
WHAT IS BREAST CANCER?

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All living cells have the potential to bear offspring by dividing and forming 2 separate cells, then 4, 8, etc. This is called 'cell proliferation'. All cells also have the potential to take on characteristics and functions different from those they originally had. This is called 'cell differentiation'. Normally, how a cell functions and when it divides are well regulated and coordinated with the rest of the body's cells and tissues.

Occasionally, however, a cell can escape the controls that normally regulate it and start to multiply or 'proliferate' wildly.

When this happens, sometimes the cells will form a self-contained mass, or a benign tumor which does not spread. Other times, the new mass of cells will start to invade other tissues. This is what characterizes a cancer. Cancers are recognized by the loss of normal appearance of the cells within them, by the way the mass of cells invades other tissues, and by the ability for clumps of cells to be released which can then travel in the body and form another cancer in another part of the body (metastasis).

"In situ" cancers are collections of cancer-like cells which are not invading other tissues. These sometimes progress to become invasive or spreading cancer, and sometimes do not. It is not known whether they are intermediate between a benign tumour and a cancer, or whether they are a latent form of cancer which needs to be "activated" to grow. Little is known about why they sometimes progress and sometimes do not.

Cancers can be caused by exposure to certain chemicals, either in the air, through the skin, or in a person's food or medicine. How these chemicals act to cause cancer is not well understood. It is known that certain chemicals can cause cancer only after they are broken down by enzymes in the body. It is also known that many cancer causing chemicals are "mutagenic", that is, they cause genetic changes which are thought to influence cells to grow into cancers instead of functioning as they normally should within the body. Radiation has also been shown to cause cancer, and certain viruses have been linked to increasing a person's likelihood of developing certain types of cancer.

Some cancers, but not others, have been found to run in families indicating that a person is genetically predisposed to developing the cancer.

Many types of cancer occur more frequently in one country or one culture than another. Studies of how often they occur after a group immigrates to another country help to show whether certain people are more likely to get the type of cancer because of genetic or environmental reasons. It has been estimated that 80% of cancers are environmentally caused.⁷

One theory of cancer causation is that it is often a 2 stage process. First, a cancer is initiated by a cancer causing substance, probably by changes in the genes of certain cells. Later, another cancer causing substance acts as a promoter, helping the cancer to grow. Certain substances have been found to act only as initiators in animal experiments, others only as promoters. Studies of dietary fat and of normal hormonal levels as causes of cancer are almost always studying them as 'promoters' and not 'initiators' of cancer.

Many cancers have long latency periods. Often a person will not develop observable cancer until 10-30 years after they have been exposed to a cancer causing

substance.

RATES OF BREAST CANCER

Breast cancer is the most common type of cancer affecting North American women. Currently, one in eleven women in North America will get breast cancer at some time in her life.

The incidence of breast cancer has been increasing since the generation of women born around 1900.¹ Between 1969 and 1979 the incidence of breast cancer rose 1% a year.² There has been a particularly steep increase in how many women under 40 are getting breast cancer.

The average age of women who get breast cancer is 60-61. Breast cancer is 100 times more frequent in women than men, but it does also occur in men.

87% of women who have breast cancer with no spread to the lymph nodes in the nearby armpit will survive at least 5 years after their diagnosis of breast cancer.³ 75% will survive at least 10 years.⁴ 56% of women whose cancer has spread to the lymph nodes in the armpit when first detected will survive at least 5 years.⁴ Only 10% of women whose cancer has spread to other organs (metastasis) when first detected will survive 5 years. There has been a slight increase in survival rates from breast cancer in North America, because more breast cancer is being detected at an earlier stage and fewer women have cancer which has spread to other organs when their breast cancer is first discovered. Overall, 55-65% of women with breast cancer survive 5 years after diagnosis.⁵

One study of breast cancer deaths between 1950 and 1973 showed that 40% women with breast cancer die rapidly within 2 years of diagnosis regardless of treatment, and the other 60% have a mortality rate which is very similar to women of the same age without breast cancer. It is not known whether the 60% would have done as well or better without the type of treatment they received — radical mastectomy.⁶

TYPES OF BREAST CANCER

About 80% of women with breast cancer have invasive duct carcinoma. This form of breast cancer starts in the ducts, or passageways, leading from the milk producing lobes to the nipples. Invasive duct carcinoma is most often first felt as a hard irregular lump in the breast.

Types of breast cancer with survival rates that are higher than that of invasive duct carcinoma are:

- mucinous carcinoma of the breast, characterized by a smooth lump full of a jelly-like substance
- medullar carcinoma, which forms an almost spherical lump
- tubular carcinoma, which forms a small irregular lump
- adenoid cystic carcinoma of the breast
- and secretory carcinoma, a rare type of cancer which usually occurs in children and adolescents.

Breast cancers with lower than average survival rates include:

- breast cancers with types of cell growth not usually found in the breast (squamous, osseous or chondroid metaplasia)
- sarcomatoid carcinomas, a type of breast cancer which is usually large when first discovered because of a rapid growth rate, and which has a 35% 5 year survival rate regardless of the stage of its discovery
- and inflammatory carcinoma, which occurs in

2% of women with breast cancer. It is a cancer which attacks the lymphatic system directly, causing the breast to become red and swollen.

About one third of breast cancers are strongly estrogen dependent, (they grow in the presence of estrogen), one third are variably estrogen dependent, and one third are not estrogen dependent.

Women with estrogen dependent cancers can be treated with an estrogen-blocking drug or by removal of the ovaries so that the woman no longer produces estrogen in large amounts, if the breast cancer recurs after it is removed. Tests for growth in the presence of progesterone, or progesterone dependence, are also performed on breast cancers.

STAGES OF BREAST CANCER

Breast cancer has been 'staged' in various ways to describe how far the disease has progressed. The size of the lump, whether and how much spread there is to the lymph nodes under the arm, and whether there is any spread to other organs (metastasis) are indications of breast cancer stage.

The following are two examples of staging systems. The second (TNM classification) is the most commonly used one at present:

Staging Scheme for Breast Cancer

- Stage I: Tumor less than two cm in diameter; nodes clinically negative; no distant metastasis
 Stage II: Tumor less than five cm in diameter; nodes, if palpable, not fixed; no distant metastasis
 Stage III: Tumor greater than five cm, any size tumor that is fixed in place or evidences invasion of the skin or any tumor that is accompanied by nodes other than the axillary nodes that are clinically positive; no distant metastasis
 Stage IV: Tumor of any size accompanied by distant metastasis

TNM Classification for Breast Cancer

T = Tumor size

- TIS: Preinvasive cancer, carcinoma in situ, noninfiltrating intraductal carcinoma or Paget's disease of the nipple with no obvious tumor
 TO: No tumor can be felt
 T1: * Tumor two cm or less
 T1a: Tumor not fixed to underlying pectoral muscles
 T2a: Tumor fixed to underlying pectoral muscles
 T2: * Tumor more than two cm, but less than five cm
 T2a/T2b: Same as above
 T3: * Tumor more than five cm
 T3a/T3b: Same as above
 T4: * Tumor of any size with direct extension to the skin or ribs or underlying muscles other than the pectoral muscles
 T4a: Tumor fixed
 T4b: Swelling, sores or cancerous nodules on the skin of the breast, peau d'orange
 T4c: Both of the above

N = axillary lymph nodes

- NO: No palpable nodes
 N1: Palpable but freely movable nodes
 N1a: Nodes not considered to contain cancer
 N1b: Nodes considered to contain cancer
 N2: Nodes that are considered to contain growths and that are fixed
 N3: Nodes other than axillary nodes considered to contain growths or swelling of the arm

M = distant metastasis

- MO: No evidence of distant metastasis
 M1: Distant metastasis (including skin involvement beyond the breast area)

*Dimpling of the skin, nipple retraction or other skin changes except those noted in T4b may occur in T1, T2, or T3 without changing the classification.

Breast cancer was originally thought to follow a set progression: from the breast, at the first stage, to the lymph nodes under the arm, and later to other organs — usually the bones, liver or lungs.

About 25% of women with small lumps contained entirely in the breast with no spread to the lymph nodes do get recurrences or spread to other organs even if the breast and lymph nodes are entirely removed. Obviously, the disease was present outside of the breast of these women when their breasts were removed. It is now thought that breast cancer affects the whole body early on, constantly shedding clumps of cancerous cells into the bloodstream and lymphatic system. Usually, a woman's immune system will prevent other tumours from being formed outside her breast while her cancer is at an early stage. If the lymph nodes under the arm are cancerous, this is a sign that her immune system is no longer working as well to combat the cancer as if her lymph nodes were free of cancer. Therefore, it is an indication of lower chances for survival.

It takes a breast cancer 3 years to grow to be 1 cm. in diameter at the fastest rate of cancer growth.⁸ Therefore, a woman with a very small tumour has had breast cancer already for a fairly long period of time. This is important for a woman to know if she is concerned about taking several weeks to check out options for treatment in case her cancer spreads during that time. A one centimeter diameter tumour has had plenty of time in the body to shed clumps of cells and possibly spread, yet the 5 year survival rate for women with cancers less than one centimeter in diameter is 95%, presumably because a woman's immune system is able to fight the spread of cancer at that stage.

CANCER RISK:

Within a group of people with the same exposure to a cancer-causing substance, certain people will develop cancer and others will not. Little is known about why some people do not ever develop cancer, with the same exposure to a cancer causing substance as someone who does develop cancer.

There are several theories as to why this may be:

1. The immune system usually is able to destroy abnormal cells before they develop into cancers. Some people's immune systems are better able to do this than others.
2. Differences in rates of metabolism and in hormonal levels can slow or speed both the growth of cancer and the rate at which cancer-causing chemicals are removed from the body.
3. Differences in enzyme levels can affect the way a chemical is broken down into cancer-causing substances or the way cancer-causing substances are broken down into harmless substances.
4. Differences in the diet can affect how a cancer-causing substance is metabolized. For instance certain vitamin deficiencies can make a person more likely to get certain types of cancer.

POSSIBLE CAUSES OF BREAST CANCER:

Dietary Fat:

It is known that the rates of breast cancer vary tremendously in different countries. Women in highly industrialized countries and of higher income levels are much more likely to get breast cancer than women in less industrialized countries or women of lower social class within one country.

There are various theories as to why this is so. The one which is most current is that these differences reflect differences in how much fat (particularly animal fat) is in a woman's diet. Differences in the amount of fat consumed in different countries correlate well with differences in the rate of breast cancer. Japan, for

instance, has a much lower rate of breast cancer than other industrialized countries, and the national diet is low in fat. However, Finland has a high fat diet and does not have a proportionally high breast cancer rate. It has been speculated that this is because in Finland, the diet is high in fat and fibre, while in other countries with a high fat diet, the diet is low in fibre.

Geographic differences in the amount of fat in the diet of different cultures are considered a very crude sort of evidence for a link between fat and breast cancer, as many other aspects of women's environments vary from country to country. There have been some studies of the diets of women who have developed breast cancer within one country compared to women who have not. In some cases these studies are inconclusive, and they may be affected by changes in a woman's eating habits once she learns she has breast cancer. One study in Canada and one in Japan do show a link between fat in the diet and breast cancer, though the design of the studies has been criticized.^{6,10} In one study of the blood levels of metabolized fats of 95,000 women who were followed over a period of time to see who developed breast cancer and who did not, no significant link was seen between blood levels of metabolized fats and breast cancer.¹¹

A study of British nuns in a religious order which ate a low-fat diet did not show any lower breast cancer rates.¹² It has been speculated that the effect of dietary fat earlier in life and in puberty may be more important than the effect in adult women.

Animal studies have shown that when animals were treated with a chemical that caused breast cancer, more animals developed breast cancer if they were on a high fat diet. The relationship was stronger for polyunsaturated vegetable fats than for animal fats, but it occurred for both types of high-fat diets.¹³

The evidence on the relationship of dietary fat, particularly animal fat, to breast cancer is inconclusive and somewhat contradictory. However, it is relatively easy for a woman trying to decrease her risk for breast cancer to limit her consumption of fats. There is certainly evidence that such a step could be helpful. And there is good evidence that a diet high in animal fats is unhealthy in general, because it increases a person's risk for heart disease.

Geographic differences in breast cancer rates in women are most often linked to diets high in animal fats. It is not known whether high fat diets are only more likely to cause cancer if women are also exposed to cancer-causing substances (as in the animal experiments), or if residues of cancer-causing substances which contaminate our environment are concentrated in animal fats. Studies on the relationship of diet to breast cancer have not looked at diet in terms of cancer-causing contaminants in food.

Other theories of how a high fat diet can increase breast cancer risk are that such a diet interferes with a woman's immune response. Diets high in polyunsaturated vegetable fats are used for patients getting kidney transplants, because they are known to help suppress part of a person's immune response. (For a kidney transplant patient, lowered immunity is helpful because it makes it less likely for a new kidney to be rejected.)

Body Hormone Levels:

Another theory of how a high fat diet could make a woman more prone to breast cancer is by changing the levels of hormones in a woman's blood. Prolactin, a hormone released from the pituitary which affects breast development, has been found to exist at higher levels in women on standard North American diets high in meat versus women on low-fat vegetarian diets. Certain animal studies have linked the effects of a high

fat diet on breast cancer to prolactin levels.¹³ Higher prolactin levels have also been linked to a type of infertility, luteal phase deficiency, which may increase a woman's risk of getting breast cancer.¹⁴

The hormone estrogen has also been examined to see if a woman's risk of getting breast cancer is higher if she has more estrogen, or more estrogen without progesterone also present to oppose its effects. The link of luteal phase deficiency to higher breast cancer risk has been discussed in terms of more unopposed estrogen being present. Also, the more body fat a woman has after menopause, the more estrogen she produces. Certain studies have shown a connection between having more body fat after menopause, and being at higher risk for getting breast cancer.⁴ Animal studies which have tried to connect greater breast cancer risk with a high fat diet to the action of estrogen have not been successful.¹³

Hormonal Drugs:

Estrogen replacement therapy for symptoms of menopause has been shown to increase a woman's risk of developing breast cancer.¹⁵ The higher the dose and the longer a woman has been on estrogen replacement therapy, the greater her increased risk. Women who develop benign breast disease while on estrogen replacement therapy have 7 times the risk of developing breast cancer as other women. The link between estrogen replacement therapy and cancer of the endometrium is much stronger than the link to breast cancer. Women must take higher doses of estrogens for longer to increase their risk for breast cancer than for endometrial cancer.

DES (diethylstilbestrol) a synthetic estrogen given to millions of women during pregnancy during the 1940's and 1950's, mostly to prevent miscarriage, has been linked to an increase in risk for breast cancer. A recent study indicates that DES mothers have a risk for breast cancer one and a half times greater than the risk for unexposed women.¹⁶

There are some suggestions that long-term use of birth control pills may increase a woman's risk for breast cancer. Several studies of the effects of the pill have not shown an increased risk. However, breast cancer often has a long latency period (the time between exposure to a cancer-causing substance and developing the cancer). It may be that not enough time had elapsed between when women were first on the pill and when their rates of breast cancer were examined. One study shows eleven times the risk of breast cancer among women with benign breast disease who have been on the pill more than six years.⁴ Another recent study shows that women who used high dose (high progestagen) birth control pills for 4-5 years before they reached the age of 25 have a substantially increased risk for breast cancer as they get older.¹⁷ High dose pills comprise about 10% of birth control pills sold.

Provera (called depo-provera in its injectable form used as a contraceptive) is a progestin, a synthetic form of progesterone, which may be linked to a higher risk for breast cancer based on results on animal studies. The drug is widely available for birth control in third world countries, although it has been banned for use as birth control in North America and in other industrialized countries.

Non-Hormonal Drugs:

The drug reserpine, taken for high blood pressure (hypertension), has been linked in some studies to a higher risk for breast cancer.⁸

Radiation:

Radiation can cause breast cancer. Women exposed to radiation from the atom bomb explosions at Hiroshima and Nagasaki have high rates of breast cancer. This is especially true of women who were adolescents (aged 14 - 19) at the time of the explosions.

Large doses of chest x-rays given as a treatment for tuberculosis have been found to have caused breast cancer in some of the women exposed. Any x-ray to the chest has a potential for increasing a woman's risk for breast cancer. The larger the dose, the greater the increased risk.

Family History:

Women with a family history of breast cancer are more likely to develop the disease. If a woman's mother and sister, or 2 close relatives, have had breast cancer in both breasts before they reached menopause, she has about a 50% chance of developing breast cancer. If a woman has 2 close relatives who develop breast cancer after menopause, her risk of developing the disease is about 16%.⁴ This compares to a 9% average risk for women in North America.

There is some evidence that a woman is at an increased risk, though to a lesser extent, if relatives on her father's side, or if more distant relatives (a grandmother or aunt) have had breast cancer. No gene or chromosome making a person more likely to get breast cancer has been discovered. It is not known whether some of the increased family risk is due to having been exposed to a similar environment and/or to a similar diet, rather than genetics. The link to family history is so strong in breast cancer which develops in both breasts before menopause that this type of cancer is very likely to be genetic.

Over 90% of the women who get breast cancer do not have a family history of breast cancer.⁴

Women of European Jewish background are at a somewhat higher risk for breast cancer than other ethnic groups in North America.

Reproductive History:

Many studies have looked at how many children women with breast cancer have had compared to other women; how young they were when they had their first child; when they first menstruated; and when they reached menopause.

Generally, women who begin to menstruate earlier and reach menopause later are thought to be more likely to develop breast cancer. Women who have had no children, or have had their first child after age 35 are thought to be at higher risk for breast cancer.⁴ In one Japanese study, single women were found to be at higher risk for breast cancer than married women, whether or not the married women had had children.¹⁰

The link of reproductive history to breast cancer risk has been shown to occur in some studies, but not others. In one study from Sweden, no difference was seen in the age at menarche (first menstruation), age at first birth, age at menopause, or number of children of women with breast cancer vs. women without breast cancer.¹⁰ This study differed from others in that the women with breast cancer were compared to women in the general population and not to women in hospital for other reasons. The authors suggest that reproductive history factors may be unrelated to breast cancer risk, but may make it more or less likely for a woman to be hospitalized for other reasons. For instance, women who first became pregnant after age 35 may not be at higher than average risk for breast cancer, but they may be healthier than most women and less likely to be in hospital for another reason. Therefore, it may be poor study design which has shown them to be at high risk for breast cancer.

In the study mentioned above, whether or not a woman had breastfed her children did not seem to change her chances of developing breast cancer. However, it is often unclear whether breastfeeding has an effect apart from the effect of pregnancy.

Women from certain fishing villages in Hong Kong traditionally only breastfed their children from the right breast. Women from these villages who develop breast cancer after menopause are much more likely to develop it in the left (unsucked) breast than the right breast.¹⁹ This relationship does not hold for pre-menopausal breast cancer. It may be that certain types of breast cancer are less likely to occur if a woman has breastfed her children, and others are unaffected.

Hypothyroidism:

A number of studies have been done to look at the link between reduced thyroid function and the development of breast cancer. Results of these studies are inconsistent, although associations have been shown between breast cancer risk and hyperthyroidism, thyroid cancer and Hashimoto's thyroiditis (an auto-immune disease resulting in mild hypothyroidism). The inconsistency of results suggests that an association between thyroid and breast cancer is likely to be indirect. More research needs to be done.²⁰

Benign Breast Disease:

Some studies have shown that women with benign breast disease are more likely to get breast cancer than other women. Other studies show no such link, except for specific conditions thought to be pre-cancerous. These conditions are: ductal hyperplasia, lobular hyperplasia and apocrine metaplasia.

Studies of the pill and estrogen replacement therapy have shown a higher risk of breast cancer for women who develop benign breast disease while taking these drugs.

CONCLUSION

Although breast cancer is quite a common disease, many aspects of the disease are still not well understood. For instance, why conditions thought to be pre-cancerous sometimes progress to breast cancer and sometimes do not is not well understood. Why breast cancer sometimes spreads to other organs very early in its development and sometimes does not is not well understood. Much of the information doctors have on the progress of the later stages of the disease is based only on the experiences of women with radical mastectomies, as that has been the treatment used for all breast cancer patients from the 1930's until recently.

Many different 'risk factors' making a woman more likely to get breast cancer have been investigated. One thing stands out in the research; it is a very incomplete explanation of why certain women get breast cancer and certain women do not.

The large variety in the rates of breast cancer in different parts of the world, and the way the rates of breast cancer in a group of women change if they immigrate to another country, suggest that a large proportion of breast cancer is environmentally caused. An individual woman trying to lessen her risk of getting breast cancer can avoid radiation exposure, avoid hormonal drugs, lower the fat content of her diet, and ensure that she gets enough iodine in her diet for healthy thyroid function. It is not known whether the higher rates of breast cancer in the industrialized countries are caused by environmental pollution by cancer-causing substances. It is also not known whether wealthier women who eat more meat and animal products are getting more breast cancer because cancer-causing chemicals are being concentrated in the meat and milk of animals. Both suggestions are possible, however. Therefore, an individual woman can also try to lessen her risks of getting breast cancer by working to oppose the contamination of the environment with cancer-causing substances.

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