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# The Soy Connection

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## 2005 U.S. Dietary Guidelines Review

By Patricia Samour, M.M.Sc., R.D., L.D.N. and Jeanene Fogli, M.S., R.D., L.D.N.

In January, the Secretaries of Agriculture and Health and Human Services (HHS) released the 2005 Dietary Guidelines for Americans (DGs). These guidelines set the nation's policy direction for the next five years for all government nutrition programs, including nutrition research, education, food assistance, labeling and nutrition promotion.

The DGs for Americans provide valuable and realistic recommendations based on the latest scientific research to help people eat well and stay healthy. The revised DGs include 41 recommendations, grouped under the nine inter-related focus areas listed below. Twenty-three of the recommendations are intended for the general public and 18 are for specific populations such as children, the elderly and pregnant women. The DGs emphasize that the nutrient needs of individuals should be met primarily through food consumption, and the recommendations focus on foods in the context of the total diet as the primary route to wellness.

*(Continued on Page 5)*

## In This Issue:

- Women and Cancer
- Dietary Guidelines
- Breast Cancer Screening
- Gallstone Risk

## HEALTH AND NUTRITION NEWS ABOUT SOY

# Soy Isoflavone Intake and the Risk of Breast and Endometrial Cancers

By Mark Messina, Ph.D.

## Introduction

The anticancer effects of soy have been rigorously investigated for the past 15 years, ever since the National Cancer Institute first organized a workshop on this subject.<sup>1</sup> Most of the focus has been on breast and prostate cancers in part because of the very low incidence rates of these cancers in Asia.<sup>2</sup> There are several putative anticarcinogens in the soybean, but unarguably, the isoflavones have received the most attention. Isoflavones have both hormonal and non-hormonal properties that are relevant to cancer prevention and treatment.<sup>3,4</sup>

In regard to breast cancer, one of the more intriguing hypotheses is that isoflavone intake during adolescence markedly reduces breast cancer risk later in life. There is both animal and epidemiologic support for this hypothesis.<sup>4</sup> Furthermore, it is consistent with the considerable data highlighting the important influence of early life events on breast cancer risk.<sup>5</sup>

However, concerns have also been expressed that the estrogen-like effects of isoflavones may increase the risk of developing hormone-related cancers in some women.<sup>6,7</sup> In particular, there is concern that isoflavones, and soyfoods, may increase risk of breast cancer in women at high-risk of this disease and/or stimulate the growth of secondary tumors in breast cancer patients. More recently, the relationship between soy intake and endometrial cancer has received attention because of research suggesting both possible benefit and harm.

This article briefly reviews the relationship between soy intake and risk of breast and endometrial cancers, including relevant research published within the past two years.

## Breast Cancer

The theoretical basis for concern that isoflavones stimulate breast cancer risk is easily understandable. Isoflavones bind to estrogen receptors<sup>8</sup> and exert estrogen-like effects under some experimental conditions, and lifelong estrogen exposure is acknowledged as playing an important role in the etiology of breast cancer.<sup>9</sup>

However, the role of estrogen therapy in postmenopausal breast cancer risk is less clear. Recent evidence suggests that the combination of estrogen plus progestin, much more so than estrogen alone, increases breast cancer risk.<sup>7,10,11</sup> These data are relevant because neither soyfoods nor isoflavones exert progestin-like effects.<sup>12</sup> Furthermore, considerable research shows that isoflavones differ from estrogen in important ways; in fact, the estrogen-like effects of isoflavones are often not evident in pre- or postmenopausal women.<sup>13</sup> Thus, on two counts, the phytoestrogenic nature of isoflavones is not grounds for concluding that soy intake raises risk of breast cancer. Nevertheless, some research does suggest that isoflavones may increase breast cancer risk.

For example, two preliminary studies in women suggested that soy

*(Continued on Page 2)*



USB Focus on

Breast Cancer

exerted estrogenic effects on breast tissue. In one, isolated soy protein had a stimulatory effect on the premenopausal female breast, characterized by increased secretion of breast fluid and the appearance of hyperplastic epithelial cells.<sup>14</sup> A major limitation of this study is the lack of a control group; furthermore, even after discontinuation of the soy diet, breast fluid secretion continued to increase. But in agreement with this study, a two-week trial also in premenopausal women, found that soy consumption affected two gene products (increased pS2 and decreased apo-D levels) in a manner similar to that affected by estrogen.<sup>15</sup> However, the authors of this study concluded that the implications of these findings were unclear because of the short duration of the study and because breast cell proliferation was not increased.

More importantly, in contrast to these two studies, two long-term trials, one conducted in pre-<sup>16</sup> and the other in postmenopausal<sup>17</sup> women, failed to show that soy or isoflavones increased breast tissue density. Breast tissue density, which can be assessed via a mammogram, is regarded as a good non-invasive marker of breast cancer risk. Factors that increase breast cancer risk, such as combined (especially estrogen plus progestin) hormone therapy, increase breast tissue density whereas those that decrease it, such as tamoxifen, decrease risk.<sup>18</sup>

In the premenopausal study, over a two-year period women consumed either their usual diet or this diet plus two servings of soyfoods daily, which provided approximately 50 mg isoflavones.<sup>16</sup> In the postmenopausal study, women were randomized to either the placebo group or a group given 43 mg isoflavones daily in supplement form.<sup>17</sup> These studies are noteworthy because of their long duration and the endpoint being a fairly well-accepted marker of breast cancer risk. These studies concur with a three-year study in postmenopausal monkeys, which

found that in contrast to conjugated equine estrogens, isoflavone-rich soy protein did not increase mammary cell proliferation.<sup>19</sup>

Unquestionably, much of the concern about the effect of isoflavones on breast cancer risk is based on animal research from the University of Illinois. This research has shown that in athymic ovariectomized mice implanted with MCF-7 cells (estrogen receptor positive breast cancer cells), isolated soy protein<sup>20</sup> and genistin<sup>21</sup> stimulate tumor growth. Conversely however, a similar animal model to this produces exactly opposite results; i.e., soy isoflavones inhibit tumor growth.<sup>22</sup> In this model, the ovaries are not removed and the mice are implanted with an estrogen pellet.

The question therefore arises as to which animal model best reflects conditions in either pre- or postmenopausal women. Of course, all animal models, regardless of the species involved, have their limitations and should not be used as the sole basis for making predictions in humans. This having been said, the model in which isoflavones inhibit tumor growth seems to be a better fit, although experts disagree on this point.

In ovariectomized mice, tumors do not grow unless the animals are exposed to a source of estrogen or estrogen-like activity. However, even in postmenopausal women not on hormone therapy, despite reduced serum estrogen levels, tumors grow quite well. Therefore, these two contrasting rodent models suggest that isoflavones stimulate tumor growth

in mice only in an estrogen environment that does not appear to exist in young or old women, whereas they inhibit tumor growth in an environment that may.

In conclusion, recently published data suggest that neither soy nor isoflavones increase breast cancer risk. However, definitive data are not available, so the impact of both soy and isoflavones on breast cancer risk remains controversial. Additional insight may be gained by examining the relationship between soy/isoflavone intake and survival among Japanese breast cancer patients. But the ideal study would be a randomized controlled trial in which the effects of soyfoods/ isoflavones on tumor recurrence in breast cancer patients were evaluated. Ethical concerns may prohibit such a study from being conducted.

Until definitive data are available, any decision about soy or isoflavone consumption by women at high risk of breast cancer or breast cancer patients should be made in consultation with the appropriate health care provider.

## Endometrial Cancer

There has been relatively little investigation of the relationship between soyfoods and risk of endometrial cancer, which is somewhat surprising considering how common endometrial cancer is and that estrogen is clearly an important risk factor for this disease. In the United States, cancer of the endometrium is the most common cancer of the female reproductive

*(Continued on Page 3)*

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# Breast and Endometrial Cancers

(Continued from Page 2)

organs. The American Cancer Society (ACS) estimates there were about 40,000 new cases of cancer of the uterine corpus (body of the uterus) diagnosed in 2004. Most of these cancers occur in the endometrium or lining of the uterus. The ACS also estimates that last year about 7,000 American women died from cancers of the uterine body.

Evidence overwhelmingly indicates the hormone estrogen plays a role in the etiology of endometrial cancer.<sup>9</sup> This conclusion is based on several observations, including the enhanced rate of endometrial cell proliferation during the follicular phase of the menstrual cycle when estrogen levels are high (and progesterone levels are low) and that women who have used estrogen replacement therapy are much more likely to develop endometrial cancer than women who have never used estrogen replacement therapy.<sup>23</sup>

Interestingly, in contrast to the effects on the breast where the addition of progestin to estrogen greatly increases cancer risk compared to estrogen alone, progestin greatly inhibits the carcinogenic effect of estrogen on the endometrium.<sup>23, 24</sup>

Because of the role of estrogen in endometrial cancer, many of the soy and isoflavone clinical trials examining different health outcomes have included effects on endometrial tissue.<sup>9</sup> These trials overwhelmingly indicate that unlike estrogen, isoflavones do not stimulate endometrial tissue proliferation.<sup>25-29</sup> However, a recent trial from Italy found that isoflavones very slightly increased the risk of simple endometrial hyperplasia.<sup>30</sup> Importantly, none of the women in this study developed atypical hyperplasia, which does often develop into cancer. There is debate about whether simple endometrial hyperplasia should be classified as a pre-cancerous condition because it so very rarely pro-

gresses to cancer, but these findings showed that isoflavones exerted a very mild estrogen-like effect in some women.<sup>31</sup>

Ordinarily, findings from one clinical study would not raise concern when they contrast with an extensive amount of research, but the Italian study was five years in duration, whereas all of the other relevant studies were conducted for less than one year. Thus, the Italian findings can not be dismissed. However, it is important to recognize that only five women out of 154 developed hyperplasia. None of the women in the placebo group did, which is a bit unexpected. If even two women had, the difference between the isoflavone and placebo groups would not likely have been statistically significant. Furthermore, there is evidence suggesting that neither soy nor isoflavones increase endometrial cancer risk; in fact, there are data suggesting the opposite.

For example, endometrial cancer rates in Asia are low relative to the West, and when Asians migrate to the high risk countries such as the United States, their risk increases.<sup>32</sup> More importantly, of the four case-control studies to examine the relation between soy intake and endometrial cancer risk, one found no association<sup>33</sup> and the other three found an inverse relationship.<sup>34-36</sup> The most recent study involved 832 cases aged 30-69 years and 846 age-matched controls located in the urban area of Shanghai, China.<sup>35</sup> Dietary information for the past five years prior to diagnosis or selection was collected through the use of a food frequency questionnaire. After adjustment for a host of factors the first quartile through fourth quartile odds ratios for soy protein intake were 1.00, 0.91, 0.85, and 0.67 ( $p$  for trend = 0.02), respectively.

One caveat of the epidemiologic data is that the results may reflect lifelong intake whereas the

intervention studies represent acute or recent consumption. This having been said, findings from a recently conducted rat study support the epidemiologic data. In this study, isoflavones appeared to inhibit atypical hyperplasia from progressing to endometrial cancer.<sup>37</sup>

In conclusion, findings from a five-year study showing that isoflavones slightly increase simple endometrial hyperplasia are noteworthy, but overall, most evidence points in the direction of soy either having no effect on or reducing risk of endometrial cancer. But at this point, the evidence in both directions is too speculative for this area of research to form a basis for a decision about consuming soyfoods.

## REFERENCES

*Complete references for this article can be found on page 7.* ☺

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# The Latest on Breast Cancer Screening and Prevention

By Guy Johnson, Ph.D.

F.Y.D.  
From Your Dietitian

**B**reast cancer trails only lung cancer as the most prevalent form of this disease in the United States.<sup>1</sup> More than 41,000 U.S. women died of breast cancer in 2001 and the National Cancer Institute (NCI) estimates that 13.4 percent of women born today will be diagnosed with the disease at some time in their lives.<sup>2</sup> The most recent recommendations for prevention and early detection of breast cancer include screening by mammography and other techniques, as well as lifestyle modifications.

## Mammography

Several large studies have suggested that annual mammograms in women with no symptoms of breast cancer can substantially reduce the number of deaths from this disease.<sup>3</sup> Based on this information, the American Cancer Society (ACS)<sup>4</sup> and the NCI<sup>5</sup> recommend annual or semi-annual mammograms beginning at age 40. However, these recommendations have been challenged on the basis of a more comprehensive review of the evidence.<sup>6,7</sup> The two most rigorously conducted studies did not show that women who received regular mammograms experienced fewer deaths due to breast cancer (or any other cause) compared to women who did not receive such screening. In addition, aggressive treatments such as mastectomy were about 20 percent more frequent among women given yearly mammograms. However, both the ACS and the NCI have carefully reviewed this criticism and continue to believe that regular mammograms are beneficial, especially for women aged 50-59.<sup>8,9</sup> The ACS' current breast cancer screening recommendations<sup>4</sup> include both mammography and clinical examination. (See *Table 1*.)

Table 1

## ACS Breast Cancer Screening Recommendations

- Yearly mammograms starting at age 40 and continuing for as long as a woman is in good health.
- Clinical breast exams (CBE) should be part of a periodic health exam, about every three years for women in their 20s and 30s and every year for women 40 and over.
- Women should report any breast change promptly to their health care providers. Breast self-exam (BSE) is an option for women starting in their 20s.
- Women at increased risk (e.g., family history, genetic tendency, past breast cancer) should talk with their doctors about the benefits and limitations of starting mammography screening earlier, having additional tests (e.g., breast ultrasound or MRI), or having more frequent exams.

## Dietary and Physical Activity Recommendations

Lifestyle factors including nutrition and physical activity are associated with the incidence of certain cancers. Risk factors for breast cancer include obesity, sedentary behavior pattern and excess consumption of alcohol. Dietary fat may also be associated with increased risk of breast cancer, but the evidence is not as clearly established.

See *Table 2* for nutrition and physical activity guidelines recommended by the ACS<sup>10</sup> to help reduce the risk of all forms of cancer:

## Screenings Are Important

Breast cancer screening should be an important part of a comprehensive health maintenance strategy developed in conjunction with your health care professional(s) and based on medical history and lifestyle preferences.

## REFERENCES

*Complete references for this article can be found on page 8.* 🍌

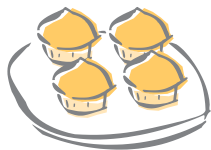
Table 2

## ACS Nutrition and Physical Activity Guidelines

- Eat a variety of healthful foods with an emphasis on plant sources.
- Eat five or more servings of a variety of vegetables and fruits each day.<sup>11</sup>
- Choose whole grains in preference to processed (refined) grains and sugars.
- Limit consumption of red meats, especially those high in fat and processed.
- Choose foods that help maintain a healthful weight.
- Adopt a physically active lifestyle.
- If you drink alcoholic beverages, limit consumption.

# Looking for Tasty Soy Recipes?

The United Soybean Board is offering complimentary copies of its “Great Health, Great Taste EVERYDAY” CD-ROM. It’s packed with recipes to help you make delicious homecooked meals with soy, plus quick cooking tips to help incorporate soy into your existing recipes.



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## Dietary Guidelines *(Continued from Page 1)*

The nine focus areas are:

- Adequate Nutrient Needs within Calorie Needs
- Weight Management
- Physical Activity
- Food Groups to Encourage
- Fats
- Carbohydrates
- Sodium and Potassium
- Alcoholic Beverages
- Food Safety

Key recommendations for the general public for five of these nine focus areas are listed below. Soyfoods can easily and healthfully be part of the American diet that will help meet these new DGs.

### ■ ADEQUATE NUTRIENTS Key Recommendations

- Consume a variety of nutrient-dense foods and beverages within and among the basic food groups while choosing foods that limit the intake of saturated and *trans* fats, cholesterol, added sugars, salt and alcohol.

- Meet recommended intakes within energy needs by adopting a balanced eating pattern, such as the USDA Food Guide or the Dietary Approaches to Stop Hypertension (DASH) Eating Plan.

*Authors' Note: Soyfoods are included in the milk, meat and beans, vegetable (legumes), carbohydrates and oils food groups for both the USDA Food Guide and the DASH Eating Plan.*

### ■ WEIGHT MANAGEMENT Key Recommendations

- To maintain body weight in a healthy range, balance calories

from foods and beverages with calories expended.

- To prevent gradual weight gain over time, make small decreases in food and beverage calories and increase physical activity.

*Authors' Note: Soyfoods such as soy protein isolate, tofu, edamame and soynuts are good choices for protein and good fats, and many may help lower an individual's serum cholesterol.*

### ■ ENCOURAGED GROUPS Key Recommendations

- Consume a sufficient amount of fruits and vegetables while staying within energy needs. Two cups of fruit and 2 1/2 cups of vegetables per day are recommended for a reference 2,000-calorie intake, with higher or lower amounts depending on the calorie level.

- Choose a variety of fruits and vegetables each day. In particular, select from all five vegetable subgroups (dark green, orange, legumes, starchy vegetables, and other vegetables) several times a week.

- Consume 3 or more ounce-equivalents of whole-grain products per day, with the rest of the recommended grains coming from enriched or whole-grain products. In general, at least half the grains should come from whole grains.

- Consume 3 cups per day of fat-free or low-fat milk or equivalent milk products.

*Authors' Note: Use non-dairy sources of calcium such as*

*calcium-fortified soy beverage, soybeans or calcium-set tofu to meet the needs of the milk group.*

### ■ FATS Key Recommendations

- Consume less than 10 percent of calories from saturated fatty acids and less than 300 mg/day of cholesterol, and keep *trans* fatty acid consumption as low as possible.

- Keep total fat intake between 20 to 35 percent of calories, with most fats coming from sources of polyunsaturated and monounsaturated fatty acids, such as fish, nuts and vegetable oils.

- When selecting and preparing meat, poultry, dry beans, and milk or milk products, make choices that are lean, low-fat, or fat-free.

- Limit intake of fats and oils high in saturated and/or *trans* fatty acids, and choose products low in such fats and oils.

*Authors' Note: Use soybean (vegetable) oil in cooking or in salad dressings. Watch for the new low linolenic acid soybeans which will soon be available and will bring healthier soybean oil products to the table.*

### ■ CARBOHYDRATES Key Recommendations

- Choose fiber-rich fruits, vegetables and whole grains often.

- Choose and prepare foods and beverages with little added sugars or caloric sweeteners, such

*(Continued on Page 6)*



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## Unsaturated Fats May Reduce Gallstone Risk

A study published last fall in the *Annals of Internal Medicine* found that men who ate the most unsaturated fat were about one-fifth less likely to develop gallstones compared with men who ate the least unsaturated fat.<sup>1</sup> Sources of unsaturated fat in the diet include soybean oil, nuts, and fish, like salmon and tuna.

Gallstones form when changes in bile, a fluid produced by the liver to help digest food, cause the bile to crystallize and form gallstones. About 80 percent of gallstones are formed mainly from hardened cholesterol.<sup>2</sup> Gallstones are common, affecting 10-15 percent of the U.S. population.<sup>3</sup>

The study tracked the eating

habits of 45,756 U.S. men, age 40-75 years, for up to 14 years. All worked as health professionals, and none had suffered from gallstones or gallbladder disease at the start of the study. Participants completed a questionnaire every two years that provided informa-

### Soybean Oil

tion on their general health, dietary intake, and their incidence of gallstones or gallbladder disease. Those in the highest one-fifth of unsaturated fat consumption had an 18 percent lower risk of

gallstones than participants in the lowest one-fifth.

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## Dietary Guidelines (Continued from Page 5)

as amounts suggested by the USDA Food Guide and the DASH Eating Plan.

- Reduce the incidence of dental cavities by practicing good oral hygiene and consuming sugar- and starch-containing foods and beverages less frequently.

*Authors' Note: Soy products such as miso, tofu, edamame and*

*soy protein isolate are examples of lean, low-fat or fat-free protein sources. Miso and edamame are also good sources of fiber.*

The 2005 Dietary Guidelines executive summary, main document and consumer brochure can be accessed at: [www.healthierus.gov/dietaryguide/lines](http://www.healthierus.gov/dietaryguide/lines).

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- 11) Note: The 2005 Dietary Guidelines for Americans recommend nine servings of vegetables and fruits a day.