reduce Breast Cancer Risk” and “Breast Cancer Early Detection.”)

Most breast cancers have several gene mutations that are acquired. That means that these mutations are not inherited. They develop as part of the cancer.

Tests to identify other acquired changes in oncogenes or tumor suppressor genes (such as p53) may help doctors more accurately predict the survival outcome of some women with breast cancer. But with the exception of the HER2 oncogene, these tests have not yet been shown to be useful in making decisions about treatment and are used only for research purposes.

Can Breast Cancer Be Prevented?

A woman at average risk for breast cancer might reduce her risk somewhat by changing those risk factors that can be changed. If you give birth to several children and breast-feed them for several months, avoid alcohol, exercise regularly, and maintain a slim body, you are decreasing your risk of getting breast cancer. Likewise, avoiding PHT will avoid increasing your risk (see the section, "What Are the Risk Factors for Breast Cancer?").

Other than these lifestyle changes, the most important action a woman can take is to follow early detection guidelines. Following the American Cancer Society's guidelines for early detection (outlined in the section, "Can Breast Cancer Be Found Early?") will not prevent breast cancer but can help find cancers when the likelihood of successful treatment is greatest.

If you are a woman with a strong family history of breast cancer or with a known genetic mutation of a BRCA gene, there are things you can do to reduce your chances of developing breast cancer. We strongly recommend genetic counseling before any of these steps. It is important to know if your mutation is BRCA1 or BRCA2. BRCA1 cancers may not be prevented by tamoxifen or raloxifene.

Also, if you have had DCIS, LCIS, or biopsies that have shown pre-malignant or pre-cancerous changes, you might also consider treatment to reduce your breast cancer risk.

Genetic testing for BRCA gene: Recently the US Preventive Services Task Force made recommendations for genetic testing. They recommended that only people with a strong family history should be evaluated. Women who are NOT of Ashkenazi (Eastern European) Jewish heritage should be referred for genetic evaluation if they have:

- Two first-degree relatives with breast cancer, one of whom was diagnosed when they were younger than 50, or
- Three or more first or second degree relatives diagnosed with breast cancer at any age, or
- A first degree relative diagnosed with cancer in both breasts, or
- Two or more first or second degree relatives diagnosed at any age, or
- A male relative with breast cancer

Women of Ashkenazi (Eastern European) Jewish heritage should be referred for genetic evaluation if they have:

- A first degree relative with breast or ovarian cancer at any age or
- Two second degree relatives on the same side of the family with breast or ovarian cancer at any age.

Breast Cancer Risk Reduction and Chemoprevention

The use of drugs to reduce the risk of cancer is called chemoprevention. The anti-estrogen drug, *tamoxifen*, is an example of this. Tamoxifen has been used for several years to reduce

the risk of recurrence in localized breast cancer and as a treatment for advanced breast cancer (see the section, "How Is Breast Cancer Treated?"). Several studies have looked at tamoxifen's ability to lower the risk of getting breast cancer in women known to be at increased risk for the disease.

Results from the Breast Cancer Prevention Trial (BCPT) have shown that women at increased risk for breast cancer are less likely to develop the disease if they take tamoxifen. Women in the study were assigned to take either tamoxifen or a placebo pill for 5 years. After 7 years of follow-up, women taking tamoxifen had 42% fewer breast cancers than women who took the placebo, although there was no difference in the risk of death due to breast cancer. Thus far, tamoxifen is the only drug approved for use in reducing breast cancer risk in high-risk women.

Because tamoxifen has side effects that include increased risks of endometrial (uterine) cancer and blood clotting, every woman should consider the possible benefits and risks of tamoxifen before deciding whether or not it is right for her.

Like tamoxifen, *raloxifene* also blocks the effect of estrogen on breast tissue. In a study looking at raloxifene for preventing osteoporosis, researchers noticed that it also lowered the risk of breast cancer. A study comparing the effectiveness of the 2 drugs, called the Study of Tamoxifen and Raloxifene (STAR) trial, found that raloxifene reduced the risk of invasive breast cancer to the same degree as tamoxifen, although it didn't have the same protective effect against non-invasive cancer (DCIS or LCIS). Raloxifene did, however, have lower risks of certain side effects such as uterine cancer and blood clots in the legs or lungs, compared to tamoxifen.

It isn't yet clear which women should take this drug. No specific guidelines have been developed, so this is a decision to be made by women and their doctors. At this time, it should only be considered for women who are postmenopausal and wish to take something to lower their risk of developing cancer. It should not be used as a substitute for tamoxifen in women with a diagnosis of invasive or in situ breast cancer, nor should it be given after concluding 5 years of tamoxifen in the adjuvant setting. This drug currently has FDA approval only for use to prevent osteoporosis in post-menopausal women, though the company that makes it plans to ask the FDA to approve it for use in breast cancer prevention by the end of 2006. For now, raloxifene is still being studied for use in reducing breast cancer risk.

Other drugs that are being studied as breast cancer chemopreventive agents in postmenopausal women are *aromatase inhibitors*. These block the production of small amounts of estrogen that postmenopausal women normally make. But they also have side effects, such as causing joint pain and stiffness and bone loss, leading to a higher risk of osteoporosis.

New studies are under way using other drugs. Some studies have found that women who take aspirin or non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, have a lower risk of breast cancer. Similar drugs (called COX-2 inhibitors) are being tested to see if they can reduce the risk of breast cancer in women who are at a high risk for this disease. Recent studies have shown, though, that COX-2 inhibitors can raise the risk of heart attacks. For more information on chemopreventive drugs see the American Cancer Society document, "Medicines to Reduce Breast Cancer Risk."

More clinical trials will be needed before doctors can be certain of the best way to prevent breast cancer in women at high risk for this disease.

Many the drugs mentioned above are discussed below under hormonal treatment.
For more information on the possible benefits and risks of chemopreventive drugs see the American Cancer Society document, "Medicines to Reduce Breast Cancer Risk."

Preventive (Prophylactic) Mastectomy for Women With Very High Breast Cancer Risk

For the few women who are at very high risk for breast cancer, prophylactic mastectomy may be an option. The purpose of the surgery is to reduce the risk by removing both breasts before breast cancer is diagnosed. The reasons for considering this type of surgery may include one or more of the following risk factors:

- mutated BRCA genes found by genetic testing
- previous cancer in one breast
- strong family history (breast cancer in several close relatives)
- biopsy specimens showing lobular carcinoma in situ (LCIS)

There is no way to know ahead of time how this surgery will affect a particular woman. Some women with BRCA mutations will develop a fatal breast cancer early in life, and a prophylactic mastectomy before the cancer occurs might add many years to their life expectancy. Although most women with BRCA mutations develop breast cancer, some don't and these women would not benefit from the surgery.

Also, it is important to realize that while this operation removes nearly all of the breast tissue, a small amount remains. So although this operation markedly reduces the risk of breast

cancer, a cancer can still develop in the breast tissue remaining after surgery. To date, this has been a rare problem.

Although women might develop breast cancer that can be found by mammograms or breast exam and be treated and cured by mastectomy, these women still face a high risk of cancer in the remaining breast. These women might consider preventive mastectomy of the remaining breast. Second opinions are strongly recommended before any woman makes the decision to have this surgery. The American Cancer Society Board of Directors has stated that "only very strong clinical and/or pathologic indications warrant doing this type of preventive operation." Nonetheless, after careful consideration, this might be the right choice for some women.

Although this document is not about ovarian cancer, it is important that women with a BRCA mutation recognize they have a high risk of developing ovarian cancer. Most doctors recommend that these women have their ovaries surgically removed once child bearing is complete.

Oophorectomy (removing ovaries) for Women With Very High Breast Cancer Risk

Women who have the BRCA1 mutation and who have their ovaries surgically removed before they are age 40 appear to have a reduced risk of breast cancer. One study has found that the risk of cancer is lowered by two-thirds for 10 years following the surgery. Longer time periods have not been studied.

Can Breast Cancer Be Found Early?

Screening refers to tests and exams used to detect a disease, such as cancer, in people who do not have any symptoms. The goal of screening exams, such as mammograms, for early breast cancer detection is to find cancers before they start to cause symptoms. Breast cancers that are detected because they can be felt tend to be larger and are more likely to have spread beyond the breast. In contrast, breast cancers found during screening exams are more likely to be small and still confined to the breast.

The size of a breast cancer and how far it has spread are the most important factors in predicting the prognosis (the outlook for chances of survival) of a woman with this disease. Finding a breast cancer as early as possible improves the likelihood that treatment will be successful. Most doctors feel that early detection tests for breast cancer save many thousands of lives each year, and that many more lives could be saved if even more women and their health care providers took advantage of these tests. Following the American Cancer Society's guidelines for the early detection of breast cancer improves the chances that breast cancer can be diagnosed at an early stage and treated successfully.

American Cancer Society Recommendations for Early Breast Cancer Detection

Women age 40 and older should have a screening mammogram every year and should continue to do so for as long as they are in good health.

- Current evidence supporting mammograms is even stronger than in the past. In particular, recent evidence has confirmed that mammograms offer substantial benefit for women in their 40s. Women can feel confident about the benefits associated with regular mammograms for finding cancer early. However, mammograms also have limitations. A mammogram will miss some cancers, and it sometimes leads to follow up of findings that are not cancer, including biopsies.

- Women should be told about the benefits, limitations, and potential harms linked with regular screening. Mammograms can miss some cancers. However, mammograms, despite their limitations, remain a very effective and valuable tool for decreasing suffering and death from breast cancer.

- Mammograms for older women should be based on the individual, her health, and other serious illnesses, such as congestive heart failure, end-stage renal disease, chronic obstructive pulmonary disease, and moderate-to-severe dementia. Age alone should not be the reason to stop having regular mammograms. As long as a woman is in good health and would be a candidate for treatment, she should continue to be screened with a mammogram.

Women in their 20s and 30s should have a clinical breast exam (CBE) as part of a periodic (regular) health exam by a health professional preferably every 3 years. After age 40, women should have a breast exam by a health professional every year.

- CBE is a complement to mammograms and an opportunity for women and their doctor or nurse to discuss changes in their breasts, early detection testing, and factors in the woman's history that might make her more likely to have breast cancer.

- There may be some benefit in having the CBE shortly before the mammogram. The exam should include instruction for the purpose of getting more familiar with your own breast. Women should also be given information about the benefits and limitations of CBE and breast self exam (BSE). Breast cancer risk is very low for women in their 20s and gradually increases with age. Women should be told to promptly report any new breast symptoms to a health professional.

BSE is an option for women starting in their 20s. Women should be told about the benefits and limitations of BSE. Women should report any breast changes to their health professional right away.

- Research has shown that BSE plays a small role in finding breast cancer compared with finding a breast lump by chance or simply being aware of what is normal for each woman. Some women feel very comfortable doing BSE regularly (usually monthly) which involves a systematic step-by-step approach to examining the look and feel of one's breasts. Other women are more comfortable simply looking and feeling their breasts in a less systematic approach, such as while showering or getting dressed or doing an occasional thorough exam. Sometimes, women are so concerned about "doing it right" that they become stressed over the technique. Doing BSE regularly is one way for women to know how their breasts normally look and feel and to notice any changes. The goal, with or without BSE, is to report any breast changes to a doctor or nurse right away.

- Women who choose to do BSE should have their BSE technique reviewed during their physical exam by a health professional. It is okay for women to choose not to do BSE or not to do it on a regular schedule. However, by doing the exam regularly, you get to know how your breasts normally look and feel and you can more readily detect any signs or symptoms If a change occurs, such as development of a lump or swelling, skin irritation or dimpling, nipple pain or retraction (turning inward), redness or scaliness of the nipple or breast skin, or a discharge other than breast milk. Should you notice any changes you should see your health care provider as soon as possible for evaluation. Remember that most of the time, however, these breast changes are not cancer.

Women at high risk (greater than 20% lifetime risk) should get an MRI and a mammogram every year. Women at moderately increased risk (15% to 20% lifetime risk) should talk with their doctors about the benefits and limitations of adding MRI screening to their yearly mammogram. Yearly MRI screening is not recommended for women whose lifetime risk of breast cancer is less than 15%.

- Women at high risk include those who:
  - have a known BRCA1 or BRCA2 gene mutation
  - have a first-degree relative (mother, father, brother, sister, or child) with a BRCA1 or BRCA2 gene mutation, and have not had genetic testing themselves
  - have a lifetime risk of breast cancer of 20%-25% or greater, according to risk assessment tools that are based mainly on family history
  - had radiation therapy to the chest when they were between the ages of 10 and 30 years
  - have Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley-Ruvalcaba syndrome, or have one of these syndromes in first-degree relatives

- Women at moderately increased risk include those who:
  - have a lifetime risk of breast cancer of 15%-20%, according to risk assessment tools that are based mainly on family history
  - have a personal history of breast cancer, ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), atypical ductal hyperplasia (ADH), or atypical lobular hyperplasia (ALH)
  - have extremely dense breasts or unevenly dense breasts when viewed by mammograms

- If MRI is used, it should be in addition to, not instead of, a screening mammogram. This is because while an MRI is a more sensitive test (it's more likely to detect cancer than a mammogram), it may still miss some cancers that a mammogram would detect.

- For most women at high risk, screening with MRI and mammograms should begin at age 30 years and continue for as long as a woman is in good health. But because the evidence is limited regarding the best age at which to start screening, this decision should be based on shared decision making between patients and their health care providers, taking into account personal circumstances and preferences.

- Several risk assessment tools, with names such as BRCAPRO, the Claus model, and the Tyrer-Cuzick model, are available to help health professionals estimate a woman's breast cancer risk. These tools give approximate, rather than precise, estimates of breast cancer risk based on different combinations of risk factors and different data sets. As a result, they may give different risk estimates for the same woman. Their results should be discussed by a woman and her doctor when being used to decide on whether to start MRI screening.

- It is recommended that women who get screening MRI do so at a facility that can do an MRI-guided breast biopsy at the same time if needed. Otherwise, the woman will have to have a second MRI exam at another facility at the time of biopsy.

- There is no evidence at this time that MRI will be an effective screening tool for women at average risk. While MRI is more sensitive than mammograms, it also has a higher false-positive rate (where the test finds something that turns out not to be cancer), which would result in unneeded biopsies and other tests in a large portion of these women.

The American Cancer Society believes the use of mammograms, MRI (in women at high risk), clinical breast exams, and finding and reporting breast changes early, according to the recommendations outlined above, offers women the best opportunity for reducing the breast cancer death rate through early detection. This combined approach is clearly better than any one examination. Without question, breast physical exam without a mammogram would miss the opportunity to detect many breast cancers that are too small for a woman or her doctor to feel, but can be seen on mammograms. While mammograms are a sensitive screening method, a small percentage of breast cancers do not show up on mammograms, but can be felt by a woman or her doctors. For women at high risk of breast cancer, such as those with BRCA gene mutations or a strong family history, both MRI and mammogram exams of the breast are recommended.

Mammograms

A *mammogram* is an x-ray of the breast. A diagnostic mammogram is used to diagnose breast disease in women who have breast symptoms. Screening mammograms are used to

look for breast disease in women who are asymptomatic; that is, they appear to have no breast problems. Screening mammograms usually involve 2 views (x-ray pictures) of each breast. For some patients, such as women with breast implants, additional pictures may be needed to include as much breast tissue as possible. Women who are breast-feeding can still get mammograms, although these are probably not quite as accurate.

Although breast x-rays have been performed for more than 70 years, the modern mammogram has only existed since 1969. That was the first year x-ray units specifically for breast imaging were available. Modern mammogram equipment designed for breast x-rays uses very low levels of radiation, usually a dose of about 0.1 to 0.2 rads per picture.

Strict guidelines are in place to ensure that mammogram equipment is safe and uses the lowest dose of radiation possible. Many people are concerned about the exposure to x-rays, but the level of radiation used in modern mammograms does not significantly increase the risk for breast cancer.

To put dose into perspective, if a woman with breast cancer is treated with radiation, she will receive around 5,000 rads (a rad is a measure of radiation dose). If she had yearly mammograms beginning at age 40 and continuing until she was 90, she will have received 20 to 40 rads. As another example, flying from New York to California on a commercial jet exposes a woman to roughly the same amount of radiation as one mammogram.

For a mammogram, the breast is pressed between 2 plates to flatten and spread the tissue. Although this may be uncomfortable for a moment, it is necessary to produce a good, "readable" mammogram. The compression only lasts a few seconds. The entire procedure for

a screening mammogram takes about 20 minutes. This procedure produces a black and white image of the breast tissue on a large sheet of film that is read, or interpreted, by a *radiologist* (a doctor specially trained to interpret images from x-rays, ultrasound, MRI, and related tests).

The doctor reading the films will look for several types of changes:

- *Calcifications*, or *microcalcifications*, are tiny mineral deposits within the breast tissue that appear as small white spots on the film. They may occur singly or in clusters. They are a sign of changes within the breast and can be either carefully watched by additional, periodic mammograms or examined by biopsy (removal of a small amount of breast tissue). They may be caused by benign breast conditions or, less often, by breast cancer.

- A *mass*, which may occur with or without calcifications, is another important change that can be seen on a mammogram. Masses can be many things, including cysts and fibroadenomas, but they may be cancer and usually should be biopsied.

- A *cyst* is a collection of fluid in a small sac in the breast. It can feel like a lump, usually soft, in the breast. Either a breast ultrasound or removal of the fluid with a needle (aspiration) is used to confirm that a mass, or lump, is a cyst and not another type of mass. It is very rare for a cyst to be cancerous. If a cyst has ultrasound features that are suggestive of cancer, fluid removed from the cyst will be examined to look for malignant cells or an ultrasound-guided biopsy of the suspicious region of the cyst will be performed.

A mammogram cannot prove that an abnormal area is cancer. To confirm whether cancer is present, a small amount of tissue must be removed and examined under a microscope. This procedure is called a *biopsy*.

You should also be aware that mammograms are imperfect at finding breast cancer. If you have a breast lump, you should have it checked by your doctor and consider having it biopsied even if your mammogram is normal.

For some women, such as those with breast implants (for augmentation or as reconstruction after mastectomy), additional pictures may be needed to include as much breast tissue as possible. Breast implants make it harder to see breast tissue on standard mammograms, but additional x-ray pictures with implant displacement and compression views can be used to more completely examine the breast tissue.

Mammograms are less effective in younger women, usually because their breasts are dense, and this can hide a tumor. This is also true for pregnant women and women who are breast feeding, although studies have shown that the breasts may or may not be any denser than before their pregnancy. Since most breast cancers occur in older women, this is usually not a major problem.

It is, however, a problem for young women who are at high risk for breast cancer (due to gene mutations, a strong family history, or other factors) because they often develop breast cancer at a younger age. For this reason, the American Cancer Society now recommends MRI in addition to mammograms for screening in these women.

For more information see the American Cancer Society document, "Mammograms and Other Breast Imaging Procedures."

When You Get a Mammogram

Medicare, Medicaid, and most private health insurance plans cover mammogram costs or a percentage of them. Low-cost mammograms are available in most communities. Call us at 1-800-ACS-2345 for information about facilities in your area.

The procedure requires that you undress above the waist. A wrap for you to wear will be provided by the facility.

A technologist will be present to position your breasts for the mammogram. Most technologists are women. You and the technologist are the only ones present during the mammogram. Women who have no breast lumps or symptoms will have a *screening* mammogram. This includes 2 pictures of each breast, a top to bottom and a side-to-side view. To get a high-quality mammogram picture with excellent image quality, it is necessary to flatten the breast slightly. A technician places the breast on the mammogram machine's lower plate, which is made of metal and has a drawer to hold the x-ray film. The upper plate, made of clear plastic, is lowered to compress the breast for a few seconds while the technician takes a picture. Although compression may be uncomfortable, most women do not say it is painful.

The whole procedure takes about 20 minutes. The actual breast compression only lasts a few seconds.

You may feel some discomfort when your breasts are compressed, but you should not feel pain. Try not to schedule a mammogram when your breasts are likely to be tender, as they may be just before or during your period.

All mammography facilities are now required to send your results to you within 30 days. You will be contacted within 5 working days if there is a problem with the mammogram.

Only 1 or 2 mammograms of every 1,000 lead to a diagnosis of cancer. However, about 10% of women will require additional mammograms. Don't be alarmed if this happens to you. Only 8% to 10% of those women will need a biopsy, and 80% of those biopsies will not be cancer.

If you are a woman aged 40 or over, you should get a mammogram every year. You can schedule the next one while you're at the facility and/or request a reminder.

Tips for Mammograms

The following are useful suggestions for making sure that you will receive a quality mammogram:

- Ask to see the FDA certificate that is issued to all facilities that meet high professional standards of safety and quality.
- Use a facility that either specializes in mammograms or performs at least 3 to 5 mammograms a day.
- If you are satisfied that the facility is of high quality, continue to go there on a regular basis so that your mammograms can be compared from year to year.
- If you change facilities, it is important to take your previous mammograms with you to the new facility so that they can be compared to the new ones.
- If you have sensitive breasts, try having your mammogram at a time of the month when your breasts will be least tender. Try to avoid the week right before your period. This will help lessen the discomfort.
- Don't wear deodorant, powder, or cream under your arms -- it may interfere with the quality of the mammogram.
- Bring a list of the places, dates of mammograms, biopsies, or other breast treatments you have had before.
- If you do not hear from your doctor within 10 days, do not assume that your mammogram was normal -- confirm this by calling your doctor or the facility.

Financial assistance for breast cancer testing for low-income women: Breast cancer testing is now more available to medically underserved women through the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). This program provides breast and cervical cancer early detection testing to women without health insurance for free or at very low cost.

The NBCCEDP attempts to reach as many women in medically underserved communities as possible, including older women, women without health insurance, and women who are members of racial and ethnic minorities. Although the program is administered within each state, the Centers for Disease Control and Prevention (CDC) provide matching funds and support to each state program.

Offered mainly through nonprofit organizations and local health clinics, this program makes testing available for breast and cervical cancer in medically underserved women. Each state's Department of Health has information on how to contact the nearest program.

In 2000, the Breast and Cervical Cancer Treatment Act was signed into law. This act adds to the NBCCEDP by providing funds to pay for treatment associated with breast and cervical cancer in medically underserved populations. This new option helps women focus their energies on fighting their disease, instead of worrying about how to pay for treatment. As with the Early Detection Program, individual states must adopt the program to receive the matching federal funds.

The program is only designed to provide screening. But if a cancer is discovered, it will cover further diagnostic testing and a surgical consultation.

To learn more about this program, please contact the CDC at 1-888-842-6355 or on the Internet at www.cdc.gov/cancer.

Clinical Breast Exam

A clinical breast exam (CBE) is an exam of your breasts by a health care professional, such as a doctor, nurse practitioner, nurse, or doctor's assistant. For this exam, you undress from the waist up. The health care professional will first look at your breasts for changes in size or shape. Then, using the pads of the fingers, the examiner will gently feel (palpate) your breasts.

Special attention will be given to the shape and texture of the breasts, location of any lumps, and whether such lumps are attached to the skin or to deeper tissues. The area under both arms will also be examined.

During the CBE is a good time for the health care professional to teach breast self-examination to the woman who does not already know how to examine her breasts. Ask your doctor or nurse to teach you and watch your technique.

Breast Awareness and Self Exam

Beginning in their 20s, women should be told about the benefits and limitations of breast self exam (BSE). Women should be aware of how their breasts normally look and feel and report any new breast change to a health professional as soon as they are found. Finding a breast change does not mean there is a cancer.

Women can notice changes by being aware of how their breasts normally look and feel and by feeling their breasts for changes (breast awareness) or by choosing to use a step-by-step approach (see below) and using a specific schedule to examine her breasts.

Women with breast implants can do BSE. It may be helpful to have the surgeon help identify the edges of the implant so that you know what you are feeling. There is some thought that the implants push out the breast tissue and actually make it easier to examine.

If you choose to do BSE, the following information provides a step-by-step approach for the exam. The best time for a woman to examine her breasts is when the breasts are not tender or swollen. Women who are pregnant, breast feeding, or have breast implants can also choose to examine their breasts regularly. Women who examine their breasts should have their technique reviewed during their periodic health exams by their health care professional. It is acceptable for women to choose not to do BSE or to do BSE occasionally.

For women who choose not to do BSE, they should still be aware of their breasts and report any changes without delay to their doctor.

How to Examine Your Breasts

- Lie down and place your right arm behind your head. The exam is done while lying down, not standing up. This is because when lying down the breast tissue spreads evenly over the chest wall and it is as thin as possible making it much easier to feel all the breast tissue.
- Use the finger pads of the 3 middle fingers on your left hand to feel for lumps in the right breast. Use overlapping dime-sized circular motions of the finger pads to feel the breast tissue.
- Use 3 different levels of pressure to feel all the breast tissue. Light pressure is needed to feel the tissue closest to the skin; medium pressure to feel a little deeper; and firm

pressure to feel the tissue closest to the chest and ribs. A firm ridge in the lower curve of each breast is normal. If you're not sure how hard to press, talk with your doctor or nurse. Use each pressure to feel the breast tissue before moving on to the next spot.

- Move around the breast in an up and down pattern starting at an imaginary line drawn straight down your side from the underarm and moving across the breast to the middle of the chest bone (sternum or breastbone). Be sure to check the entire breast area going down until you feel only ribs and up to the neck or collar bone (clavicle).
- There is some evidence to suggest that the up and down pattern (sometimes called the vertical pattern) is the most effective pattern for covering the entire breast, without missing any breast tissue.
- Repeat the exam on your left breast, using the finger pads of the right hand.
- While standing in front of a mirror with your hands pressing firmly down on your hips, look at your breasts for any changes of size, shape, contour, or dimpling, or redness or scaliness of the nipple or breast skin. (The pressing down on the hips position contracts the chest wall muscles and enhances any breast changes.)
- Examine each underarm while sitting up or standing and with your arm only slightly raised so you can easily feel in this area. Raising your arm straight up tightens the tissue in this area and makes it difficult to examine.

This procedure for doing breast self exam is different than in previous procedure recommendations. These changes represent an extensive review of the medical literature and input from an expert advisory group. There is evidence that the woman's position (lying down), area felt, pattern of coverage of the breast, and use of different amounts of pressure increase the sensitivity of BSE as measured with silicone models. Lying down also increased the sensitivity of CBE using patient models with known small non-cancerous lumps in their breasts.

Magnetic Resonance Imaging (MRI)

For certain women at high risk for breast cancer, screening MRI is recommended along with a yearly mammogram. It is not generally recommended as a screening tool by itself, as it may miss some cancers that mammograms would detect.

MRI uses magnets and radio waves, instead of x-rays, to produce very detailed, cross-sectional images of the body. The most useful MRI exams for breast imaging use a contrast material (gadolinium DTPA) that is injected into a small vein in the arm before or during the exam. This improves the ability of the MRI to clearly show breast tissue details.

While MRI is more sensitive in detecting cancers than mammograms, it also has a higher false-positive rate (where the test finds something that turns out not to be cancer), which results in more recalls and biopsies. This is why it is not recommended as a screening test for women at average risk of breast cancer, as it would result in unneeded biopsies and other tests in a large portion of these women.

Just as mammography uses x-ray machines designed especially to image the breasts, breast MRI also requires special equipment. Higher quality images are produced by dedicated breast MRI equipment than by machines designed for head, chest, or abdominal MRI scanning. However, many hospitals and imaging centers do not have dedicated breast MRI equipment available. It is important that screening MRIs are done at facilities that are capable of performing an MRI-guided breast biopsy at the time of the exam if anything abnormal is found. Otherwise, the scan will need to be repeated at another facility at the time of the biopsy.

MRI is also more expensive than mammography. Most major insurance companies will likely pay for these screening tests if a woman can be shown to be at high risk, but it's not yet clear if all companies will. At this time there are concerns about costs of and limited access to high-quality MRI breast screening services for women at high risk of breast cancer.

How Is Breast Cancer Diagnosed?

If screening tests or your signs and symptoms suggest breast cancer, your doctor will use one or more methods to determine if the disease is present and to evaluate the stage of the cancer.

Signs and Symptoms

Although widespread use of screening mammograms has increased the number of breast cancers found before they cause any symptoms, some breast cancers are not found by mammogram, either because the test was not done or because, even under ideal conditions, mammograms cannot find every breast cancer.

The most common sign of breast cancer is a new lump or mass. A painless, hard mass that has irregular edges is more likely to be cancerous, but some cancers are tender, soft, and rounded. For this reason, it is important that a health care professional experienced in diagnosing breast diseases check any new breast mass or lump.

Other signs of breast cancer include a generalized swelling of part of a breast (even if no distinct lump is felt), skin irritation or dimpling, nipple pain or retraction (turning inward), redness or scaliness of the nipple or breast skin, or a discharge other than breast milk. Sometimes a breast cancer can spread to underarm lymph nodes and cause swelling there even before the original tumor in the breast tissue is large enough to be felt.

Medical History and Physical Exam

The first step in evaluation of a woman with suspected breast cancer is a complete medical history and physical exam. Your doctor will ask questions about your symptoms, any other health problems, and risk factors for benign breast conditions and breast cancer (such as whether any of your relatives had benign breast conditions, breast cancer, ovarian cancer, or other cancers).

Your breast will be thoroughly examined to locate any lump or suspicious area and to feel its texture, size, and relationship to the skin and chest muscles. Any changes in the nipples or the skin of your breast will be noted. The lymph nodes under the armpit and above the collarbones may be palpated (felt), because enlargement or firmness of these lymph nodes might indicate spread of breast cancer. Your doctor will also perform a complete physical exam to judge your general health and whether there is any evidence the cancer has spread.

In addition to the medical history and physical exam, imaging tests and biopsies may be done.

Imaging Tests to Diagnose Breast Disease

Mammograms: Although mammograms are mostly used for screening, they can also be used to examine the breast of a woman who has a breast problem. This can be a breast mass, nipple discharge, or an abnormality that was found on a screening mammogram. In some cases, special images known as cone views with magnification are used to make a small area of altered breast tissue easier to evaluate.

A diagnostic mammogram may show that a lesion (area of abnormal tissue) has a high likelihood of being benign (not cancer). In these cases, it is common to ask the woman to

come back sooner than usual for a recheck, usually in 4 to 6 months. On the other hand, a diagnostic mammogram may show that the abnormality is not worrisome at all, and the woman can then return to having routine yearly mammograms. Finally, the diagnostic work-up may suggest that a biopsy is needed to tell if the lesion is cancer. Even if the mammograms show no tumor, if you or your doctor can feel a lump, then usually a biopsy will be needed to make sure it isn't cancer. One exception would be if an ultrasound exam finds that the lump is a cyst.

Magnetic resonance imaging (MRI): MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body. A contrast material called *gadolinium* is often injected to better see details.

Patients have to lie inside a tube, which is confining and may upset people with claustrophobia (a fear of enclosed spaces). The machine also makes a buzzing noise that you may find disturbing. Some places provide headphones with music to block this out. MRIs are very expensive, although insurance plans generally pay for them once cancer is diagnosed.

Although MRI machines are quite common, they need to be specially adapted to look at the breast. They can be used to better examine cancers found by mammogram, or can be used along with mammograms for screening women who have a high risk of developing breast cancer.

MRI is also used for women who have been diagnosed with breast cancer. It is used to better determine the actual size of the cancer and to look for any other cancers in the breast.

Breast ultrasound: Ultrasound has become a valuable tool to use with mammography because it is widely available and less expensive than other options, such as MRI. Usually, breast ultrasound is used to target a specific area of concern found on the mammogram. Ultrasound also helps distinguish between cysts and solid masses and between benign and cancerous tumors. Ultrasound may be most helpful in women with high breast density (thickness). The National Cancer Institute (NCI) is sponsoring a clinical trial to evaluate the benefits and risks of adding screening breast ultrasound to screening mammograms in women with dense breasts and a higher risk of breast cancer.

Ultrasound, also known as *sonography*, uses high-frequency sound waves to outline a part of the body. High-frequency sound waves are transmitted into the area of the body being studied and echoed back. These echoes are picked up by the ultrasound probe. A computer changes the sound waves into an image that is displayed on a screen. You are not exposed to radiation during this test.

Ductogram: This test, also called a *galactogram*, is sometimes helpful in determining the cause of bloody nipple discharge. In this test a fine plastic tube is placed into the opening of the duct at the nipple. A small amount of contrast medium is injected, which outlines the shape of the duct on an x-ray image, which will show if there is a mass inside the duct.

Full-field digital mammogram (FFDM): A full-field digital mammogram is similar to a standard mammogram in that x-rays are used to produce an image of your breast. The

differences are in the way the image is recorded, viewed by the doctor, and stored. Standard mammograms are recorded on large sheets of photographic film. Digital mammograms are recorded and stored on a computer. After the exam, the doctor can view them on a computer screen and adjust the image size, brightness, or contrast to see certain areas more clearly. Digital images can also be sent electronically to another site for a remote consult with breast specialists. While many centers do not offer the digital option at this time, it is expected to become more widely available in the future.

Because digital mammograms cost more than standard mammograms, studies are now under way to determine which form of mammogram will benefit more women in the long run. Some studies have found that women who have a FFDM have to return less often for additional imaging tests because of inconclusive areas on the original mammogram. A recent large study from the National Cancer Institute found that a FFDM was more accurate in finding cancers in women younger than 50 and in women with dense breast tissue, although the rates of inconclusive results were similar between a FFDM and a film mammogram. It is important to remember that a standard film mammogram also is effective for these groups of women, and that they should not miss their regular mammogram if a digital mammogram is not available.

Computer-aided detection and diagnosis (CAD): Over the past 2 decades, computer-aided detection and diagnosis (CAD) has been developed to help radiologists detect suspicious changes on mammograms. This is done most commonly with screen-film mammograms and less often with digital mammograms. Generally, the computer device will scan the mammogram first. It can find tumors that the radiologist can’t spot. The radiologist, knowing the results of the CAD, will then review the films to look for lesions the CAD missed. The

radiologist will then decide the seriousness of the lesions the CAD found. Early research results suggest that CAD systems help radiologists diagnose more early stage cancers than mammograms alone.

Scintimammography: In scintimammography, a radioactive tracer is injected into a vein to detect breast cancer cells. The tracer attaches to breast cancers and is detected by a special camera. This is a very new technique and is still considered experimental. It may or may not be helpful in evaluating abnormal mammograms.

Tomosynthesis: This technology is an extension of a digital mammogram. Tomosynthesis allows the breast to be viewed as many thin slices and has the possibility of providing a more accurate and earlier diagnosis of breast cancer. This technology is still considered experimental and is not yet commercially available.

Other Tests

Nipple discharge exam: If you have spontaneous nipple discharge, some of the fluid may be collected and looked at under a microscope to see if any cancer cells are in it. Most nipple discharges or secretions are not cancer. In general, if the secretion appears clear green in color, or milky, cancer is very unlikely. If the discharge is red or red-brown, suggesting that it contains blood, it might possibly be caused by cancer, although an injury, infection, or benign tumor are more likely causes.

Even when no cancer cells are found in a nipple discharge, it is not possible to say for certain that a breast cancer is not present. If a patient has a suspicious mass, a biopsy is necessary, even if the nipple discharge does not contain cancer cells.

Ductal lavage and nipple aspiration: Ductal lavage is an experimental test developed for women who have no symptoms of breast cancer but are at very high risk for the disease. It is not a test to screen for or diagnose breast cancer, but it may help give a more accurate picture of a woman's risk of developing it.

Ductal lavage can be done in a doctor's office or an outpatient facility. An anesthetic cream is applied to numb the nipple area. Gentle suction is then used to help draw tiny amounts of fluid from the milk ducts up to the nipple surface. The fluid droplets that appear help locate the milk ducts' natural openings on the surface of the nipple. A tiny tube (called a catheter) is then inserted into a milk duct opening on the nipple. A small amount of anesthetic is infused into the duct to numb the inside. Saline (salt water) is slowly delivered through the catheter to gently "rinse" the duct and collect cells. The ductal fluid is withdrawn through the catheter and placed into a collection vial. The vial is then sent to a lab, where the cells are viewed under a microscope.

Ductal lavage is not considered appropriate for women who aren't at high risk for breast cancer. It is not clear whether it will ever be a useful tool. The test has not been shown to detect cancer early. It is much more useful as a test of cancer risk rather than as a screening test for cancer. More studies are needed to better define the usefulness of this test.

Nipple aspiration also looks for abnormal cells arising in the ducts, but is much simpler, in that nothing is inserted into the breast. The device for nipple aspiration uses small cups that are placed on the woman's breasts. The device warms the breasts, gently compresses them, and applies light suction to bring nipple fluid to the surface of the breast. The nipple fluid is

then collected and sent to a lab for analysis. As with ductal lavage, the procedure may be useful as a test of cancer risk but is not appropriate as a screening test for cancer. The test has not been shown to detect cancer early.

Biopsy

A biopsy is done when mammograms, ultrasound, or the physical exam finds a breast change (or abnormality) that is possibly cancer. A biopsy is the only way to tell if cancer is really present. All biopsy procedures remove a tissue sample for examination under a microscope. There are several types of biopsies, such as fine needle aspiration biopsy, core (large needle) biopsy, and surgical biopsy. Each type of biopsy has its own advantages and disadvantages.

The choice of which to use depends on your specific situation. Some of the factors your doctor will consider include how suspicious the lesion appears, how large it is, where in the breast it is located, how many lesions are present, other medical problems you may have, and your personal preferences. You might want to discuss the advantages and disadvantages of different biopsy types with your doctor.

Fine needle aspiration biopsy (FNAB): A thinner needle is used for FNAB than the ones used for blood tests. The needle can be guided into the area of the breast change while the doctor is feeling (palpating) the lump. The doctor can be a pathologist, radiologist, or surgeon. If the lump can't be felt easily, the doctor might use ultrasound or a method called stereotactic needle biopsy to guide the needle, although most of the time if a stereotactic device is used, a large needle (core) biopsy is done.

Ultrasound lets the doctor watch the needle on a screen as it moves toward and into the mass. For stereotactic needle biopsy, computers map the exact location of the mass using mammograms taken from 2 angles. Then a computer guides the needle to the right spot.

A local anesthetic (numbing medicine) may or may not be used. Because such a thin needle is used for the biopsy, the process of getting the anesthetic may actually be more uncomfortable than the biopsy itself.

Once the needle is in place, fluid is drawn out. If the fluid is clear, the lump is probably a benign cyst. Bloody or cloudy fluid can mean either a benign cyst or, very rarely, a cancer. If the lump is solid, small tissue fragments are drawn out. A pathologist (a doctor specializing in diagnosing disease from tissue samples) will examine the biopsy tissue or fluid to determine if it is cancerous.

Fine needle aspiration biopsies can sometimes miss a cancer and take benign cells from nearby the cancer. If it does not provide a clear diagnosis, or your doctor is still suspicious, a second biopsy or a different type of biopsy should be performed.

Stereotactic core needle biopsy: A core biopsy can sample breast changes felt by the doctor, as well as smaller ones pinpointed by ultrasound or mammogram. Depending on whether the abnormal area can be felt, about 3 to 5 cores are usually removed.

The needle used in core biopsies is larger than that used in FNAB. It removes a small cylinder of tissue (about 1/16- to 1/8-inch in diameter and ½-inch long) from a breast abnormality. The biopsy is done with local anesthesia in an outpatient setting.

Two new stereotactic biopsy methods can remove more tissue than a core biopsy. The *Mammotome*® is also known as *vacuum-assisted biopsy*. For this procedure the skin is numbed and a small incision (about ¼ inch) is made. A probe is inserted through the incision into the abnormal area of breast tissue. A cylinder of tissue is suctioned into the probe then a rotating knife within the probe cuts the tissue sample from the rest of the breast. The Mammotome procedure is done as an outpatient. No stitches are needed and there is minimal scarring. This method usually removes about twice as much tissue as core biopsies. The *ABBI* method (short for Advanced Breast Biopsy Instrument) uses a probe with a rotating circular knife and thin heated electrical wire to remove a large cylinder of abnormal tissue.

In some centers, the biopsy is guided by an MRI, which locates the tumors, plots its coordinates, and aims the stereotactic biopsy device into the tumor.

Surgical biopsy: Sometimes, a surgeon is needed to remove all or part of the lump for microscopic examination. An *excisional biopsy* removes an entire *lesion* (breast abnormality such as a mass or area containing calcifications), as well as a surrounding margin of normal-appearing breast tissue. In rare circumstances, this type of biopsy can be done in the doctor's office, but it is more commonly done in the hospital's outpatient department under a local anesthesia (you are awake during the procedure, but your breast is numb). Intravenous sedation is often given to make you less aware of the procedure.

During an excisional breast biopsy the surgeon may use a procedure called *wire localization* if there is a small lump that is hard to locate by touch or if an area looks suspicious on the x-ray but cannot be felt. After the area is numbed with local anesthetic, a thin hollow needle is

placed into the breast and x-ray views are used to guide the needle to the suspicious area. A thin wire is inserted through the center of the needle. A small hook at the end of the wire keeps it in place. The hollow needle is then removed, and the surgeon uses the wire to guide him to the abnormal area to be removed.

If a benign condition is diagnosed, no further treatment is needed. If the diagnosis is cancer, there is time for you to learn about the disease and to discuss all treatment options with your cancer care team, friends, and family. There is no need to rush into treatment. You may wish to obtain a second opinion before deciding on what treatment is best for you.

Imaging Tests to Detect Breast Cancer Spread

Chest x-ray: This test may be done to see whether the breast cancer has spread to your lungs.

Bone scan: This procedure helps show if a cancer has metastasized (spread) to your bones. The patient receives an injection of radioactive material called *technetium diphosphonate*. The amount of radioactivity used is very low and causes no long-term effects. The radioactive substance is attracted to diseased bone cells throughout the entire skeleton. Areas of diseased bone will be seen on the bone scan image as dense, gray to black areas, called "hot spots."

These areas may suggest metastatic cancer is present, but arthritis, infection, or other bone diseases can also cause a similar pattern. To distinguish among these conditions, the cancer care team may use other imaging tests or take bone biopsies. Bone scans can find metastases

earlier than regular x-rays but sometimes, even when the cancer has spread to the bones, the bone scan won't show it. Other imaging studies such as CT or MRI will be needed.

Computed tomography (CT): The CT scan is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body. The machine creates several pictures of the part of your body that is being studied. This test can help tell if your cancer has spread into your liver or other organs. Often after the first set of pictures is taken you will receive an intravenous injection of a *contrast agent*, or "dye," that helps better outline structures in your body. A second set of pictures is then taken.

CT scans can also be used to precisely guide a biopsy needle into a suspected metastasis. For this procedure, called a *CT-guided needle biopsy*, you remain on the CT scanning table while a radiologist advances a biopsy needle toward the location of the mass. CT scans are repeated until the doctors are sure that the needle is within the mass. A fine needle biopsy sample (tiny fragment of tissue) or a core needle biopsy sample (a thin cylinder of tissue about ½-inch long and less than 1/8-inch in diameter) is removed and sent to be examined under a microscope.

CT scans take longer than regular x-rays. You need to lie still on a table, and the part of your body being examined is placed within the scanner, a doughnut-shaped machine that completely surrounds the table. The test is painless, but you may find it uncomfortable to hold still in certain positions for minutes at a time.

You will need an IV (intravenous) line through which the contrast dye is injected. The injection can also cause some flushing (redness and warm feeling). Some people are allergic and get hives or, rarely, more serious reactions like trouble breathing and low blood pressure can occur. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays. You may be asked to drink 1 to 2 pints of a solution of contrast material. This helps outline the intestine so that it is not mistaken for tumors.

Magnetic resonance imaging (MRI): This is described above as a way of looking for breast cancer as a supplement to mammograms. Traditionally, MRI scans have been used to look for cancer spread, just like CT scans. MRI scans are particularly helpful in looking at the brain and spinal cord. MRI scans are a little more uncomfortable than CT scans. First, they take longer -- often up to an hour. Second, you have to lie inside a narrow tube, which is confining and can upset people with claustrophobia (a fear of enclosed spaces). The machine also makes a buzzing noise that you may find disturbing. Some centers provide headphones with music to block this out.

Positron emission tomography (PET): PET uses glucose (a form of sugar) that contains a radioactive atom, which is injected into a vein and travels throughout the body. A special camera can detect the radioactivity. Cancer cells of the body absorb large amounts of the radioactive sugar, because of the high amount of energy that they use. PET is useful when your doctor thinks the cancer has spread but doesn't know where. A PET scan can be used instead of several different x-rays because it scans your whole body. Some of the newer machines are able to perform both a PET and CT scan at the same time (PET/CT scan). This allows the radiologist to compare areas of higher radioactivity on the PET with the appearance of that area on the CT.

It is important to follow the eating, drinking, and activity directions you are given before the PET scan.

This test can be used as a diagnostic aid to a mammogram, especially in looking for cancer in axillary lymph nodes. So far, most studies show it isn't very sensitive in finding small deposits of cancer in lymph nodes, although it can find big ones.

Laboratory Examination of Breast Cancer Tissue

Types of breast cancer: The tissue removed during the biopsy is examined in the lab to see whether the cancer is *in situ* (not invasive) or invasive. The biopsy is also used to determine the cancer's type. The different types of breast cancer are defined in the section, "What Is Breast Cancer?"

The most common types, invasive ductal and invasive lobular cancer, are treated in the same way. In some cases, breast cancer types that tend to have a more favorable prognosis (medullary, tubular, and mucinous cancers) are treated differently. For example, hormone therapy or chemotherapy may be recommended for small stage I cancers with unfavorable microscopic features, but not for small cancers of the types associated with a more favorable prognosis.

Grades of breast cancer: A pathologist looks at the tissue sample under a microscope and then assigns a grade to it. The *grade* helps predict the patient's prognosis because cancers that closely resemble normal breast tissue tend to grow and spread more slowly. In general, a

lower grade number indicates a slower-growing cancer that is less likely to spread, while a higher number indicates a faster-growing cancer that is more likely to spread.

Histologic tumor grade (sometimes called its *Bloom-Richardson grade*, *Scarff- Bloom-Richardson grade*, or *Elston-Ellis grade*) is based on the arrangement of the cells in relation to each other: whether they form tubules; how closely they resemble normal breast cells (nuclear grade); and how many of the cancer cells are in the process of dividing (mitotic count). This system of grading is used for invasive cancers but not for in situ cancers.

- Grade 1 (well-differentiated) cancers have relatively normal-looking cells that do not appear to be growing rapidly and are arranged in small tubules.
- Grade 2 (moderately differentiated) cancers have features between grades 1 and 3.
- Grade 3 (poorly differentiated) cancers, the highest grade, lack normal features and tend to grow and spread more aggressively.

The tumor grade is most important in patients with small tumors without lymph node involvement. Patients with small, well-differentiated tumors may require no further treatment after the tumor is removed, while patients with moderately or poorly differentiated tumors usually receive additional hormonal or chemotherapy.

Ductal carcinoma in situ (DCIS) is sometimes given a *nuclear grade*, which describes how abnormal the cancer cells appear. The presence or absence of *necrosis* (areas of dead or degenerating cancer cells) is also noted.

Some researchers have suggested combining information about the nuclear grade and necrosis with information about the *surgical margin* (how close the cancer is to the edge of the lumpectomy specimen) and the size (amount of breast tissue affected by DCIS). In situ

cancers with high nuclear grade, necrosis, cancer at or near the edge of the lumpectomy sample, and large areas of DCIS are more likely to come back after lumpectomy.

Estrogen and progesterone receptors: Receptors are parts of cells that can attach to certain substances, such as hormones, that circulate in the blood. Normal breast cells and some breast cancer cells have receptors that attach to estrogen and progesterone. These 2 hormones play an important role in the growth and treatment of breast cancer.

An important step in evaluating a breast cancer is to test a portion of the cancer removed during the biopsy or initial surgical treatment for the presence of these receptors. The tumor is tested for these receptors in a test called a hormone receptor assay. Breast cancers that contain estrogen and progesterone receptors are often referred to as ER-positive and PR-positive tumors, or simply hormone receptor positive. Women with these cancers tend to have a better prognosis and are much more likely to respond to hormone therapy than women with cancers without these receptors (see section, "How Is Breast Cancer Treated?"). All breast cancers, with the exception of lobular carcinoma in situ, should be tested for hormone receptors at the time of the breast biopsy or surgery. About two thirds of breast cancers contain estrogen receptors. This percent is higher in older women and lower in younger ones.

HER2/neu testing: About 15% to 25% of breast cancers have too much of a growth-promoting protein called HER2/neu. This protein is produced by the cell under the instruction of the HER2/neu gene. Normally, we all have 2 copies of the HER2/neu gene in every cell in our bodies (one copy per chromosome 17). Tumors with increased levels of HER-2/neu are referred to as “HER-2 positive.”

In women with HER2/neu positive breast cancers, there are too many copies of the HER2/neu gene being produced (more than 2 genes for every chromosome 17). This is referred to as gene amplification, or having a HER2 positive breast cancer. These cancers tend to grow and spread more aggressively than other breast cancers with a normal amount of the HER2/neu gene. They can be treated with a drug called trastuzumab (Herceptin) that prevents the HER2/neu protein from stimulating breast cancer cell growth. Recent studies have shown that trastuzumab, given after breast cancer surgery for HER-2 positive tumors, reduces the risk of recurrence when the tumor measures larger than 1 cm in diameter or when the cancer has spread to the lymph nodes. Studies also suggest that chemotherapy containing certain drugs (such as doxorubicin or epirubicin) may be especially effective against breast cancers that are HER-2 positive (see the section, "How Is Breast Cancer Treated?" for information on these drugs).

HER2/neu testing is done on thin slices of the biopsy sample that have been treated with special antibodies that identify the HER2/neu protein or with pieces of DNA that identify the HER2/neu gene. The test that uses antibodies to detect HER2/neu protein is called *immunohistochemistry*. The DNA test for extra copies of the HER2/neu gene is called *fluorescent in situ hybridization* (usually called FISH for short). Many breast cancer specialists feel the FISH test is more accurate than the immunohistochemistry test. HER2/neu testing should be performed on all newly diagnosed breast cancers.

Tests of ploidy and cell proliferation rate: The *ploidy* of cancer cells refers to the amount of DNA they contain. If there's a normal amount of DNA, the cells are said to be *diploid*. If the amount is abnormal, then the cells are described as *aneuploid*. Although they may help

determine prognosis, these tests rarely change treatment and are considered optional. They are not recommended by the National Comprehensive Cancer Network (NCCN).

- *Flow cytometry* uses lasers and computers to measure the amount of DNA in cancer cells suspended in liquid as they flow past the laser beam.
- *Image cytometry* uses computers to analyze digital images of the cells from a microscope slide.

Flow cytometry can also measure the *S-phase fraction,* which is the percentage of cells in a sample that are replicating (copying) their DNA. DNA replication means that the cell is getting ready to divide into 2 new cells. The rate of cancer cell division can also be estimated by a *Ki-67* test, which identifies cells in the S-phase, as well as cells getting ready to replicate DNA, cells that have just completed DNA replication, and cells in the process of dividing. A high S-phase fraction or Ki-67 labeling index means that the cancer cells are dividing more rapidly, which indicates a more aggressive cancer.

Other tests to predict breast cancer prognosis: Many new prognostic factors, such as changes of the p53 tumor suppressor gene, the epidermal growth factor receptor, and microvessel density (number of small blood vessels that supply oxygen and nutrition to the cancer) are currently being studied (see section, "What's New in Breast Cancer Research and Treatment?").

Tests of gene patterns: Researchers have found that looking at the patterns of a number of genes at the same time can help predict whether or not an early stage breast cancer is likely to come back after initial treatment. This can help when deciding whether additional (adjuvant) treatment such as chemotherapy might be helpful. Two such tests (Oncotype DX and MammaPrint), which look at different sets of genes, are now available. While some doctors

are using them, others are waiting for more research to prove they are helpful. Large clinical trials of these tests are now under way.

How Is Breast Cancer Staged?

Cancers are divided into different groups, called *stages*, based on whether the cancer is invasive or non-invasive, the size of the tumor, how many lymph nodes are involved, and whether there is spread to other parts of the body. *Staging* is the process of finding out how widespread a cancer is when it is diagnosed. The stage of a cancer is the most important factor in considering treatment options. A *staging system* is a standardized way for the cancer care team to summarize information about how far a cancer has spread.

Depending on the results of your physical exam and biopsy, your doctor may want you to have certain imaging tests such as a chest x-ray, mammograms of both breasts, bone scans, and computed tomography (CT) or magnetic resonance imaging (MRI) scans. (All are discussed in the section, “Imaging Tests to Detect Breast Cancer Spread.”) Blood tests to evaluate your overall health and help detect whether the cancer has spread to certain organs may also be done.

The 2002 American Joint Committee on Cancer (AJCC) TNM System

The most common system used to describe the stages of cancers is the American Joint Committee on Cancer (AJCC) TNM system. This staging system classifies cancers based on their T, N, and M stages:

- *T* stands for *tumor* (its size and how far it has spread within the breast and to nearby organs).

- *N* stands for spread to lymph *nodes* (bean-shaped collections of immune system cells that help fight infections and cancers).
- *M* is for *metastasis* (spread to distant organs).

The stage of a breast cancer can be based on the results of physical exam and imaging tests (called clinical stage) or on the results of these and surgery (called pathologic stage). The approach to staging used here is based on the pathologic stage, the findings after surgery, when the pathologist has looked at the breast mass and lymph nodes.

Additional letters or numbers appear after T, N, and M to provide more details about the tumor, lymph nodes, and metastasis:

- The letter T followed by a number from 0 to 4 describes the tumor's size and spread to the skin or to the chest wall under the breast. Higher T numbers indicate a larger tumor and/or wider spread to tissues near the breast.
- The letter N followed by a number from 0 to 3 indicates whether the cancer has spread to lymph nodes near the breast and, if so, how many lymph nodes are affected.
- The letter M followed by a 0 or 1 indicates whether the cancer has spread to distant organs, for example, the lungs or bones, or to lymph nodes that are not next to the breast, such as those above the collarbone.

Once the T, N, and M categories have been determined, this information is combined in a process called *stage grouping* to determine your disease stage. The stages refer to the extent of the disease and similar stages have a similar outlook and thus are treated in a similar way. Stage is expressed as stage 0 and in Roman numerals from stage I (the least advanced stage) to stage IV (the most advanced stage).

Breast Cancer T, N, M Categories and Stage Groupings

Primary tumor (T):

TX: Primary tumor cannot be assessed.

T0: No evidence of primary tumor (this sometimes happens).

Tis: Pure Carcinoma in situ; intraductal carcinoma, lobular carcinoma in situ, or Paget disease of the nipple with no associated tumor mass.

T1: Tumor 2 cm (3/4of an inch) or less in greatest dimension.

T2: Tumor more than 2 cm but not more than 5 cm (2 inches) in greatest dimension.

T3: Tumor more than 5 cm in greatest dimension.

T4: Tumor of any size growing into the chest wall or skin.

Regional (nearby) lymph nodes (N) pathologic staging (based on looking at them under a microscope):

NX: Regional lymph nodes cannot be assessed (for example, removed previously).

N0: Cancer has not spread to regional lymph nodes.

N1: Cancer has spread to 1 to 3 axillary lymph node(s) under the arm.

N2: Cancer has spread to 4 to 9 lymph nodes under the arm.

N3: Cancer has spread to 10 or more lymph nodes under the arm or also involves lymph nodes in other areas around the breast.

Metastasis (M):

MX: Presence of distant spread (metastasis) cannot be assessed.

M0: No distant spread.

M1: Spread to distant organs is present.

Summary of Breast Cancer Stages

Stage 0: Tis, N0, M0: *Ductal carcinoma in situ (DCIS)* is the earliest form of breast cancer. In DCIS, cancer cells are located within a duct and have not invaded the surrounding fatty breast tissue. *Lobular carcinoma in situ (LCIS)*, which is sometimes classified as stage 0 breast cancer, but most oncologists believe it is not a true breast cancer. In LCIS, abnormal

cells grow within the lobules or milk-producing glands, but they do not penetrate through the wall of these lobules. Paget disease of the nipple is stage 0. In all cases the cancer has not spread to lymph nodes or distant sites.

Stage I: T1, N0, M0: The tumor is 2 cm (about 3/4 of an inch) or less in diameter and has not spread to lymph nodes or distant sites.

Stage IIA: T0, N1, M0 / T1, N1, M0 / T2, N0, M0: No tumor is found in the breast but it is in 1 to 3 axillary lymph nodes,; or the tumor is less than 2 cm and has spread to 1 to 3 axillary lymph nodes; or cancer is found by sentinel node biopsy as microscopic disease in internal mammary nodes but not on imaging studies or by clinical exam; or the tumor is larger than 2 cm in diameter and less than 5 cm but hasn't spread to axillary nodes. In all cases, the cancer hasn't spread to distant sites.

Stage IIB: T2, N1, M0 / T3, N0, M0: The tumor is larger than 2 cm in diameter and less than 5 cm and has spread to 1 to 3 axillary lymph nodes or found by sentinel node biopsy as microscopic disease in internal mammary nodes or the tumor is larger than 5 cm and does not grow into the chest wall and has not spread to lymph nodes. The cancer hasn't spread to distant sites.

Stage IIIA: T0-2, N2, M0 / T3, N1-2, M0: The tumor is smaller than 5 cm in diameter and has spread to 4 to 9 axillary lymph nodes; or it is found through imaging studies or clinical exam to have spread to internal mammary nodes; or the tumor is larger than 5 cm and has spread to 1 to 9 axillary nodes, or to internal mammary nodes. In all cases, the cancer hasn't spread to distant sites.

Stage IIIB: T4, N0-2, M0: The tumor has grown into the chest wall or skin and may have spread to no lymph nodes or to as many as 9 axillary nodes. It may or may not have spread to internal mammary nodes. The cancer hasn't spread to distant sites.

Stage IIIC: T0-4, N3, M0: The tumor is any size, has spread to 10 or more nodes in the axilla or to 1 or more lymph nodes under the clavicle (infraclavicular) or above the clavicle (supraclavicular) or to internal mammary lymph nodes, which are enlarged because of the cancer. All of these are on the same side as the breast cancer. The cancer hasn't spread to distant sites.

Inflammatory breast cancer is classified as stage III, unless it has spread to distant organs or lymph nodes that are not near the breast, in which case it would be stage IV.

Stage IV: T0-4, N0-3, M1: The cancer, regardless of its size, has spread to distant organs such as bone, liver, or lung, or to lymph nodes far from the breast.

Breast Cancer Survival by Stage

The numbers below are based on patients diagnosed many years ago and can be expected to be a little different for women diagnosed more recently. One reason for this is that the staging system was revised in 2002. Another reason is that treatments have greatly improved since 1998. Because of these improved treatments, the survival rates for women diagnosed now should be better. These numbers come from the American College of Surgeons National Cancer Data Base.

Stage	5-year Relative Survival Rate
0	100%
I	100%
IIA	92%
IIB	81%
IIIA	67%
IIIB	54%
IV	20%

(Survival rates are not yet available for stage IIIC breast cancer because this stage was defined only a few years ago.)

The 5-year survival rate refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. This means that they may or may not be cancer-free during this 5 year period. Five-year rates are used to produce a standard way of discussing prognosis. Of course, many people live much longer than 5 years. Five-year relative survival rates assume that people will die of other causes and compares the observed survival with that expected for people without breast cancer. That means that relative survival only talks about deaths from breast cancer.

How Is Breast Cancer Treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Local versus Systemic Therapy

Local therapy is intended to treat a tumor at the site without affecting the rest of the body.

Surgery and radiation therapy are examples of local therapies.

Systemic therapy refers to drugs, which can be given by mouth or directly into the bloodstream to reach cancer cells that may have spread beyond the breast. Chemotherapy, hormone therapy, and immunotherapy are systemic therapies.

When patients who have no detectable cancer after surgery are given systemic therapy, it is called *adjuvant therapy*. Doctors believe that cancer cells may break away from the primary breast tumor and begin to spread through the body via the bloodstream even in the early stages of the disease. These cells can't be felt by physical exam or seen on x-rays or other imaging methods, and they cause no symptoms. But they can establish new tumors in other organs or the bones. The goal of adjuvant therapy is to kill these hidden cells.

Not every patient needs adjuvant therapy, however. Generally speaking, if the tumor is larger than one-half inch or the cancer has spread to lymph nodes, it is more likely to have spread through the bloodstream. But there are other features, some of which have been previously discussed, that may determine whether or not a patient should receive adjuvant therapy. Recommendations regarding systemic therapy are discussed in the sections on these treatments and in the section on treatment by stage.

Some patients are given systemic therapy, usually chemotherapy, before surgery to shrink a tumor. This is called neoadjuvant therapy.

Surgical Procedures for Breast Cancer

Most women with breast cancer have some type of surgery. Operations for local treatment include breast-conserving surgery, mastectomy, and axillary (armpit) lymph node sampling

and removal. In addition, women may decide to have breast reconstruction at the same time they have the mastectomy, or later on.

Breast conservation therapy: *Lumpectomy* removes only the breast lump and a surrounding margin of normal tissue. If examination of the tissue removed by lumpectomy finds there is cancer at the edge of the piece of tissue removed (*margin*), the surgeon may need to remove additional tissue. This operation is called a *re-excision*. Radiation therapy is usually given after a lumpectomy. If there is to be chemotherapy, the radiation is usually delayed until the chemotherapy is completed.

Partial or s*egmental mastectomy* or *quadrantectomy* removes more breast tissue than a lumpectomy (up to one-quarter of the breast). Radiation therapy is usually given after surgery.

Side effects of these operations include temporary swelling, tenderness, and hardness due to scar tissue that forms in the surgical site.

For most women with stage I or II breast cancer, breast conservation therapy (lumpectomy and radiation therapy) is as effective as mastectomy. Survival rates of women treated with these 2 approaches are the same. However, breast conservation therapy is not an option for all women with breast cancer (see "Choosing between lumpectomy and mastectomy" in this section).

Radiation therapy as a part of breast-conserving therapy can sometimes be omitted. Women who may consider lumpectomy without radiation therapy have all of the following:

- age 70 years or older
- a tumor 2 cm or less that has been completely removed
- a tumor that contains hormone receptors and hormone therapy is given
- no lymph node involvement

Mastectomy: In a *simple* or *total mastectomy* the surgeon removes the entire breast, including the nipple, but does not remove underarm lymph nodes or muscle tissue from beneath the breast. Sometimes this is done for both breasts, especially in women at very high risk for breast cancer. This surgery usually isn't much more physically difficult to recover from than having one breast removed. Either a single or double simple mastectomy has few side effects. Most women, if they are hospitalized, can go home the next day.

Modified radical mastectomy involves removing the entire breast and some of the axillary (underarm) lymph nodes. This is the most common surgery for women with breast cancer who are having the whole breast removed.

Radical mastectomy is an extensive operation removing the entire breast, axillary lymph nodes, and the *pectoral* (chest wall) muscles under the breast. This surgery was once very common. But because of the disfigurement and side effects it causes, and because modified radical mastectomy has been proven to be as effective as radical mastectomy, it is rarely done today.

Possible side effects of mastectomy and lumpectomy include wound infection, *hematoma* (accumulation of blood in the wound), and *seroma* (accumulation of clear fluid in the wound). If axillary lymph nodes are also removed, additional side effects may occur (see "Axillary lymph node dissection" in this section).

Choosing between lumpectomy and mastectomy: The advantage of a lumpectomy is that it saves the appearance of the breast. A disadvantage is the need for several weeks of radiation therapy after surgery. However, a small percentage of women who have a mastectomy still need radiation therapy to the breast area.

When deciding between a lumpectomy or mastectomy, be sure to get all the facts. You may have an initial gut feeling for mastectomy to "take it all out as quickly as possible." Women tend to prefer mastectomy more often than do their surgeons because of this feeling. But the fact is that in most cases, mastectomy does not provide any better chance of long-term survival or a better outcome from treatment. Large research studies with thousands of women participating and over 20 years of accumulated information show that when lumpectomy can be performed, mastectomy does not provide any better chance of survival from breast cancer than lumpectomy. It is because of these outcomes that most women (around 70% in one study) do not have the breast removed.

Although most women and their doctors prefer lumpectomy and radiation therapy, your choice will depend on a number of factors, such as:

- how you feel about losing your breast
- how you feel about getting radiation therapy
- how far you have to travel for radiation therapy
- whether you think you will want to have more surgery to reconstruct your breast after having a mastectomy
- your preference for mastectomy as a way to 'get rid of all your cancer as quickly as possible
- your fear of recurrence

Lumpectomy or breast conservation therapy is usually not recommended for:

- women who have already had radiation therapy to the affected breast

- women with 2 or more areas of cancer in the same breast that are too far apart to be removed through 1 surgical incision, while keeping the appearance of the breast satisfactory
- women whose initial lumpectomy along with (one or more) re-excision has not completely removed the cancer
- women with certain serious connective tissue diseases such as scleroderma, which make them especially sensitive to the side effects of radiation therapy
- pregnant women who would require radiation while still pregnant (risking harm to the fetus)
- women with a tumor larger than 5 cm (2 inches) that doesn't shrink very much with neoadjuvant chemotherapy
- women with a cancer that is large relative to her breast size

Axillary lymph node dissection: To determine if the breast cancer has spread to axillary (underarm) lymph nodes, some of these lymph nodes are removed (in an operation called axillary dissection) and examined under the microscope. This is an important part of staging and determining treatment and outcomes. When the lymph nodes are affected, there is an increased likelihood that cancer cells have spread through the bloodstream to other parts of the body.

As noted previously, axillary lymph node dissection is part of a radical or modified radical mastectomy procedure and is usually combined with a breast-conserving procedure, such as lumpectomy. Anywhere from about 10 to 40 lymph nodes are removed during axillary lymph node dissection.

Whether or not cancer cells are present in the lymph nodes under the arm is an important factor in selecting adjuvant therapy. It was once believed that removing as many lymph nodes as possible would reduce the risk of spread to other parts of the body and improve the

chance of curing the cancer. It is now known that breast cancer cells that have spread beyond the breast and axillary lymph nodes are best treated by systemic therapy. Axillary dissection is used as a test to help guide other breast cancer treatment decisions.

The main side effect of removing axillary lymph nodes is *lymphedema* (swelling of the arm). About 25% to 30% of women who have underarm lymph nodes removed develop lymphedema. It also occurs in up to 5% of women who have sentinel lymph node biopsy. Sometimes there is temporary swelling, which lasts for only a few weeks and then goes away. Other times, the swelling is long lasting. Ways to help prevent or reduce the effects of lymphedema are discussed in the section, "What Happens After Treatment for Breast Cancer?" If your arm is swollen, tight, or painful after lymph node surgery, be sure to tell someone on your cancer care team right away.

You may also have temporary or permanent limitations in arm and shoulder movement after surgery. Numbness of the upper, inner arm skin is another common side effect because the nerve controlling sensation here travels through the lymph node area.

Sentinel lymph node biopsy (SLNB): Although lymph node dissection is a safe operation and has low rates of serious side effects, doctors have developed another way of learning if cancer has spread to lymph nodes without removing all of them. This procedure is called the *sentinel lymph node biopsy*.

In this procedure the surgeon finds and removes the "sentinel node" -- the first lymph node into which a tumor drains, and the one most likely to contain cancer cells. The surgeon injects a radioactive substance and/or a blue dye into the area around the tumor. Lymphatic

vessels carry these substances into the sentinel node and provide the doctor with a "lymph node map." The doctor can either see the blue dye or detect the radioactivity with a Geiger counter in the nodes that the substances flow into. These nodes (often 2 or 3) are then removed and sent for examination by the pathologist.

If the sentinel node(s) contains cancer, the surgeon will perform an *axillary dissection* -- removal of more lymph nodes in the armpit. This may be done at the same time or several days after the original sentinel node biopsy. The timing of the axillary dissection depends on how easily the cancer can be seen in the lymph node at the time of surgery. Sometimes it is obvious and other times it will only be found by thorough microscopic study by a pathologist.

If the sentinel node is cancer-free, the patient will not need more lymph node surgery and can avoid the side effects of full lymph node surgery, which are discussed later on (see “Lymphedema” in the section, "What Happens After Treatment for Breast Cancer?").

This limited sampling of lymph nodes is not always appropriate. It is most suitable if there is a single tumor less than 5 cm in the breast, no prior chemotherapy or hormone therapy has been given, and the lymph nodes do not feel enlarged.

Sentinel lymph node biopsy is a complex technique that requires a great deal of skill. Therefore, doctors recommend that sentinel lymph node biopsy be done only by a team known to have experience with this technique. If you are considering having such a biopsy, ask your health care team if this is something they do regularly.

Reconstructive surgery and breast implant surgery: If a woman has a mastectomy, she may want to consider having the breast mound rebuilt; this is called *breast reconstruction*. These procedures are not done to treat cancer but to restore the breast's appearance after mastectomy. If you are going to have a mastectomy and are thinking about having reconstruction, it is important to consult with a plastic surgeon who is an expert in breast reconstruction before the mastectomy is done.

Decisions about the type of reconstruction and when it will be done depend on each woman's medical situation and personal preferences. Your breast can be reconstructed at the same time as the mastectomy (*immediate reconstruction*) or at a later time (*delayed reconstruction*). Reconstruction may use implants and/or tissue from other parts of your body (a*utologous tissue reconstruction*).

See the American Cancer Society document, "Breast Reconstruction After Mastectomy" for more information. You may also find it helpful to talk with a woman who has had the type of reconstruction you might be considering. Our Reach to Recovery volunteers can help you with this.

What to Expect With Surgery

For many, the thought of surgery can be very frightening. But with a better understanding of what to expect before, during, and after the operation, many fears can be relieved.

Before surgery: Today, the common procedure for biopsy lets you find out if you have breast cancer within a few days of your biopsy, but the extent of the breast cancer will not be known until after the surgery for local treatment.

You usually meet with your surgeon a few days before the operation to discuss the procedure. This is a good time to ask specific questions about the surgery and review potential risks. You will be asked to sign a consent form, giving the doctor permission to perform the surgery. Take your time and review the form carefully to be certain that you understand what you are signing.

Sometimes, doctors send material for you to review in advance of your appointment, so you will have plenty of time to read it and won't feel rushed. You may also be asked to give consent for researchers to use any tissue or blood that is not needed for diagnostic purposes. Although this may not be of direct use to you, it may be very helpful to women in the future.

You may be asked to donate blood before some operations, such as a mastectomy combined with natural tissue reconstruction, if the doctors think a transfusion might be needed. You might feel more secure knowing that if a transfusion is needed, you will receive your own blood. If you do not receive your own blood, it is important you know that in the United States, blood transfusion from another person is nearly as safe as receiving your own blood. Ask your doctor about your possible need for a blood transfusion.

Your doctor will review your medical records and ask you about any medicines you are taking. This is to be sure that you are not taking anything that will interfere with the surgery. For example, if you are taking a blood-thinning medicine (even aspirin), you may be asked to stop taking the drug about a week or two before the surgery. Be sure you tell your doctor about everything you take, including vitamins and herbal supplements. Usually, you will be

told not to eat or drink anything for 8 to 12 hours before the surgery, especially if you are going to have general anesthesia (will be "asleep" during surgery).

You will also meet with the anesthesiologist or nurse anesthetist, the health professional who will be giving you the anesthesia during your surgery. The type of anesthesia used depends largely on the kind of surgery being done and your medical history.

General anesthesia is usually given whenever the surgery involves a mastectomy or an axillary node dissection. You will have an IV (intravenous) line put in, which the medical team will use to give medications that may be needed during the surgery. Usually you will be hooked up to an electrocardiogram (EKG) machine and have a blood pressure cuff on your arm, so your heart rhythm and blood pressure can be checked during the surgery.

Surgery: For your surgery, you may be offered the choice of an outpatient procedure or you may be admitted to the hospital. How long you stay in the hospital depends on the surgery being performed, your overall state of health and whether you have any other medical problems, how well you do during the surgery, and how you feel after the surgery. Decisions about the length of your stay should be made by you and your doctor and not dictated by what your insurance will pay, but it is important to check your insurance coverage before surgery.

As a general rule, women having a mastectomy and/or axillary lymph node dissection stay in the hospital for 1 or 2 nights and then go home. However, some women may be placed in a 23-hour, short-stay observation unit before going home. In this situation, care is continued at home with a home care nurse visiting you to monitor and provide care.

Lumpectomy and sentinel lymph node biopsy are usually done in an outpatient surgery center, and an overnight stay in the hospital is usually not necessary.

The length of the operation depends on the type of surgery being done. For example, a mastectomy with axillary lymph node dissection will take from 2 to 3 hours. After your surgery, you will be taken to the recovery room, where you will stay until you are awake and your condition and vital signs (blood pressure, pulse, and breathing) are stable.

After surgery: You will have a dressing (bandage) over the surgery site that may snugly wrap around your chest. You may have one or more drains (plastic or rubber tubes) from the breast or underarm area to remove blood and lymph fluid that collects during the healing process. Care of the drains includes emptying and measuring the fluid and identifying problems the doctor or nurse needs to know about. Most drains stay in place for 1 or 2 weeks. When drainage has decreased to about 30 cc (1 fluid ounce) each day, the drain will usually be removed.

Doctors rarely put the arm in a sling to hold it in place. Most doctors will want you to start moving the arm so that it won't get stiff. Women who have a lumpectomy or mastectomy are surprised by how little pain they have in the breast area. But they are less happy with the strange sensations (numbness, pinching/pulling feeling) in the underarm area.

Care of the surgery site and arm should be discussed with your doctor. Written instructions about care after surgery are usually given to you and your caregivers. These instructions should include:

- the care of the surgical wound and dressing
- how to monitor drainage and take care of the drains
- how to recognize signs of infection
- when to call the doctor or nurse
- when to begin using the arm and how to do arm exercises to prevent stiffness
- when to resume wearing a bra
- when to begin using a prosthesis and what type to use (after mastectomy)
- what to eat and not to eat
- use of medications, including pain medicines and possibly antibiotics
- any restrictions of activity
- what to expect regarding sensations or numbness in the breast and arm
- what to expect regarding feelings about body image
- a follow-up appointment and referral to a Reach to Recovery volunteer. Through our Reach to Recovery program, a specially trained volunteer who has had breast cancer can provide information, comfort, and support (see the American Cancer Society document, "Reach to Recovery" for more information).

Most patients see their doctor within 7 to 14 days following the surgery. Your doctor should explain the results of your pathology report and talk to you about the need for further treatment. If you will need more treatment, you will be referred to a medical oncologist and/or radiation oncologist.

Chemotherapy

Even in the early stages of the disease, cancer cells can break away from the primary breast tumor and spread through the bloodstream. These cells don’t cause symptoms, they don’t show up on an x-ray, and they can’t be felt during a physical exam. But if they are allowed to grow, they can establish new tumors in other places in the body. Systemic therapy given to patients who have no evidence of spread of cancer, but who are at increased risk of developing spread of the cancer is called adjuvant therapy. The goal of adjuvant therapy is to kill undetected cells that have traveled from the breast. Chemotherapy is a form of adjuvant systemic therapy.

Chemotherapy is treatment with cancer-killing drugs that may be given intravenously (injected into a vein) or by mouth. The drugs travel through the bloodstream to reach cancer cells in most parts of the body. Chemotherapy may also be recommended based on the size of the tumor, grade of the tumor, and presence or absence of lymph node involvement. When used as adjuvant therapy after breast conservation therapy or mastectomy, chemotherapy reduces the risk of breast cancer recurrence. The chemotherapy is given in cycles, with each period of treatment followed by a recovery period. The usual course of chemotherapy lasts between 3 to 6 months.

Chemotherapy can also be used as the main treatment for women whose cancer has already spread outside the breast and underarm area at the time it is diagnosed, or if it spreads after initial treatments. The length of these treatments is not definite, but depends on whether the cancer shrinks and how much it shrinks.

Chemotherapy given before surgery is called *neoadjuvant therapy*. The major benefit of neoadjuvant chemotherapy is that it can shrink large cancers so that they are small enough to be removed by lumpectomy instead of mastectomy. Another possible advantage of neoadjuvant chemotherapy is that doctors can see how the cancer responds to chemotherapy. If the tumor does not shrink, then different chemotherapy drugs may be substituted. So far, there is no evidence, however, that this improves survival.

In most cases, chemotherapy is most effective, either as an adjuvant or neoadjuvant therapy, when combinations of more than one chemotherapy drug are used together. Clinical research studies over the last 30 years have determined which combinations of chemotherapy drugs are most effective. However, the "best" combination may not have yet been discovered, so

there continue to be clinical research studies comparing one of today's most effective treatments against something that may be better.

The most commonly used combinations are:

- Cyclophosphamide (Cytoxan), methotrexate (Amethopterin, Mexate, Folex), and fluorouracil (Fluorouracil, 5-FU, Adrucil) [abbreviated CMF]
- Cyclophosphamide, doxorubicin (Adriamycin), and fluorouracil [abbreviated CAF]
- Doxorubicin (Adriamycin) and cyclophosphamide [abbreviated AC]
- Doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel (Taxol) or docetaxel (Taxotere) [abbreviated AC -->T] or docetaxel concurrent with AC [abbreviated TAC]
- Doxorubicin (Adriamycin), followed by CMF
- Cyclophosphamide, epirubicin (Ellence), and fluorouracil [abbreviated CEF] with or without docetaxel
- Cyclophosphamide and Docetaxel (TC)
- Gemcitabine (Gemzar) and paclitaxel (Taxol) [abbreviated GT]

Some other chemotherapy drugs used for treating women with breast cancer include carboplatin (Paraplatin), cisplatin (Platinol), vinorelbine (Navelbine), capecitabine (Xeloda), pegylated liposomal doxorubicin (Doxil), and albumin-bound paclitaxel (Abraxane).

Doctors give chemotherapy in cycles, with each period of treatment followed by a rest period. The chemotherapy begins on the first day of each cycle, and then the body is given time to recover from the effects of chemotherapy. The chemotherapy drugs are then repeated to start the next "cycle." The time between giving the chemotherapy drugs is generally 2 or 3 weeks and varies according the specific chemotherapy drug or combination of drugs. Some drugs are given more often. These cycles generally last for a total time of 3 to 6 months when given as adjuvant therapy, depending on the drugs used.

The side effects of chemotherapy depend on the type of drugs, the amount taken, and the length of treatment. Some women have many side effects while other women have few side

effects. Temporary side effects might include fatigue, nausea and vomiting, loss of appetite, hair loss, and mouth sores. Changes in the menstrual cycle may be temporary or permanent. Because chemotherapy can damage the blood-producing cells of the bone marrow, patients may have low blood cell counts. This is the most common serious side effect and can result in an increased chance of infection (due to a shortage of white blood cells), bleeding or bruising after minor cuts or injuries (due to a shortage of blood platelets), and fatigue (due to low red blood cell counts).

There are very effective remedies for many of the temporary side effects of chemotherapy. For example, there are several drugs that can prevent or reduce nausea and vomiting. A group of drugs called *growth factors* can help the patient's bone marrow recover after chemotherapy and can treat problems caused by low blood counts.

Premature menopause (not having any more menstrual periods) and infertility (not being able to become pregnant) are potential permanent complications of chemotherapy. Some chemotherapy drugs are more likely to do this than others. You cannot depend on chemotherapy to prevent pregnancy, and getting pregnant while receiving chemotherapy could lead to birth defects and interfere with treatment. Therefore, premenopausal women who are sexually active should use birth control while receiving chemotherapy and need to discuss the type of birth control with their oncologist. It is safe to have children after chemotherapy, but it’s not safe to get pregnant while on treatment. The older a woman is when she receives chemotherapy, the more likely it is that she will become infertile or menopausal as a result. When this happens, it can also lead to rapid bone loss from osteoporosis. Again, there are medicines available to prevent this possible side effect.

Adriamycin (doxorubicin) may cause permanent heart damage if used for a long time or in high doses, but doctors carefully control the dose of this drug. They use echocardiograms and other heart tests in order to monitor the heart and will stop the medication at the first sign of damage.

Another side effect of chemotherapy is "chemo brain." Researchers have reported that many women who have received chemotherapy for breast cancer will experience a slight decrease in mental functioning. There may be some difficulty in concentration and memory. This may last a long time, but it rarely interferes with a woman's ability to do intellectual tasks. Recently, other researchers have been unable to confirm these findings. Still, whether or not "chemo brain" is a real issue, women do function well after chemotherapy. In studies that have found "chemo brain" to be a side effect of treatment, the symptoms usually disappeared after 1 to 2 years.

Very rarely, 1 to 2 years after treatment for breast cancer, certain chemotherapy drugs may cause acute myeloid leukemia, a life-threatening cancer of white blood cells. Chemotherapy's benefits in preventing many breast cancers from coming back and in saving lives from breast cancer far exceed the risk of this serious, but rare complication.

Many women do not feel as healthy after receiving chemotherapy as they did before. There is often a residual feeling of body pain or achiness and a mild loss of physical functioning. This is a very subtle change that is only revealed by close questioning of women who have undergone chemotherapy.

Fatigue is another problem for women who have received chemotherapy. This may last up to several years, but it can be helped. An exercise program is useful. Naps and conserving energy are also recommended. If there are problems with sleep, these can be treated. Sometimes there is depression which can be relieved with drugs and psychotherapy.

Sometimes the fatigue, particularly during treatment, can be caused by anemia – lowered red blood cell count. A drug called erythropoietin (Procrit) can help reverse this. However, there are side effects, such as increased number of blood clots, usually in the legs. Patients should ask their doctor about the likely benefits and risks in their case

Radiation Therapy

Radiation therapy is treatment with high-energy rays or particles that destroy cancer cells. This treatment may be used to destroy cancer cells that remain in the breast, chest wall, or underarm area after surgery. Radiation may also be needed after mastectomy in cases with either a cancer larger than 5 cm in size, or when cancer is found in the lymph nodes.

In some cases, the area treated by radiation therapy may also include supraclavicular lymph nodes (nodes above the collarbone) and internal mammary lymph nodes (nodes beneath the sternum or breast bone in the center of the chest). When given after surgery, radiation therapy is usually not started until the tissues have been able to heal for about a month. Radiation therapy is usually delayed until chemotherapy is complete.

The extent of radiation depends on whether or not a lumpectomy or mastectomy was performed and whether or not lymph nodes are involved. If a lumpectomy was done, the

entire breast receives radiation and an extra boost of radiation is given to the area in the breast where the cancer was removed to prevent it from coming back in that area.

External beam radiation: This is the usual type of radiation therapy for women with breast cancer. The radiation is focused from a machine outside the body on the area affected by the cancer. This usually includes the whole breast and, depending on the size and extent of the cancer, may include the chest wall and underarm area as well. Radiation therapy is much like getting a diagnostic x-ray, but the radiation is more intense. The procedure itself is painless.

Before your treatments start, the radiation team carefully takes measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. They will make some ink marks or small tattoos on your skin that they will use later as a guide to focus the radiation on the right area. Patients who receive breast radiation after lumpectomy are usually treated 5 days a week in an outpatient center for about 6 or 7 weeks, with each treatment lasting a few minutes.

A new technique to give radiation over a much shorter period of time (5 days total) and to only the part of the breast with the cancer is currently being done in clinical research trials. This is called *partial breast irradiation*. It is hoped that partial breast irradiation will prove to be equal to the current, standard whole breast irradiation. However, partial breast irradiation is still experimental. Women are interested in this are encouraged to participate in the major national clinical trial of partial breast irradiation that started in 2005 and should ask their doctor about this.

Lotions, powders, deodorants, and antiperspirants can interfere with external beam radiation therapy, so you should avoid using them until treatments are complete.

The main side effects of external beam radiation therapy are swelling and heaviness in the breast, sunburn-like skin changes in the treated area, and fatigue. You should avoid exposing the treated skin to the sun because it can make the skin changes worse. These changes to the breast tissue and skin usually go away in 6 to 12 months. There may also be some aching in the breast and rarely, a rib fracture related to radiation therapy.

A rare complication is the development of another cancer called angiosarcoma. In one group of 20,000 patients, 9 patients developed this cancer about 4 to 8 years after post-lumpectomy radiation. It is treated with mastectomy but can be fatal. For more information see the American Cancer Society document, "Sarcoma -- Adult Soft Tissue Cancer."

In some women, the breast becomes smaller and firmer after radiation therapy. Radiation therapy of axillary lymph nodes also can cause lymphedema (see the section, "What Will Happen After Treatment for Breast Cancer?"). Radiation therapy is not given during pregnancy because it can harm a fetus.

Brachytherapy: Brachytherapy, also known as *internal* or *interstitial radiation*, is another way to deliver radiation therapy. Instead of aiming radiation beams from outside the body, radioactive seeds or pellets are placed directly into the breast tissue next to the cancer. Often this is used to add an extra "boost" of radiation to the tumor site. This method is also being studied in clinical trials as the only source of radiation for women who have had

lumpectomy. So far the results have been promising, but more experience is needed with this technique before it can be recommended as standard treatment.

Another method of brachytherapy being used is called *Mammosite*. It consists of a balloon attached to a thin tube. The balloon is inserted into the lumpectomy space and filled with a salt water solution. A source of radioactivity is then temporarily placed into the balloon through the tube. The radioactive material is inserted and removed twice daily for 5 days. The balloon is then deflated and removed.

Hormone Therapy

Hormone therapy is another form of adjuvant systemic therapy. The hormone *estrogen* is produced mainly by a woman's ovaries until menopause. After menopause it is made mostly in the body’s fat tissue, where a testosterone-like hormone made by the adrenal gland is converted into estrogen. Estrogen promotes the growth of about two thirds of breast cancers (those containing estrogen or progesterone receptors and called hormone receptor positive cancers). Because of this, several approaches to blocking the effect of estrogen or lowering estrogen levels are used to treat breast cancer.

Tamoxifen: The antiestrogen drug that has been used most often is tamoxifen (Nolvadex). It is taken daily in pill form. Taking tamoxifen after surgery, usually for 5 years, reduces the chances of the cancer coming back by about 50% for women with early breast cancer, if the cancer contained estrogen or progesterone receptors. Tamoxifen is also used to treat metastatic breast cancer and to prevent the development of breast cancer in a woman at high risk.

This drug does have known side effects. Tamoxifen can increase the risk of developing cancer of the lining of the uterus (*endometrial cancer*). This cancer is usually diagnosed at a very early stage and is generally curable by surgery. Tamoxifen can also increase the risk of uterine sarcoma, a rare cancer of the connective tissue of the uterus. If you are taking tamoxifen, tell your doctor right away about any unusual vaginal bleeding (a common symptom of both of these cancers). Most uterine bleeding is not due to cancer, but this symptom always needs prompt evaluation.

Blood clots are another serious side effect of tamoxifen. Other side effects may include weight gain (although recent studies have not found this), hot flashes, vaginal discharge, and mood swings. Early cataracts may occur rarely. Nonetheless, for most women with breast cancer, the benefits of taking tamoxifen far outweigh the risks.

Some patients whose cancer has spread to their bones may experience a "tumor flare" with pain and inflammation in the muscles and bones when treated with tamoxifen. It usually subsides quickly. However, the patient may also develop a high calcium level in the blood that cannot be controlled. If this occurs, the treatment may need to be stopped.

Toremifene: Toremifene (Fareston), another anti-estrogen drug closely related to tamoxifen, may be an option for postmenopausal women with breast cancer that has metastasized. Toremifene is an anti-estrogen medicine that is used in tumors that are estrogen-receptor positive or whose estrogen-receptor status is unknown.

Fulvestrant: Fulvestrant (Faslodex) is a newly approved drug that also acts via the estrogen receptor, but instead of blocking it, this drug eliminates it. It is often effective even if the

breast cancer is no longer responding to tamoxifen. It is given by injection once a month. Hot flashes, mild nausea, and fatigue are the major side effects. It is only given to women who are already in menopause. It is currently only approved for use in women with advanced breast cancer.

Aromatase inhibitors: Three drugs that stop estrogen production in postmenopausal women have been approved for use in treating both early and advanced breast cancer. These drugs are letrozole (Femara), anastrozole (Arimidex), and exemestane (Aromasin). They work by blocking an enzyme responsible for producing small amounts of estrogen in postmenopausal women. They cannot stop the ovaries of premenopausal women from producing estrogen. For this reason they are only effective in postmenopausal women.

These drugs have been compared with tamoxifen as adjuvant hormone therapy in postmenopausal women with early breast cancer. Clinical trials have been performed comparing tamoxifen with one of the aromatase inhibitors "head to head" for a total of 5 years, and as an additional treatment after 2 to 6 years of tamoxifen. In each of these studies there has been a clear advantage to using either the aromatase inhibitor instead of tamoxifen for a total of 5 years or switching to it after several years of tamoxifen, rather than keeping postmenopausal women on tamoxifen alone for 5 years. Clinical trials continue to be done to try to figure out which of these strategies is the best. The aromatase inhibitors have fewer side effects than tamoxifen because they don’t cause endometrial cancer and very rarely cause blood clots. They can, however, cause osteoporosis and bone fractures because they remove all estrogens from a postmenopausal woman.

Many doctors prefer aromatase inhibitors over tamoxifen as the first hormonal treatment for postmenopausal women whose breast cancer has come back but only if the cancer is hormone receptor positive.

Ovarian ablation: Removing estrogens from premenopausal women is another effective way of treating breast cancer in hormone-responsive cancer. This can be done surgically, by removing the ovaries. It also can be done with drugs called luteinizing hormone-releasing hormone (LHRH) analogs. The usual drugs are goserelin (Zoladex) or leuprolide (Lupron). These drugs block the mechanism that causes ovaries to make estrogens. They are now being tested as adjuvant therapies. Chemotherapy drugs may also damage the ovaries of premenopausal women so they no longer produce estrogen.

Megestrol acetate: Megestrol acetate (Megace) is a progesterone-like drug used for hormone treatment of advanced breast cancer, usually for women whose cancers do not respond to the other hormone treatments. Its major side effect is weight gain, and it is sometimes used to reverse weight loss in patients with advanced cancer.

Other ways to control hormones: Androgens (male hormones) may be considered after other hormone treatments for advanced breast cancer have been tried. Androgens cause masculine characteristics to occur, for example, more body hair and a deeper voice. They are sometimes effective.

Targeted Therapy

As we have learned more about the gene changes that cause cancer, researchers have been able develop newer drugs that specifically target these changes. These targeted drugs work

differently than standard chemotherapy drugs. They often have different (and less severe) side effects. They are most often used along with chemotherapy at this time.

Drugs That Target the HER2/neu Protein

Trastuzumab (Herceptin) is a monoclonal antibody that attaches to a growth-promoting protein known as HER2/neu, which is present in small amounts on the surface of the breast cancer cells of about 15% to 25% of patients. (Monoclonal antibodies are manmade versions of immune system proteins (antibodies) designed to target specific substances located on some cells.) Breast cancers with too much of this protein tend to grow and spread more aggressively. Trastuzumab can prevent the HER2/neu protein from making breast cancer cells grow and may also stimulate the immune system to more effectively attack the cancer. It is an important treatment option for some patients with HER2-positive tumors.

Trastuzumab can shrink some breast cancer metastases that return after chemotherapy or continue to grow during chemotherapy. Treatment that combines trastuzumab with chemotherapy may be more effective than chemotherapy alone in some patients.

Recently, clinical trials have found that adding one year of trastuzumab treatment to chemotherapy lowers the recurrence rate and death rate over chemotherapy alone after surgery in women with HER2/neu-positive early breast cancers. Using trastuzumab along with chemotherapy has become standard adjuvant treatment for these women.

Compared with chemotherapy drugs, the side effects of trastuzumab are relatively mild. They may include fever and chills, weakness, nausea, vomiting, cough, diarrhea, and headache. These side effects are usually associated with the first dose and not seen again. Some women

being treated with trastuzumab, however, have experienced heart damage leading to a problem called congestive heart failure. For most women, this effect on the heart has been temporary and has improved when the drug is stopped; however, it is not always reversible. The risk of heart problems is about 3 times higher when trastuzumab is given with anthracyclines, a class of chemotherapy drugs that includes doxorubicin (Adriamycin) and epirubicin (Ellence). Major symptoms are shortness of breath and severe fatigue. Women experiencing these symptoms should call their doctor right away. A recent study found that trastuzumab may have the same benefit if it is given for only 9 weeks and without the side effect of heart damage.

Lapatinib (Tykerb) is another drug that targets the HER2/neu protein. This drug is given as a pill, most often along with the chemotherapy drug capecitabine (Xeloda). It is used in women with HER2-positive breast cancer that is no longer helped by chemotherapy and trastuzumab. The most common side effects with this drug include diarrhea, nausea, vomiting, rash, and hand-foot syndrome, which may include numbness, tingling, redness, swelling and discomfort of hands and feet. In rare cases it may cause a decrease in heart function (that can lead to shortness of breath), although this seems to go away once treatment is finished.

Drugs That Target Tumor Blood Vessels (Angiogenesis)

Bevacizumab (Avastin) is another monoclonal antibody that may be used in patients with metastatic breast cancer. It is used in combination with the chemotherapy drug paclitaxel (Taxol). This antibody is directed against vascular endothelial growth factor (VEGF), a protein that helps tumors form new blood vessels to get nutrients (a process known as angiogenesis). Bevacizumab is given by intravenous infusion.

Rare, but possibly serious side effects include bleeding, holes forming in the colon (requiring surgery to correct), and slow wound healing. More common side effects include high blood pressure, tiredness, blood clots, bleeding, low white blood cell counts, headaches, mouth sores, loss of appetite, and diarrhea.

Bisphosphonates

Two drugs that help strengthen bones are used in breast cancer treatment to strengthen bones that have been weakened by invading breast cancer cells. They are pamidronate (Aredia) and zoledronic acid (Zometa). They are given intravenously and help reduce the risk of bone fractures if the cancer has spread to the bone. Recently, there have been reports of a serious side effect called osteonecrosis of the jaw. The jaw bone deteriorates and can become painful. Doctors don't know why this happens, but it seems to occur mainly in people who have had dental procedures while taking the drug. If bisphosphonates are recommended and you need dental work, do it before starting on the drug.

Hormonal treatment with the aromatase inhibitors may also weaken the bones by causing loss of calcium from the bone (called osteoporosis) and thus increase the risk of a fracture. Therefore, patients treated with an aromatase inhibitor should have their bone strength tested (called a bone density test) to determine if medication to strengthen their bones, such as bisphosphonates, would be appropriate. Some patients may go into early menopause due to the side effects of chemotherapy. Menopause is associated with bone loss, too. These patients may also undergo a bone density test to evaluate the presence of osteoporosis. There are a number of medications, including some oral forms of bisphosphonates, to treat the loss of calcium from bone that is not caused by direct breast cancer in the bone.

High-Dose Chemotherapy With Autologous Bone Marrow or Peripheral Blood Stem Cell Support

Although it is possible to use very high doses of chemotherapy or radiation to kill cancer cells, such treatments also kill blood-producing stem cells in the bone marrow. Damage to bone marrow stem cells lowers the white blood cell count, which makes it much easier for the patient to get severe infections that could be fatal. It also makes them bleed easily. This, too, can be fatal.

One way to get around this is to remove some of the patient's stem cells from either the peripheral (circulating) blood or bone marrow and then return them into a vein after high-dose chemotherapy. The stem cells are then able to find their way back into the bone marrow where they soon re-establish themselves and restore the body's ability to produce blood cells.

It was thought that this would be a good way to treat women whose breast cancer was diagnosed at an advanced stage, for example, if they had many lymph nodes involved. However, several studies evaluating this treatment have showed no benefit. Women who received the high-dose chemotherapy did not live any longer than women who received standard dose chemotherapy without stem cell support.

High-dose chemotherapy with stem cell support also causes more serious side effects than standard dose chemotherapy. Research in this area is still being conducted. Recent studies found that in certain women whose cancer had spread to many lymph nodes, high-dose chemotherapy did not lower the death rate. Although newer studies may show a drop in death rate, it will likely be very small. And the toxicity from this treatment is very high. Recently, a

study from Germany treated women who had 9 or more cancer-involved lymph nodes with 2 courses of high-dose chemotherapy and stem cell support. Women receiving this treatment had a better survival than those who received conventional treatment. Still, this is only one study. Experts in the field currently recommend that women with breast cancer not receive high-dose chemotherapy except as part of a clinical trial.

Clinical Trials

The purpose of clinical trials: Studies of promising new or experimental treatments in patients are known as clinical trials. A clinical trial is only done when there is some reason to believe that the treatment being studied may be valuable to the patient. Treatments used in clinical trials are often found to have real benefits. Researchers conduct studies of new treatments to answer the following questions:

- Is the treatment helpful?
- How does this new type of treatment work?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are the side effects greater or less than the current standard treatment?
- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

Types of clinical trials: There are 3 phases of clinical trials in which a treatment is studied before it is eligible for approval by the FDA (Food and Drug Administration).

Phase I clinical trials: The purpose of a phase I study is to find the best way to give a new treatment and how much of it can be given safely. The cancer care team watches patients carefully for any harmful side effects. The treatment has been well tested in lab and animal studies, but the side effects in patients are not completely known. Doctors conducting the clinical trial start by giving very low doses of the drug to the first patients and increasing the

dose for later groups of patients until side effects appear. Although doctors are hoping to help patients, the main purpose of a phase I study is to test the safety of the drug.

Phase II clinical trials: These studies are designed to see if the drug works. Patients are given the highest dose that doesn't cause severe side effects (determined from the phase I study) and closely observed for an effect on the cancer. The cancer care team also looks for side effects.

Phase III clinical trials: Phase III studies involve large numbers of patients -- often several hundred. One group (the control group) receives the standard (most accepted) treatment. The other group receives the new treatment. All patients in phase III studies are closely watched. The study will be stopped if the side effects of the new treatment are too severe or if one group has had much better results than the others.

If you are in a clinical trial, you will have a team of experts taking care of you and monitoring your progress very carefully. The study is especially designed to pay close attention to you.

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to find out. While most side effects disappear in time, some can be permanent or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enroll in a clinical trial.

Deciding to enter a clinical trial: Enrollment in any clinical trial is completely up to you. Your doctors and nurses will explain the study to you in detail and will give you a form to read and sign indicating your desire to take part. This process is known as giving your informed consent. Even after signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason. Taking part in the study does not prevent you from getting other medical care you may need.

To find out more about clinical trials, ask your cancer care team. Among the questions you should ask are:

- Is there a clinical trial for which I would be eligible?
- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do? Has it been used before?
- Will I know which treatment I receive?
- What is likely to happen in my case with, or without, this new treatment?
- What are my other choices and their advantages and disadvantages?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to be hospitalized? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

The American Cancer Society offers a clinical trials matching service for patients, their family, and friends. You can reach this service at 1-800-303-5691 or on our Web site at http://clinicaltrials.cancer.org. Based on the information you provide about your cancer type, stage, and previous treatments, this service can compile a list of clinical trials that match your medical needs. In finding a center most convenient for you, the service can also take into account where you live and whether you are willing to travel.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinical_trials/.

Complementary and Alternative Therapies

Complementary and alternative therapies are a diverse group of health care practices, systems, and products that are not part of usual medical treatment. They may include products such as vitamins, herbs, or dietary supplements, or procedures such as acupuncture, massage, and a host of other types of treatment. There is a great deal of interest today in complementary and alternative treatments for cancer. Many are now being studied to find out if they are truly helpful to people with cancer.

You may hear about different treatments from family, friends, and others, which may be offered as a way to treat your cancer or to help you feel better. Some of these treatments are harmless in certain situations, while others have been shown to cause harm. Most of them are of unproven benefit.

The American Cancer Society defines *complementary medicine* or methods as those that are used along with your regular medical care. If these treatments are carefully managed, they may add to your comfort and well-being. *Alternative medicines* are defined as those that are used instead of your regular medical care. Some of them have been proven not to be useful or even to be harmful, but are still promoted as “cures.” If you choose to use these alternatives, they may reduce your chance of fighting your cancer by delaying, replacing, or interfering with regular cancer treatment.

Before changing your treatment or adding any of these methods, discuss this openly with your doctor or nurse. Some methods can be safely used along with standard medical treatment. Others, however, can interfere with standard treatment or cause serious side effects. That is why it's important to talk with your doctor. More information about specific complementary and alternative therapies used for cancer is available through our toll-free number or on our Web site.

Breast Cancer Treatment by Stage

Stage 0 (Ductal Carcinoma in Situ [DCIS] or Lobular Carcinoma in Situ [LCIS])

The 2 types of stage 0 breast cancer, DCIS and LCIS, are treated quite differently.

No immediate or active treatment is recommended for most women with LCIS because this condition is not a true cancer. But because having LCIS increases your risk of developing invasive cancer later on, close follow-up is essential. This usually includes a yearly mammogram and a clinical breast exam. Close follow-up of both breasts is important because women with LCIS in one breast have an equal risk of developing breast cancer on the same or opposite side.

These women may wish to consider taking tamoxifen or participating in a clinical trial for breast cancer prevention (with tamoxifen or raloxifene, for example). For more information on drugs to prevent breast cancer see the American Cancer Society document, "Medicines to Reduce Breast Cancer Risk." They may also wish to discuss other possible prevention strategies (such as optimizing their body weight, an exercise program, or preventive surgery) with their doctor.

Some medical centers have clinical trials to test the value of magnetic resonance imaging (MRI) for patients with LCIS. Some women with LCIS may choose to have a bilateral simple mastectomy (removal of both breasts but not axillary lymph nodes), especially if they have other risk factors, such as strong family history, in an attempt to prevent invasive cancer from developing. Depending on the woman's preference, she may consider immediate or delayed breast reconstruction.

Treatment of DCIS depends on mammogram and biopsy results. In most cases, a woman can choose between breast-conserving therapy (lumpectomy, usually followed by radiation therapy) and simple mastectomy. Lymph node removal (axillary dissection) is usually not necessary. Lumpectomy without radiation therapy is usually considered an option only for women with small areas of low-grade DCIS with surgical margins around the DCIS of at least greater than 1 mm. Mastectomy may be necessary if the area of DCIS is very large, if the breast has several areas of DCIS, or if lumpectomy cannot completely remove the DCIS (that is, the lumpectomy specimen and re-excision specimens have positive margins).

After a lumpectomy, a mammogram should be done to ensure that the disease has been removed. The surgical specimen is also x-rayed to make sure it contains all the abnormalities, such as calcifications, seen on the original mammogram.

Women having mastectomy for DCIS may have immediate or delayed reconstruction. Studies have shown that 5 years of treatment with tamoxifen can lower the risk of another DCIS or invasive cancer developing in either breast after treatment of DCIS with lumpectomy and radiation therapy, but only if the original DCIS was estrogen receptor positive.

Invasive Breast Cancer

If the cancer is small enough, breast-conserving surgery is appropriate. If it is too large, a mastectomy will be needed, unless preoperative (neoadjuvant) chemotherapy can shrink the tumor enough to allow breast-conserving surgery. In either case, the lymph nodes will need to be checked and removed if they contain cancer. Radiation will be needed for almost all patients who have breast-conserving surgery and some who have mastectomy. Adjuvant therapy after surgery will also be recommended for all cancers larger than 1 cm (0.4 inches) and for some that are smaller.

Stage I

This can be treated with either breast-conserving surgery, sometimes called lumpectomy (removal of the cancer and a narrow margin of surrounding normal breast tissue), or mastectomy. The lymph nodes will need to be evaluated. Sentinel lymph node sampling may be used instead of standard axillary lymph node dissection. Radiation therapy is usually given after lumpectomy. Although some women try to avoid the radiation, a very large study has shown that not receiving radiation increases a woman's chance of dying from the cancer. Breast reconstruction can be done after a mastectomy, either at the time of surgery or later.

If the tumor is less than 1 cm (nearly 1/2 inch) in diameter, adjuvant systemic chemotherapy is not usually offered. Some doctors suggest adjuvant chemotherapy if a cancer smaller than 1 cm has any unfavorable features (such as, microscopic study shows high grade, the estrogen-receptor assay is negative, or the tumor is HER2/neu positive). If the tumor is larger, depending on the features mentioned above, adjuvant chemotherapy or hormone therapy, or both, may be recommended. Most doctors will discuss the pros and cons of

adjuvant hormone therapy (either tamoxifen or an aromatase inhibitor) with all women who have an estrogen-receptor positive breast cancer, no matter how small the tumor.

While not yet recommended for routine use, another aid that may be used to help doctors decide whether to give chemotherapy to women with lymph node negative, hormone-receptor positive, invasive breast cancer is called Oncotype DX. This test is performed on a sample of your breast cancer and tests for the function of 21 specific genes within your cancer. How these genes are functioning in relation to one another can predict the risk of your cancer returning somewhere else in your body, as well as your expected benefit from hormone therapy or chemotherapy. The test will not yet tell your doctor which is the best hormone therapy or chemotherapy to recommend. A large clinical trial is being started to see if this test can really tell which women can do without chemotherapy in situations where doctors are often uncertain. This occurs most often in women with small tumors and uninvolved lymph nodes.

Stage II

Surgery and radiation therapy options for stage I and stage II tumors are similar, except that in stage II, radiation therapy may be considered even after mastectomy if the tumor is large (over 5 cm) or has spread to many lymph nodes (4 or more). Adjuvant systemic therapy is also recommended. Adjuvant therapy may involve hormone therapy, chemotherapy, trastuzumab, or all three, depending on the patient's age, estrogen-receptor assay results, and HER2/neu status.

An option for some women who would like to have breast-conserving therapy for tumors larger than 2 cm (4/5 inch -- T2 or T3) is to have neoadjuvant (before surgery)

chemotherapy, hormone therapy, and/or trastuzumab to shrink the tumor. The size of these tumors relative to some women's breasts may, however, make lumpectomy difficult or impossible.

If the neoadjuvant treatment shrinks their tumors enough, women may then be able to have lumpectomy, which is followed by radiation therapy and hormone therapy if the tumor is hormone-receptor positive. If the tumor does not shrink enough to permit lumpectomy, then mastectomy followed by different chemotherapy, radiation therapy, and hormone therapy is the usual treatment. A woman’s survival from breast cancer is not affected by whether she gets her chemotherapy before or after her breast surgery.

Stage III

Smaller stage IIIA breast cancers may be removed by lumpectomy. Modified radical mastectomy (with or without reconstruction) is another option. Surgery is usually followed by adjuvant systemic chemotherapy, and/or hormone therapy, and/or trastuzumab, and radiation therapy.

Larger stage IIIA, as well as stage IIIB and IIIC cancers may be treated with neoadjuvant (before surgery) chemotherapy. Then a modified radical mastectomy is done, with or without reconstruction. A lumpectomy may be an option. In any case, surgery is followed by radiation therapy, even if a total mastectomy is done. Hormone therapy will be discussed with all women with estrogen-receptor positive breast cancers.

Adjuvant Therapy for Stage I - III Breast Cancer

Adjuvant drug therapy may be recommended, based on the tumor's size, spread to lymph nodes, and/or prognostic features. If it is, you may receive chemotherapy, and/or trastuzumab, and/or hormone therapy.

Hormone therapy: Hormone therapy is not likely to be effective for women with hormone receptor-negative tumors. Hormone therapy is frequently offered to all women with hormone receptor-positive invasive breast cancer regardless of size or the number of lymph nodes involved.

Women who are still having periods and have hormone receptor-positive tumors can be treated with tamoxifen, which blocks the effects of estrogen being made by the ovaries, or with luteinizing hormone-releasing hormone (LHRH) analogs, which medically make the ovaries temporarily nonfunctional. Another alternative is surgical removal of their ovaries (oophrectomy).

Women not having periods, or who are known to be in menopause at any age, and have hormone receptor-positive tumors will generally receive hormone therapy with an aromatase inhibitor. (Monitoring levels of hormones such as estradiol and FSH may be required to make sure that a woman is truly postmenopausal.) If the aromatase inhibitor is given alone, the period of treatment is 5 years. If the woman cannot take an aromatase inhibitor, an alternative is tamoxifen for 5 years as adjuvant therapy.

Some women may benefit from receiving both drugs (although not at the same time). Recent studies have shown that postmenopausal women who take an aromatase inhibitor after taking tamoxifen for 2 to 6 years may further lower the risk that their breast cancer will come back.

It is not known exactly how long the aromatase inhibitor should be taken, but in current studies it has been taken for up to 5 years. Other studies have shown a benefit for an aromatase inhibitor given after tamoxifen. Postmenopausal women were given the drug for 2 to 3 years after receiving tamoxifen for 2 to 3 years. These women had a lower cancer recurrence rate, both local and distant, than did women who took tamoxifen for the full 5-year period. You might want to discuss these new treatments with your doctor.

Chemotherapy: Chemotherapy is usually recommended for all women with an invasive breast cancer whose tumor is hormone receptor-negative, or with those women with hormone receptor-positive tumors who may receive additional benefit from receiving chemotherapy in addition to their hormone therapy. The specific drug regimens and the length of therapy are frequently determined by the size of the cancer, the aggressiveness of the cancer, and the number of involved lymph nodes. The specific chemotherapy regimens usually discussed are listed above in the chemotherapy section. As a general rule, CMF (cyclophosphamide, fluorouracil, and methotrexate) is given for 6 months. AC (doxorubicin and cyclophosphamide) is given for 3 months. Patients with more aggressive tumors or those women with lymph node involved cancers will frequently be offered a taxane (paclitaxel or docetaxel) in addition to doxorubicin and cyclophosphamide, either in sequence or all at the same time. The length of these regimens ranges from 4 to 6 months.

Most doctors recommend that hormone therapy be started after the chemotherapy is completed.

Women who have HER2/neu positive cancers should receive trastuzumab as part of their program. In general the chemotherapy regimen that has been used is doxorubicin and

cyclophosphamide together for 4 treatments, followed by paclitaxel for 12 weekly treatments or every 3 weeks for 4 treatments. The trastuzumab, which is given weekly for about 1 year, may be slightly more effective if it is started at the same time as the paclitaxel. But doctors worry that giving the trastuzumab so soon after doxorubicin can lead to heart problems. Clinical trials of non-doxorubicin chemotherapy combinations are being studied in an effort to find effective treatments with fewer side effects.

For help in deciding if adjuvant therapy is right for you, you might want to visit the Mayo Clinic Web site at www.mayoclinic.com and type "adjuvant therapy" into the search box. You will find a page that will help you to understand your benefits from adjuvant therapy. Another online guide can be found at www.adjuvantonline.com. This Web site provides information regarding your risk of the cancer returning within the next 10 years and what benefits you might expect from hormone therapy and/or chemotherapy.

Stage IV

Systemic therapy is the main treatment, using chemotherapy, hormone therapy, or both. Immunotherapy with trastuzumab alone or in combination with chemotherapy is another option for women whose cancer cells have high levels of the HER2/neu protein. Trastuzumab may allow women to live longer if it is given with the first chemotherapy for stage IV disease. It is not yet known whether it also should be given at the same time as hormone therapy, or how long a woman should remain on therapy.

Another new form of therapy has also recently been shown to be of benefit for women with advanced cancer who are receiving chemotherapy. This class of drugs is called anti-VEGF therapy. They work by blocking factors made by cancers (called VEGF–vascular endothelial

growth factor), which stimulate a new blood supply to the cancer. These drugs seem to be able to block the cancer's ability to provide itself a healthy blood supply. Recently, results of a study were reported using a drug called bevacizumab along with paclitaxel. Women who received both of these drugs together had a doubling of the amount of time their cancer was under control versus just receiving the chemotherapy alone.

None of the systemic therapies given for breast cancer is without side effects; including hormone therapy, chemotherapy, or the newer biologic therapies, trastuzumab and bevacizumab. Your doctor will explain to you the benefits and risks of all of these therapies before prescribing them.

Radiation and/or surgery may also be used to provide relief of certain symptoms. Treatment to relieve symptoms depends on where the cancer has spread. For example, pain due to bone metastases may be treated with external beam radiation therapy and/or bisphosphonates such as pamidronate (Aredia) or zoledronic acid (Zometa). Bisphosphonates are drugs that can help prevent bone damage or fractures caused by metastatic breast cancer. These are recommended for all patients whose breast cancer has spread to their bones. (For more information about treatment of bone metastases, see the American Cancer Society document, "Bone Metastasis.")

Patients in otherwise good health are encouraged to take part in clinical trials of other promising treatments being studied.

Recurrent Breast Cancer

Breast cancer can come back locally (in the breast or near the mastectomy scar) or in a distant area.

Treatment of women whose breast cancer has recurred locally depends on their initial treatment. If the woman had breast conservation therapy, local recurrence in the breast is usually treated with mastectomy. If the initial treatment was mastectomy, recurrence near the mastectomy site is treated by removing the tumor whenever possible, usually followed by radiation therapy, but only if none had been given after the original surgery. In either case, hormone therapy, and/or trastuzumab, and/or chemotherapy may be used after surgery and/or radiation therapy.

Women who have a distant recurrence involving organs such as the bones, lungs, brain, etc., are treated the same as those found to have stage IV breast cancer involving these organs at the time of initial diagnosis.

Treatment of Breast Cancer During Pregnancy

Breast cancer is diagnosed in about 1 pregnant woman out of 3,000. Radiation therapy during pregnancy is known to increase the risk of birth defects, so it is not recommended for pregnant women with breast cancer. For this reason, breast conservation therapy (lumpectomy and radiation therapy) is not considered an option if treatment cannot be delayed until it is safe to deliver the baby. However, breast biopsy procedures and even modified radical mastectomy are safe for the mother and fetus.

For a long time it was assumed that chemotherapy was dangerous to the fetus. However, several recent studies have found that using certain chemotherapy drugs during the second

and third trimesters (the fourth to ninth months) does not increase the risk of birth defects. Because of concern about the potential damage to the fetus, the safety of chemotherapy during the first trimester (the first 3 months) of pregnancy has not been studied. Similarly, hormone therapy should not be started until after the patient has given birth. Current treatment recommendations depend upon how long the woman has been pregnant. For more information, see the American Cancer Society document, "Pregnancy and Breast Cancer."

More Treatment Information

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from 20 of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN Web site (www.nccn.org).

The American Cancer Society collaborates with the NCCN to produce a version of some of these treatment guidelines, written specifically for patients and their families. These less-technical versions are available on both the NCCN Web site (www.nccn.org) and the ACS Web site (www.cancer.org). A print version can also be requested from the ACS at 1-800-ACS-2345.

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What Should You Ask Your Doctor About Breast Cancer?

It is important for you to have frank, open discussions with your cancer care team. Don't be afraid to ask questions, no matter how trivial you might think they are. Some questions to consider:

- What type of breast cancer do I have?
- Has my cancer spread to lymph nodes or internal organs?
- What is the stage of my cancer and how does it affect my treatment options and prognosis?
- Am I eligible for any clinical trials?
- What treatments are appropriate for me? What do you recommend? Why?
- What are the risks or side effects that I should expect?
- How effective will breast reconstruction surgery be if I need or want it?
- What should I do to get ready for treatment?
- Should I follow a special diet?
- Will I be able to have children after my treatment?
- What are the chances my cancer will come back with the treatment programs we have discussed?
- Will I go through menopause as a result of the treatment?
- Will I have normal sensation in my breasts after my treatment?

Be sure to write down any questions that occur to you that are not on this list. For instance, you might want specific information about anticipated recovery times so that you can plan your work schedule. Or you may want to ask about second opinions or about clinical trials for which you may qualify. Taking another person and/or a tape recorder to the appointment can be helpful. Collecting copies of your medical records, pathology reports, and radiology reports may be useful in case you wish to seek a second opinion at a later time.

What Happens After Treatment for Breast Cancer?

Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called recurrence.) This is a very common concern among those who have had cancer. For

more information on this please refer to the American Cancer Society document, “Living With Uncertainty: The Fear of Cancer Recurrence.”

It may take a while before your confidence in your own recovery begins to feel real and your fears are somewhat relieved. Even with no recurrences, people who have had cancer learn to live with uncertainty.

Follow-up Care

After treatment is completed, it is very important to go to all scheduled follow-up appointments. During these appointments, your doctors will ask questions about any symptoms, do physical exams, and order laboratory or imaging tests as needed to look for recurrences or side effects. Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can be permanent. You should never hesitate to tell your doctor or other members of your cancer care team about any symptoms or side effects that concern you.

At first, your follow-up appointments will probably be scheduled for every 4 to 6 months. The longer you have been free of cancer, the less often the appointments are needed. After 5 years, they are done once a year. You will need to continue to have yearly mammograms.

If you are taking tamoxifen, you should have yearly pelvic exams because this drug can increase your risk of uterine cancer. Be sure to tell your doctor right away about any abnormal vaginal bleeding you are having. Although excessive or irregular vaginal bleeding is usually caused by a non-cancerous condition, it may also be the first sign of uterine cancer.

If you are taking an aromatase inhibitor, you should consider testing your bone density.

Other tests such as blood tumor marker studies, blood tests of liver function, bone scans, and chest x-rays are not usually needed unless symptoms or physical exam findings suggest it is likely the cancer has recurred. These and other tests may be done as part of evaluating new treatments by clinical trials.

If initial exams and tests suggest a recurrence, a chest x-ray, CT scan, PET scan, MRI scan, bone scan, and/or a biopsy may be done. Your doctor may also measure the tumor marker CA-15-3, CA 27-29, or CEA with a blood test. The blood level of this substance goes up in some women if their cancer has spread to bones or other organs such as the liver. Depending on the location of a recurrent cancer, treatment may involve surgery, radiation therapy, hormone therapy, and/or chemotherapy. For more information on recurrence please see the American Cancer Society document, “When Your Cancer Comes Back: Cancer Recurrence.”

Lymphedema

Lymphedema, or swelling of the arm due to buildup of fluid, may occur any time after treatment for breast cancer. Any treatment that involves axillary dissection or radiation to the axillary lymph nodes carries the risk of lymphedema because normal drainage of lymph from the arm is changed.

The onset of lymphedema is often subtle and unpredictable. There is no good way to predict who will and will not develop lymphedema. It can occur right after surgery, months, or even years later. The potential for developing lymphedema remains throughout a woman's lifetime.

With care, lymphedema can often be avoided or, if it develops, kept under control. Injury or infection involving the affected arm or hand can contribute to the development of lymphedema or aggravate existing lymphedema, so preventive measures should focus on protecting the arm and hand. Most doctors recommend that women avoid having blood drawn from or blood pressures taken on the arm on the side of the lymph node surgery or radiation.

One of the first symptoms of lymphedema may be a feeling of tightness in the arm or hand on the same side that was treated for breast cancer. Any swelling, tightness, or injury to the arm or hand should be reported promptly to your doctor or nurse. To learn more, see the American Cancer Society document, "Lymphedema: What Every Woman With Breast Cancer Should Know."

Quality of Life

Women who have undergone treatment for breast cancer should be reassured that their quality of life, once treatment has been completed, can be normal. Extensive studies have proven this. Women who have had chemotherapy may, however, notice a slight decrease in certain areas of function.

Some studies suggest that younger women, who represent about one fourth of breast cancer survivors, tend to have more problems adjusting to the stresses of breast cancer and its treatment. They have more psychosocial problems and trouble with emotional and social functioning. Some can feel isolated. Also, chemotherapy may have caused early menopause

which requires adjustment. There may also be sexual difficulties. All these may need help with counseling and support groups directed to younger breast cancer survivors.

Emotional Aspects of Breast Cancer

It is important that your focus on tests and treatments does not prevent you from considering your emotional, psychological, and spiritual health as well. Once your treatment ends, you may find yourself overwhelmed by emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through your treatment.

Now you may find that you think about the potential of your own death, or the effect of your cancer on your family, friends, and career. You may also begin to re-evaluate your relationship with your spouse or partner. Unexpected issues may also cause concern -- for instance, as you become healthier and have fewer doctor visits, you will see your health care team less often. That can be a source of anxiety for some.

This is an ideal time to seek out emotional and social support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or individual counselors.

Almost everyone who has been through cancer can benefit from getting some type of support. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend

or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or realistic to go it all by yourself. And your friends and family may feel shut out if you decide not include them. Let them in -- and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-ACS-2345 and we can put you in touch with an appropriate group or resource.

Body image: A woman's choice of treatment will likely be influenced by her age, the image she has of herself and her body, and her hopes and fears. For example, some women may select breast-conserving surgery with radiation therapy over a mastectomy for cosmetic and body image reasons. On the other hand, some women who choose mastectomy may want the affected area removed, regardless of the effect on their body image. They may be more concerned about the effects of radiation therapy than body image.

Other issues that women worry about include hair loss from chemotherapy and skin changes of the breast from radiation therapy. In addition to these body changes, women may also be dealing with concerns about the outcome of their treatment. These are all genuine concerns that affect how a woman makes decisions about her treatment, how she views herself, and how she feels about her treatment.

Sexuality: Concerns about sexuality are often very worrisome to a woman with breast cancer. Several factors may place a woman at higher risk for sexual problems after breast cancer. It is important to remember that some treatments for breast cancer, such as

chemotherapy, can change a woman's hormone levels and may negatively affect sexual interest and/or response. A diagnosis of breast cancer when a woman is in her 20s or 30s is especially difficult because choosing a partner and childbearing are often very important during this period.

Relationship issues are also important because the diagnosis can be very distressing for the partner, as well as the patient. Partners are usually concerned about how to express their love physically and emotionally after treatment, especially surgery.

Suggestions that may help a woman adjust to changes in her body image include looking at and touching herself; seeking the support of others, preferably before surgery; involving her partner as soon as possible after surgery; and openly communicating feelings, needs, and wants created by her changed image.

Sexual impact of surgery and radiation: Because breast cancer is the most common cancer in women (excluding skin cancer), sexual problems have been linked to mastectomy more often than to any other cancer treatment. Losing a breast, or occasionally both breasts, can be traumatic.

The most common sexual side effects stem from damage to a woman's feelings of attractiveness. In our culture, we are taught to view breasts as a basic part of beauty and femininity. If her breast has been removed, a woman may be insecure about whether her partner will accept her and find her sexually pleasing.

The breasts and nipples are also sources of sexual pleasure for many women. Touching the breasts is a common part of foreplay in our culture. A few women can reach orgasm just from the stroking of their breasts. For many others, breast stimulation adds to sexual excitement.

Breast surgery or radiation to the breasts does not physically decrease a woman's sexual desire. Nor does it decrease her ability to have vaginal lubrication, normal genital feelings, or reach orgasm. Some good news from recent research is that within a year after their surgery, most women with early stage breast cancer have good emotional adjustment and sexual satisfaction. They report a quality of life similar to women who never had cancer.

Treatment for breast cancer can interfere with pleasure from breast caressing. After a mastectomy, the whole breast is gone. Some women still enjoy being stroked around the area of the healed scar. Others dislike being touched there and may no longer even enjoy being touched on the remaining breast and nipple.

Some women who have had a mastectomy feel self-conscious being the partner "on top" during sex. The area of the missing breast is more visible in that position.

A few women have chronic pain in their chests and shoulders after radical mastectomy. During intercourse, supporting these areas with pillows may help. Also, avoid positions where your weight rests on your chest or arms.

If surgery removed only the tumor (segmental mastectomy or lumpectomy) and was followed by radiation therapy, the breast may be scarred. It also may be a different shape or size.

During radiation therapy, the skin may become red and swollen. The breast also may be a little tender. Breast and nipple feeling, however, should remain normal.

Sexual impact of breast reconstruction: Breast reconstruction restores the shape of the breast, but it cannot restore normal breast sensation. The nerve that supplies feeling to the nipple runs through the deep breast tissue, and it gets disconnected during surgery. In a reconstructed breast, the feeling of pleasure from touching the nipple is lost. A rebuilt nipple has much less feeling.

In time, the skin on the reconstructed breast will regain some sensitivity but probably will not give the same kind of pleasure as before mastectomy. Breast reconstruction often makes women more comfortable with their bodies, however, and helps them feel more attractive.

Effect on your partner: Breast cancer can be a growth experience for couples under certain circumstances. The relationship may be enhanced if the partner participates in decision making and accompanies the woman to surgery and other treatments.

About Breast Forms and Bras

For women who have had a mastectomy, breast forms are an important alternative to breast reconstruction. Some women may not want further surgery, knowing that breast reconstruction can require several procedures to complete.

Your doctor will tell you when you have healed enough to be fitted for a permanent breast form or prosthesis. Most of these forms are made from materials that approximate the

movement, feel, and weight of natural tissue. A properly weighted form provides the balance your body needs for correct posture and anchors your bra, preventing it from riding up.

At first, these forms may feel too heavy, but in time they will feel natural. Prices vary considerably. High price doesn't necessarily mean that the product is the best for you. Take time to shop for a good fit, comfort, and an attractive, natural appearance in the bra and under clothing. Your clothes should fit the way they did before surgery.

The right bra for you may very well be the one you have always worn. It may or may not need adjustments. If there is tenderness during healing, a bra extender can help by increasing the circumference of the bra so that it does not bind the chest too tightly. Heavy-breasted women can relieve pressure on shoulder straps by slipping a bra shoulder pad under one or both straps.

If you decide to wear your breast form in a pocket in your bra, you can have your regular bra adapted. There are also special mastectomy bras with the pockets already sewn in. If the breast form causes any kind of skin irritation, use a bra with a pocket. If your bra has underwires, you may be able to wear it, but be sure to clear this with your doctor.

You might want to wear your prosthesis under nightgowns but would like something more comfortable than a regular bra. Most department stores carry a soft bra, sometimes called a leisure or night bra.

Be sure to read your insurance policy to see what is covered and how you must submit claims. Also, ask your doctor to write prescriptions for your prosthesis and for any special

mastectomy bras. When purchasing bras or breast forms, mark the bills and any checks you write "surgical." Medicare and Medicaid can be used to pay for some of these expenses if you are eligible. The cost of breast forms and bras with pockets may be tax deductible. If you have a bra altered, the charge may be tax deductible.

Keep careful records of all related expenses. If you submit a claim for a prosthesis or bra to your insurance company, in some cases the insurance company WILL NOT cover reconstruction, should you choose this procedure in the future. Make sure you get all the facts before submitting any insurance claims.

Be sure to call your Reach to Recovery volunteer about any questions you have. She will give you suggestions, additional reading material, and advice. Remember that she's been there and will probably understand.

Pregnancy After Breast Cancer

Because of the well-established link between estrogen levels and growth of breast cancer cells, many doctors have advised breast cancer survivors not to become pregnant for at least 2 years after treatment. This would allow any early return of the cancer to be diagnosed and this, in turn, could affect a woman’s decision to become pregnant. But this 2 year wait period is arbitrary and earlier pregnancy may not be harmful.

Although few studies have been performed, nearly all have found that pregnancy does not increase the risk of recurrence after successful treatment of breast cancer. Women are advised to discuss their risk of recurrence with their doctors. In some cases, counseling can

help women with the complex issues and uncertainties regarding motherhood and breast cancer survivorship.

Postmenopausal Hormone Therapy After Breast Cancer

The known link between estrogen levels and breast cancer growth has discouraged many women and their doctors from choosing or recommending postmenopausal hormone therapy (PHT), also called hormone replacement therapy (HRT). Unfortunately, many women experience menopausal symptoms after treatment for breast cancer. This can occur naturally or develop as a result of menopausal women stopping PHT. Chemotherapy can also cause early menopause in premenopausal women.

In the past, doctors have offered PHT after breast cancer treatment to women suffering from severe symptoms because early studies had shown no harm. However, in early 2004 a well-designed study (the HABITS study) found that breast cancer survivors taking PHT were much more likely to develop a new or recurrent breast cancer than women who were not taking the drugs. For this reason, most doctors now feel that for women previously treated for breast cancer, taking PHT would be unwise.

Women should consider discussing with their doctors alternatives to PHT to help with specific menopausal symptoms. Some doctors have suggested that phytoestrogens (estrogen-like substances from certain plant sources, such as soy products) may be safer than the estrogens used in PHT. However, there is not enough information available on phytoestrogens to evaluate their safety for breast cancer survivors.

Two of the drugs that have proven somewhat effective in treating hot flashes are the antidepressant, Effexor, and a drug called Neurontin. There is, however, recent data showing that some anti-depressants can interact with tamoxifen and make it less effective. If you are taking tamoxifen and experience hot flashes, you should ask your doctor about any possible interactions between your tamoxifen and any other drugs you may be taking.

Seeing a New Doctor

At some point after your cancer diagnosis and treatment, you may find yourself in the office of a new doctor. Your original doctor may have moved or retired, or you may have moved or changed doctors for some reason. It is important that you be able to give your new doctor the exact details of your diagnosis and treatment. Make sure you have the following information handy:

- a copy of your pathology report from any biopsy or surgery
- if you had surgery, a copy of your operative report
- if you were hospitalized, a copy of the discharge summary that every doctor must prepare when patients are sent home from the hospital
- finally, since some drugs can have long-term side effects, a list of your drugs, drug doses, and when you took them

Lifestyle Changes to Consider During and After Treatment

You can’t change the fact that you have had cancer. What you can change is how you live the rest of your life -- making healthy choices and feeling as well as possible, physically and emotionally. Having cancer and dealing with treatment can be time-consuming and emotionally draining, but it can also be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even begin this process during cancer treatment.

Make Healthier Choices

Think about your life before you learned you had cancer. Were there things you did that might have made you less healthy? Maybe you drank too much alcohol, or ate more than you needed, or smoked, or didn't exercise very often. Emotionally, maybe you kept your feelings bottled up, or maybe you let stressful situations go on too long.

Now is not the time to feel guilty or to blame yourself. However, you can start making changes today that can have positive effects for the rest of your life. Not only will you feel better but you will also be healthier. What better time than now to take advantage of the motivation you have as a result of going through a life-changing experience like having cancer?

You can start by working on those things that you feel most concerned about. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society's Quitline® tobacco cessation program at 1-800-ACS-2345.

Diet and Nutrition

Eating right can be a challenge for anyone, but it can get even tougher during and after cancer treatment. For instance, treatment often may change your sense of taste. Nausea can be a problem. You may lose your appetite for a while and lose weight when you don't want to. On the other hand, some people gain weight even without eating more. This can be frustrating, too.

If you are losing weight or have taste problems during treatment, do the best you can with eating and remember that these problems usually improve over time. You may want to ask your cancer team for a referral to a dietitian, an expert in nutrition who can give you ideas on how to fight some of the side effects of your treatment. You may also find it helps to eat small portions every 2 to 3 hours until you feel better and can go back to a more normal schedule.

One of the best things you can do after treatment is to put healthy eating habits into place. You will be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Try to eat 5 or more servings of vegetables and fruits each day. Choose whole grain foods instead of white flour and sugars. Try to limit meats that are high in fat. Cut back on processed meats like hot dogs, bologna, and bacon. Get rid of them altogether if you can. If you drink alcohol, limit yourself to 1 or 2 drinks a day at the most. And don't forget to get some type of regular exercise. The combination of a good diet and regular exercise will help you maintain a healthy weight and keep you feeling more energetic.

Weight

For a woman diagnosed with breast cancer, achieving or maintaining a desirable weight may be one of the most important things you can do. Most studies have found that women who are overweight or obese at the time of diagnosis are more likely to have their disease recur and are more likely to die from breast cancer. Overweight women should be encouraged to lose weight after treatment. In some cases, a modest weight loss program may even be started during treatment, if the doctor approves.

Study results have been mixed as to how strongly weight gain affects breast cancer recurrence or survival. Two large studies have found that those who gained significant amounts of weight after diagnosis were more likely to relapse and more likely to die than were women who gained less weight. However, other recent studies have not found an effect of weight gain on prognosis.

Rest, Fatigue, Work, and Exercise

Fatigue is a very common symptom in people being treated for cancer. This is often not an ordinary type of tiredness but a “bone-weary” exhaustion that doesn’t get better with rest. For some, this fatigue lasts a long time after treatment, and can discourage them from physical activity.

However, exercise can actually help you reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel physically and emotionally improved and can cope better. Also, recent studies suggest that breast cancer survivors who are physically active have lower rates of recurrence and lower death rates than those who are inactive.

If you are ill and need to be on bed rest during treatment, it is normal to expect your fitness, endurance, and muscle strength to decline some. Physical therapy can help you maintain strength and range of motion in your muscles, which can help fight fatigue and the sense of depression that sometimes comes with feeling so tired.

Any program of physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis 3 times a week. If you haven't exercised in a few years but can still get around, you may want to think about taking short walks.

Talk with your health care team before starting, and get their opinion about your exercise plans. Then, try to get an exercise buddy so that you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, though, you will need to balance activity with rest. It is okay to rest when you need to. It is really hard for some people to allow themselves to do that when they are used to working all day or taking care of a household. (For more information about fatigue, please see the publication, "Cancer Related Fatigue and Anemia Treatment Guidelines for Patients.")

Exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- It strengthens your muscles.
- It reduces fatigue.
- It lowers anxiety and depression.
- It makes you feel generally happier.
- It helps you feel better about yourself.

And long term, we know that exercise plays a role in preventing some cancers. The American Cancer Society, in its guidelines on physical activity for cancer prevention, recommends that to reduce the risk for breast cancer adults should take part in moderate to vigorous physical activity for 45 to 60 minutes on 5 or more days of the week. Moderate

activities are those that take about as much effort as a brisk walk. Vigorous activities use larger muscle groups, make you sweat, and cause a noticeable increase in heart rate and breathing.

What Happens if Treatment Is No Longer Working?

If cancer continues to grow after one kind of treatment, or if it returns, it is often possible to try another treatment plan that might still cure the cancer, or at least shrink the tumors enough to help you live longer and feel better. On the other hand, when a person has received several different medical treatments and the cancer has not been cured, over time the cancer tends to become resistant to all treatment. At this time it's important to weigh the possible limited benefit of a new treatment against the possible downsides, including continued doctor visits and treatment side effects.

Everyone has his or her own way of looking at this. Some people may want to focus on remaining comfortable during their limited time left.

This is likely to be the most difficult time in your battle with cancer -- when you have tried everything medically within reason and it's just not working anymore. Although your doctor may offer you new treatment, you need to consider that at some point, continuing treatment is not likely to improve your health or change your prognosis or survival.

If you want to continue treatment to fight your cancer as long as you can, you still need to consider the odds of more treatment having any benefit. In many cases, your doctor can estimate the response rate for the treatment you are considering. Some people are tempted to try more chemotherapy or radiation, for example, even when their doctors say that the odds

of benefit are less than 1%. In this situation, you need to think about and understand your reasons for choosing this plan.

No matter what you decide to do, it is important that you be as comfortable as possible. Make sure you are asking for and getting treatment for any symptoms you might have, such as pain. This type of treatment is called “palliative” treatment.

Palliative treatment helps relieve these symptoms, but is not expected to cure the disease; its main purpose is to improve your quality of life. Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, radiation therapy might be given to help relieve bone pain from bone metastasis. Or chemotherapy might be given to help shrink a tumor and keep it from causing a bowel obstruction. But this is not the same as receiving treatment to try to cure the cancer.

At some point, you may benefit from hospice care. Most of the time, this can be given at home. Your cancer may be causing symptoms or problems that need attention, and hospice focuses on your comfort. You should know that receiving hospice care doesn’t mean you can’t have treatment for the problems caused by your cancer or other health conditions. It just means that the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult stage of your cancer.

Remember also that maintaining hope is important. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. In a way, pausing at this time in your cancer treatment is an

opportunity to refocus on the most important things in your life. This is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do.

What's New in Breast Cancer Research and Treatment?

Causes of Breast Cancer

Studies continue to uncover lifestyle factors and habits that alter breast cancer risk. Ongoing studies are looking at the effect of exercise, weight gain or loss, and diet on breast cancer risk. Studies on the best use of genetic testing for BRCA1 and BRCA2 mutations continue at a rapid pace. Other genes are being identified. This will occur more rapidly now that the human genome has been sequenced.

Perhaps the most important finding, though, has been that combined estrogen and progestin (not estrogen alone) when used as postmenopausal hormone therapy increases a woman's risk of developing breast cancer.

A large, long-term study funded by the National Institute of Environmental Health Sciences (NIEHS) is now underway to help find the causes of breast cancer. Known as the Sister Study, it will follow 50,000 women for at least 10 years and will collect information about genes, lifestyle, and environmental factors that may cause breast cancer. To be eligible for the study, a woman must:

- live in the United States
- be between the ages of 35 and 74
- have a sister (related by blood) who has had breast cancer
- not have had breast cancer herself

Women who want to find out more about the Sister Study can call 1-877-4-SISTER (1-877-474-7837) or visit the Sister Study Web site (www.sisterstudy.org).

Chemoprevention

Recent results of studies that are still in progress suggest that selective estrogen-receptor modulators (SERMs) lower breast cancer risk in women with certain breast cancer risk factors. Further research with SERMs, such as tamoxifen (also used in breast cancer treatment) and raloxifene and drugs such as aromatase inhibitors, is expected to lead to ways to prevent many breast cancers. So far, most women are reluctant to take these medications because of concern about side effects.

MRI-assisted Breast Biopsy

A new biopsy technique now makes it possible to obtain tissue samples during a vacuum-assisted breast biopsy procedure with magnetic resonance imaging (MRI)-assisted guidance. This method allows many samples to be taken through a single small incision in the skin, using only local anesthesia (numbing of the area). This biopsy technique is being studied in women with a personal or family history of breast cancer, those who have undergone previous breast surgery, and women with dense breast tissue who cannot get accurate screenings with tests such as ultrasound or mammograms.

Breast Reconstruction Surgery

Although the number of women with breast cancer choosing breast conservation therapy has been steadily increasing, there are some women who, for medical or personal reasons, choose mastectomy. Some of them also choose to have reconstructive surgery to restore the breast's appearance.

Technical advances in microvascular surgery (reattaching blood vessels) have made free flap procedures an option for breast reconstruction. Recent studies suggest that a new procedure known as skin-sparing mastectomy is as effective as the usual type of modified radical mastectomy for many women. This new procedure offers the advantage of less scar tissue and a reconstructed breast that seems more natural.

For several years, concern over a possible link between breast implants and immune system diseases has discouraged some women from choosing implants as a method of breast reconstruction. Recent studies have thoroughly reviewed this complex issue. Although women should be aware that implants can cause some side effects (such as firm or hard scar tissue formation), they can be assured that women with implants do not have any greater risk for immune system diseases than women who have not had this surgery.

Similarly, the concern that breast implants increase the risk of breast cancer recurrence or formation of new cancers is not supported by current evidence.

Dose Dense Chemotherapy

Recent research has suggested that giving chemotherapy more often (every 2 weeks) at the usual doses may work better in preventing recurrence than the usual schedule (every 3 weeks). Clinical trials are in progress to define the role of dose density in adjuvant therapy. Because of this aggressive schedule, growth factors must be given to prevent low blood counts, a common and serious side effect of chemotherapy.

Monoclonal Antibodies

Antibodies are proteins produced by immune system cells that attach to certain chemicals that the body recognizes as not being part of its own normal tissues. Antibodies help your body resist infections, and even cancer.

Monoclonal antibodies are a special type of antibody that can be mass-produced in laboratories. Trastuzumab is the first monoclonal antibody drug used to treat women with breast cancer. It works by preventing the HER2/neu protein from promoting excessive growth of breast cancer cells and may also help the immune system fight the cancer.

Other monoclonal antibodies that recognize the HER2/neu protein are being tested in clinical trials, as are monoclonal antibodies that block other growth-promoting molecules of breast cancer cells. Monoclonal antibodies that have been designed to guide immune system cells, chemotherapy drugs, or radiation therapy directly to the tumor are also being tested.

Angiogenesis

In order for cancers to grow, blood vessels must develop to nourish the cancer cells. This process is called *angiogenesis*. Looking at angiogenesis in breast cancer specimens can help predict prognosis. Some studies have found that breast cancers surrounded by many new, small blood vessels are likely to be more aggressive. Bevacizumab is an anti-angiogenesis drug that doctors have recently begun using in combination with the chemotherapy drug paclitaxel in patients with metastatic breast cancer.

New drugs are being developed that may be useful in stopping breast cancer growth by preventing new blood vessels from forming. Several of these drugs are being tested in

clinical trials, and studies of new, more potent anti-angiogenesis drugs are expected to begin soon.

Gene-expression Studies and New Breast Cancer Classifications

One of the mysteries of breast cancer is that doctors cannot always accurately predict which women have a higher risk that their cancer will come back. That is why almost every woman, except for those with small tumors, receives some sort of treatment after surgery. To better pick out who will need adjuvant therapy, researchers have looked at many aspects of breast cancers. The best test seems to be one that looks at the genes in breast cancer cells. Scientists have been able to link certain patterns of genes with more aggressive cancers -- those that tend to come back and spread to distant sites. Preliminary studies suggest that some women with favorable patterns might be able to avoid adjuvant therapy after surgery, but most experts feel that more research is needed before this new technology should be used routinely.

Research using sophisticated technology for detecting patterns of gene expression has suggested some new ways of classifying breast cancers. The current types of breast cancer are based on appearance of tumors under a microscope. It appears that a new classification, based on molecular features, may be better able than the current classification to predict prognosis and response to several types of breast cancer treatment. The new research suggests four types of breast cancers:

Luminal A and Luminal B types: The luminal types are estrogen receptor positive, usually low grade, and tend to grow slowly. The gene expression patterns of these cancers are similar to normal cells that line the breast ducts and glands (the lining of a duct or glad is called its

lumen). Luminal A cancers have the best prognosis. Luminal B cancers generally grow somewhat faster than the luminal A cancers and their prognosis is not quite as good.

HER2 type: These cancers have extra amounts of HER2 DNA, RNA, and protein. They usually have a high grade appearance under the microscope. These cancers tend to grow rapidly and have a poor prognosis, although they often can be treated successfully with trastuzumab.

Basal type: These cancers lack estrogen receptors and have normal amounts of HER2. These are high-grade cancers that grow rapidly and have a poor prognosis. This type is common among women with BRCA gene mutations. For reasons that are not well understood, this cancer is particularly common among young African-American women.

Research continues in this area as scientists look for ways to apply new technology to better understand and improve the treatment of breast cancer.

Additional Resources

More Information From Your American Cancer Society

We have selected some related information that may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-ACS-2345.

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Breast Cancer Dictionary (also available in Spanish)

Breast Cancer Early Detection (also available in Spanish)

Breast Cancer Prosthesis and Hair Loss Accessory List

Breast Reconstruction After Mastectomy (also available in Spanish)

Exercises After Breast Surgery (also available in Spanish)

NCCN/ACS Breast Cancer Treatment Guidelines for Patients (also available in Spanish)

Non-cancerous Breast Conditions (also available in Spanish)

Sexuality and Cancer: For the Woman Who Has Cancer and Her Partner (also available in Spanish)

Talking with Your Doctor (also available in Spanish)

Understanding Chemotherapy (also available in Spanish)

Understanding Radiation Therapy (also available in Spanish)

The following books are available from the American Cancer Society. Call us at 1-800-ACS-2345 (1-800-227-2345) to ask about costs or to place your order.

A Breast Cancer Journey: Your Personal Guidebook, Second Edition

Caregiving: A Step-By-Step Resource for Caring for the Person With Cancer at Home

National Organizations and Web Sites*

In addition to the American Cancer Society, other sources of patient information and support include:

National Breast Cancer Coalition
1101 17th Street, NW, Suite 1300
Washington, DC 20036
Telephone: 1-800-622-2838
Internet Address: www.stopbreastcancer.org

National Cancer Institute
Telephone: 1-800-4-CANCER (1-800-422-6237)
Internet Addresses: www.cancer.gov

Susan G. Komen Breast Cancer Foundation
Telephone: 1-800-IM AWARE (1-800-462-9273)

Internet Address: www.komen.org

Y-Me National Breast Cancer Organization
Telephone: 1-800-221-2141, 1-800-986-9505 (Spanish)
Internet Address: www.y-me.org

Centers for Disease Control and Prevention (CDC)
Telephone: 1-800-232-4636
Internet Address: www.cdc.gov

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

The American Cancer Society is happy to address almost any cancer-related topic. If you have any more questions, please call us at 1-800-ACS-2345 at any time, 24 hours a day.

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For additional assistance please contact your American Cancer Society
1 · 800 · ACS·2345 or www.cancer.org