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FACT SHEET #1

Cornell University Program on
Breast Cancer and Environmental Risk Factors
in New York State (BCERF)

Phytoestrogens and the Risk of Breast Cancer

Phytoestrogens are estrogen-like chemicals found in plant foods such as beans, seeds, and grains. Foods made from soybeans have some of the highest levels of phytoestrogens and have been studied the most. In spite of initial optimism, it is not clear whether eating foods rich in phytoestrogens decreases breast cancer risk. This is an active area of research with much work needed to resolve this issue. This fact sheet presents the most current information and indicates where more research would be helpful.

What are phytoestrogens?

Phytoestrogens are a group of chemicals found in plants that can act like the hormone estrogen. Estrogen is a hormone necessary for childbearing and is involved with bone and heart health in women. However, higher exposure to estrogens over a lifetime is linked with increased breast cancer risk. (See BCERF Fact Sheet #10, *What Factors Might Affect a Woman's Exposure to Estrogen*).

What foods contain phytoestrogens?

More than 300 foods have been shown to contain phytoestrogens. Most food phytoestrogens are from one of three chemical classes, the isoflavonoids, the lignans or the coumestans. Isoflavonoid phytoestrogens are found in beans from the legume family; soybeans and soy products are the major dietary source of this type of phytoestrogens. Lignan phytoestrogens are found in high fiber foods such as cereal brans and beans; flaxseeds contain large amounts of lignans. The coumestan phytoestrogens are found in various beans such as split peas, pinto beans, and lima beans; alfalfa and clover sprouts are the foods with the highest amounts of coumestans.

Can phytoestrogens from soy foods affect breast cancer risk?

It is currently unclear whether phytoestrogens from soy foods affect breast cancer risk. Studies looking directly at breast cancer risk and soy in the diet are not in agreement. Almost half of the studies have reported no effect of soy on breast cancer risk. In addition, animal and cellular studies of soy phytoestrogens have generated both enthusiasm and concern. Animal studies have shown that soy phytoestrogens can decrease breast cancer formation in rats. However, animal and human studies suggest that soy phytoestrogens can behave like estrogens and potentially increase breast cancer risk. Some scientists have suggested that women should be cautious about eating large amounts of the soy products or soy supplements, because of the possible harmful effects of soy phytoestrogens. These concerns and areas of research are discussed below in more detail.

How do phytoestrogens act in the body?

There are many different ways that phytoestrogens may work in the body. The chemical structure of phytoestrogens is similar to estrogen, and they may act as mimics (copies) of estrogen. On the other hand, phytoestrogens also have effects that are different from those of estrogen.

Working as estrogen mimics, phytoestrogens may either have the same effects as estrogen or block estrogen's effects. Which effect the phytoestrogen produces can depend on the dose of the phytoestrogen. The phytoestrogen can act like estrogen at low doses but block estrogen at high doses. Estrogen activates a family of proteins called estrogen receptors. Recent studies have shown that phytoestrogens interact more with some members of the estrogen receptor family, but more information is needed about how these receptors work, especially in breast cancer. Finally, phytoestrogens acting as estrogen mimics may affect the production and/or the breakdown of estrogen by the body, as well as the levels of estrogen carried in the bloodstream.

Phytoestrogens - acting differently from estrogens - may affect communication pathways between cells, prevent the formation of blood vessels to tumors or alter processes involved in the processing of DNA for cell multiplication. Which of these effects occur is unknown. It is very possible that more than one of them may be working. Also, the effects in various parts of the body may be different.

What have human studies on soy in the diet and breast cancer risk found?

The results of the case-control human studies of the connection between eating soy products and breast cancer risk are

conflicting. Some studies have reported no link and others have reported a decrease in the risk of breast cancer among women eating soy compared to women who did not eat soy; no studies have reliably demonstrated an increase in the risk of breast cancer among women eating soy. In addition to the conflicting results, there are four problems with these studies. First, the number of studies is small, only ten studies have examined soy in the diet and breast cancer risk. Second, most of the studies examined small numbers of women, only four of the studies included more than 200 patients. Third, all but two of the studies were limited to women from Asia. The effect of soy in Asian women may not best reflect much of the population of Western countries like the US. Women in Asia differ in important ways. Many of them have eaten soy products all their lives and their usual diets contain large amounts of soy products. Also, Asian women have low rates of breast cancer compared to Western women, which may be related to other factors besides soy in their diet. Fourth, most of these studies are limited by their focus on the general diet of women rather than soy products in detail. More carefully controlled studies are needed that examine the effect of soy products on breast cancer risk in women from cultures outside of Asia and more indepth studies are needed of Asian women.

What is the effect of eating soy on women's hormone levels and growth within the breast?

Soy phytoestrogens could change breast cancer risk by changing the production and/or breakdown of reproductive hormones such as estrogen. The results of studies examining hormone changes among women eating soy have not been consistent, but recent studies suggest there may be a small decrease in the levels of estrogens in the body. Some studies have also shown that eating soy phytoestrogens is associated with a decrease in the formation of forms of estrogens that may directly lead to cancer causing mutations.

One of the ways higher estrogen exposure may be linked to breast cancer risk is through its ability to increase growth of milk ducts in the breast. Most breast cancer arises from these ducts. Several but not all studies examining the effect of soy phytoestrogens on breast growth in women have suggested that phytoestrogens have a weak estrogen-like effect. The longest examination followed 28 women for a year. These women received a soy supplement for six months. While they were taking this supplement the women were found to have more growth of the milk ducts in their breasts. These studies are not conclusive, but such growth could increase breast cancer risk. More study is needed to evaluate the possible effects of soy phytoestrogens on growth within the breast and hormone levels in the body.

What are the results of the animal and cellular studies examining soy phytoestrogens and breast cancer?

Animals that were given soy phytoestrogens developed fewer mammary (breast) tumors in many, but not all, studies. The decrease in tumor formation was dependent on the age at which the animals were given the soy. Animals given a soy phytoestrogen before sexual maturity had about half as many tumors as animals given a soy phytoestrogen as adults. A similar effect of the age of treatment was also seen when animals were given a synthetic estrogen or estrogen together with progesterone. More studies are needed to understand this effect of phytoestrogens and of estrogen itself.

Studies of breast cells in tissue culture have shown that soy phytoestrogens can either encourage or discourage growth within the breast. This effect depends on the amount of the soy phytoestrogen the cells are exposed to (See "How do phytoestrogens act in the body?" below). It is unclear if these effects on cells in the laboratory are the same or different from breast cells in the body.

Have other classes of phytoestrogens been examined for their effect on breast cancer risk?

Both lignan (from brans, beans, and seeds) and coumestan phytoestrogens (from beans and sprouts) have been studied for a possible effect on breast cancer risk. Two studies have found higher levels of lignan phytoestrogens in the urine of women who may be at lower risk for breast cancer, such as Japanese women and women eating a macrobiotic diet. Other studies compared women without cancer to women with breast cancer; the women with breast cancer had significantly lower levels of lignan phytoestrogens in their urine. Phytoestrogen levels in urine are an accurate measure of phytoestrogens in the body, but it is uncertain how levels in the women with cancer compare to levels in these women during the decades when cancer was developing.

A lignan phytoestrogen found in flaxseed, secoisolariciresinol diglycoside (SDG) has been shown to interfere with mammary (breast) tumor formation in rats. SDG has similar effects on the development of mammary gland as the soy phytoestrogen genistein. (But see the discussion of potential SDG/flaxseed toxicity in the question on pregnancy and nursing below.)

Coumestans are the least studied phytoestrogens. Treatment of rats with a coumestan phytoestrogen had no effect on mammary (breast) tumor formation but this phytoestrogen has been examined in only one study of this type. Some coumestans have strong interactions with estrogen receptors. This makes them like the strongest estrogens made by the body and suggests that they may also have estrogen-like actions.

Is there any harm in taking phytoestrogen supplements or eating large amounts of foods with phytoestrogens?

Care should be taken in the use of phytoestrogen supplements that may contain phytoestrogens at levels far higher than in food. Since phytoestrogens can have estrogen-like effects in humans, use of these supplements for a long time could increase breast cancer risk.

Moderate consumption of foods high in phytoestrogens is unlikely to have any adverse effects and these foods are generally healthful.

Is there a certain time during a woman's life when eating phytoestrogens can be of the greatest benefit?

One recent study of Chinese women suggests that eating large amounts of soy during adolescence may reduce the risk of breast cancer. Studies in animals have demonstrated that the period of breast development is critical for mammary tumor inhibition by phytoestrogens. It is currently unclear if the results in Chinese women reflect a similar critical period or a lifetime of eating soy products.

Human epidemiological studies suggest that if breast cancer risk reduction is linked to eating soy phytoestrogens, the effect may be greater on premenopausal breast cancer. More studies are needed to determine if soy phytoestrogen and other phytoestrogens act largely on premenopausal breast cancer and whether the effectiveness of phytoestrogens is related to the period of life when they are eaten.

Should breast cancer survivors eat more phytoestrogens?

No studies have examined the health effects of eating phytoestrogens among breast cancer survivors. Drugs or chemicals that cause growth of breast tissue are generally not recommended for breast cancer survivors. Phytoestrogen supplements have been shown to cause growth of breast tissue in animals and healthy women.

No human studies have assessed the effects of combining tamoxifen (an anti-estrogenic drug prescribed for many breast cancer survivors and some women at high risk for breast cancer) and phytoestrogens in breast cancer survivors. Women taking tamoxifen are usually not included in studies where concentrated supplements of phytoestrogens are given. Studies examining the actions of tamoxifen and genistein in the laboratory using isolated breast cancer cells have produced conflicting results. In some studies the two chemicals acted together, and in others their effects were opposing. More studies are needed to understand potential favorable or conflicting actions between these two chemicals.

Should I eat more phytoestrogens if I am taking estrogen for treatments such as birth control or postmenopausal hormone therapy?

The effects of phytoestrogens on women taking birth control pills or being treated with postmenopausal hormonal therapy have not been examined. Both of these treatments use estrogen, and since phytoestrogens can act like the hormone estrogen, phytoestrogens might disrupt or amplify the effect of the estrogen in individuals with a diet very high in phytoestrogens. However, such effects have not been reported in groups of women who have diets high in phytoestrogens.

Should infants and young children eat phytoestrogens?

The regulatory bodies of several countries, including Great Britain, Switzerland, Australia, and New Zealand, have suggested that soy infant formulas be used only in children who are not breast fed and are definitely intolerant to cow's milk. Soy formulas contain much higher amounts of phytoestrogens than is seen in human breast milk. In addition, infants fed soy formula have blood levels of phytoestrogens that are far greater than normal levels of estrogen in infants. No studies have examined the health effects of children eating phytoestrogen-rich foods. Long-term studies that look at the health benefits and risks of soy-based infant formulas and eating phytoestrogen-rich foods as a child are needed.

Should I eat phytoestrogens if I am pregnant or breast-feeding?

Pregnant or breast-feeding women should not use phytoestrogen supplements or consume substantial amounts of flaxseeds on a regular basis. In animal studies, the phytoestrogens found in high amounts in flaxseeds have been shown to cause developmental abnormalities and some studies of soy phytoestrogens have shown a possible increase in susceptibility to cancer in offspring. Eating moderate amounts of soy or flax products should present no problem. Women in China and Japan regularly eat foods containing soy phytoestrogens during pregnancy and while breast-feeding and no adverse health affects have been reported in these countries.

Do phytoestrogens have other health benefits?

Phytoestrogens are actively being researched for beneficial effects on cardiovascular and bone health. Studies are also examining various phytoestrogens for relieving some of the symptoms associated with menopause.

What can women do now?

It is unclear what role foods containing phytoestrogens play in decreasing breast cancer risk. Women can help themselves stay healthy by eating plenty of fruits, vegetables, whole grains, and beans and by getting plenty of exercise and maintaining a healthy weight.

What scientific studies need to be done?

The following aspects of phytoestrogens especially need further study:

- Effects of phytoestrogens, especially from soy, on breast cancer risk in humans
- Actions of soy phytoestrogens on breast development in humans
- Health effects of soy phytoestrogens on individuals who used soy formula as an infant
- Consequences of phytoestrogens on breast cancer survival

An extensive bibliography on "Phytoestrogens and the Risk of Breast Cancer" is available on the BCERF web site: http://www.cfe.cornell.edu/bcerf/

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