

ALTERNATIVE THERAPIES IN WOMEN'S HEALTH

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INSIDE

What constitutes a diet low in saturated fat
page 51

Table: Comparison of high-fat and low-fat foods
page 52

Can a cup of green tea keep the doctor away?
page 53

More than one-third of Americans use CAM, says government survey
page 55

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The Role of Fat Intake in Breast Cancer

*By Lynn Keegan, RN, PhD, HNC, FAAN,
and Gerald T. Keegan, MD, FACS*

BREAST CANCER IS THE SECOND MOST COMMON CANCER IN THE world and the most common cancer in women. Incidence rates are about five times higher in western countries than in developing countries and Japan.¹ International and regional variation may be related to reproductive risk factors, such as age at menarche, parity and age at birth, and breastfeeding,^{2,3} but differences in dietary habits and physical activity also might be contributing factors. Multiple studies have suggested that obesity increases risk of breast cancer in postmenopausal women by around 50%. Peculiarly, although obesity in postmenopausal women has been found to increase risk of breast cancer, the opposite has been found in premenopausal women where obesity is associated with a moderate risk reduction.

The question as to whether high fat intake increases the risk of breast cancer has been quite controversial and the results have been conflicting. Some studies have even suggested that there is no causative link between fat intake and the development of breast cancer.⁴ The converse hypothesis—that low fat intake is associated with a lower breast cancer risk—has been demonstrated recently, but in this study dietary fat alone was not the sole determinant, since it was found that the combination of high fiber and low fat had the lowest risk.⁵ A diet containing more than 30% of the total calories from fat could be considered a high-fat diet. Different methods of assessing fat intake have further confused the data.⁶ The emerging information seems to suggest that saturated fat found in butter, high-fat milk, and meat, and fat used as a food additive rather than fats in general may be the offending culprit.⁷

Mechanisms of Action

Hormonal mechanisms as well as genetic and environmental factors play key roles in the etiology of breast cancer. One commonly proposed mechanism of action is related to the increased serum concentrations of free estradiol.³ Other hormonal factors,

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including insulin-like growth factors (IGF-1) and insulin itself, may be interacting causative factors in the development of breast cancer. Although dietary fat has not been shown conclusively to change the levels of circulating estrogens,⁸ obese women with more adipose tissue have more aromatase, a substance that catalyses the conversion of androgens to estrogens. This conversion becomes the main source of endogenous estrogens in postmenopausal women.⁹ Although not directly related, the combination of excess energy intake secondary to consumption of foods with a high glycemic index and low physical activity may lead to insulin resistance and hyperinsulinemia. Hyperinsulinemia can increase the risk of breast and other cancers due to the mitogenic effects of insulin.^{10,11}

A difficulty with many studies is that the mechanism of action of fat intake on breast cancer is likely to be different in premenopausal vs. postmenopausal women. Studies on the relationship of body mass to the risk of breast cancer are complex and show opposing effects of a high basic metabolic index on premenopausal and postmenopausal risk.^{12,13} Studies actually have shown a U-shaped relationship between relative

weight in adolescence and later risk of breast cancer. Women who were either much heavier or much thinner than average were at reduced risk.¹⁴ Multiple reasons could be suggested for this variance including the common element of delayed menarche as well as completely different mechanisms producing the protective effect.¹⁵

Clinical Trials—Animal Studies

In experimental animals, restriction of caloric intake has been a very effective tool in reducing spontaneous tumor recurrence. Reduced caloric intake in general, not necessarily just fat restriction, is accompanied by lower levels of circulating insulin, IGF-I and II, and epidermal growth factor. In addition, with the caloric restriction there is modification of the cellular responsiveness to estrogens, enhancement of the immunologic response, lower rates of cell proliferation, increased DNA repair, reduced expression of oncogenes, and enhanced expression of the tumor suppressive genes.¹⁵⁻¹⁷ Theoretically, the modification of these factors could contribute to a lower incidence of breast cancer. The evidence, however, for the role of fat intake and changes in the risk of breast cancer does not stand up to close scrutiny.

A study in Hong Kong using a Noble rat model of sex-hormone-induced cancer to examine the effect of a high-fat diet on the incidence and latency of prostate and mammary cancers in male and female animals found a very high incidence of hormone-induced cancers of both prostate and mammary gland, irrespective of diet.¹⁸ Alpha-tocopherol levels also were measured in female breast tissue to determine whether a high intake of polyunsaturated fatty acids depleted the antioxidant defense in target tissues, possibly suggesting a potentiating mechanism for carcinogenesis. The authors concluded that not only was there was no significant association between fat intake and the development of either prostate or breast cancer, but breast alpha-tocopherol was unaffected by dietary fat. The results did not support a role for dietary fat in promoting sex-hormone-induced prostate or mammary carcinogenesis.

Clinical Trials—Human Studies

Human studies are far less definitive in their conclusions. Many studies are impaired by not making a differentiation between saturated and unsaturated fats.

Currently the best data come from the European Prospective Investigation of Cancer and Nutrition Norfolk study, which tried to make this distinction by using a detailed analysis of food diaries in more than 1,300 women.⁶ The researchers concluded that women who

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consumed more than 90 g/d of fat had twice the risk of breast cancer of those who had eaten less than 40 g/d. Data from a segment of the Nurses' Health Study from 1991 to 1999 based on questionnaires on dietary habits concluded a significant premenopausal risk from the intake of animal and dairy products.⁷ The study found no relationship between breast cancer risk and the amount of vegetable fat intake.

A recently published comprehensive statistical analysis on the relationship of caloric restriction and breast cancer in women hospitalized for anorexia nervosa

concluded that severe caloric restriction in humans conferred protection from invasive breast cancer.¹⁵ Low caloric intake prior to first birth followed by subsequent pregnancy appeared to be associated with an even more pronounced reduction in risk. This study confirmed an earlier finding in prepubertal girls who were exposed to the Norwegian famine in World War II, who consumed 22% fewer calories, and who subsequently were found to have a lower rate of breast cancer than women from earlier or later birth cohorts.¹⁹ Although low caloric intake may correlate with low fat intake, the presumed

What Constitutes a Diet Low in Saturated Fat

By Lynn Keegan, RN, PhD, HNC, FAAN,
and Gerald T. Keegan, MD, FACS

EXPERTS RECOMMEND A DIET THAT PROVIDES NO MORE than 30% of total calories from fat. For example, at 2,000 calories per day, the suggested upper limit of calories from fat is about 600 calories. Sixty-five grams of fat contribute about 600 calories (65 g of fat x 9 calories/g = about 600 calories). On the U.S. Food and Drug Administration Nutrition Facts Label, 65 g of fat is the Daily Value for a 2,000-calorie intake.

Some foods and food groups in the U.S. Department of Agriculture Food Guide Pyramid are higher in fat than others. Fats, oils, and some types of desserts and snack foods that contain fat provide calories but few nutrients. Many foods in the milk group and in the meat and beans group (which includes eggs, nuts, meat, poultry, and fish) also are high in fat, as are some processed foods in the grain group. Choosing lower fat options among these foods allows one to eat the recommended servings from these groups and increase the amount and variety of grain products, fruits, and vegetables in the diet without going over calorie needs.

Fats contain both saturated and unsaturated (monounsaturated and polyunsaturated) fatty acids. Saturated fat raises blood cholesterol more than other forms of fat. Reducing saturated fat to less than 10% of calories will help lower blood cholesterol. The fats from meat, milk, and milk products are the main sources of saturated fats in most diets. Many bakery products also are sources of saturated fats. Vegetable oils supply smaller amounts of saturated fat. On the Nutrition Facts Label, 20 g of saturated fat (9% of caloric intake) is the Daily Value for a 2,000-calorie diet.

Monounsaturated and Polyunsaturated Fat

Olive and canola oils are particularly high in monounsaturated fats; most other vegetable oils, nuts, and high-fat fish are good sources of polyunsaturated fats. Both kinds of unsaturated fats reduce blood cholesterol when they replace saturated fats in the diet. The fats in most fish are low in saturated fatty acids and contain a certain type of polyunsaturated fatty acid (omega-3) that is under study because of a possible association with a decreased risk for heart disease in certain people. Mono- and polyunsaturated fat sources should replace saturated fats within this limit.

Partially hydrogenated vegetable oils, such as those used in many margarines and shortenings, contain a particular form of unsaturated fat known as trans-fatty acids that may raise blood cholesterol levels, although not as much as saturated fat.

To reduce intake of fat, saturated fat, and cholesterol, follow these recommendations.

- Use fats and oils sparingly.
- Refer to the Nutrition Facts Label to choose foods lower in fat, saturated fat, and cholesterol.
- Eat plenty of grain products, vegetables, and fruits.
- Choose low-fat milk products, lean meats, fish, poultry, beans, and peas to get essential nutrients without substantially increasing calorie and saturated fat intakes.

Low-Calorie Alternative Foods

Low-calorie alternatives provide new ideas for old favorites. When making food choices, remember to consider vitamins and minerals. Some foods provide most of their calories from sugar and fat but provide few, if any, vitamins and minerals. Table I is a brief example of how to choose lower fat foods. Remember to read labels to find out just how many calories and fats are in specific products. ❖

positive correlation does not necessarily indicate causality.

Conclusion

The relationship of fat intake to breast cancer is not fully established either in terms of demographics or mechanisms of action. The best current studies suggest that saturated fats from red meat and dairy products are related to an increased risk of breast cancer. No clear evidence incriminates vegetable fat intake in increased risk. Multiple other factors play significant interactive roles.

Recommendations

Health professionals should advise their patients of the importance of maintaining a low fat, low-glycemic index diet. Patients need to be reminded of the importance of fiber intake and regular physical exercise. Patients with a family history of breast cancer need to continue to have regular examinations and routine mammograms. ❖

Table 1 Comparison of high-fat and low-fat foods	
Higher Fat Foods	Lower Fat Foods
<i>Dairy Products</i>	
Evaporated whole milk	Evaporated fat-free skim milk
Whole milk	Low- or reduced-fat milk
Sour cream	Plain low-fat yogurt
<i>Cereals, Grains, and Pastas</i>	
Pasta with alfredo sauce	Pasta with marinara sauce
Granola	Bran flakes, oatmeal, or reduced-fat cereals
<i>Meat, Fish, and Poultry</i>	
Regular ground beef	Extra lean ground beef
Chicken or turkey with skin and/or fried	Chicken or turkey without skin; broiled
Oil-packed tuna	Water-packed tuna
Whole eggs	Egg whites or egg substitutes
<i>Baked Goods</i>	
Doughnuts, muffins, scones, or pastries	English muffins, bagels, or low-fat pastries
Cake (pound, chocolate, yellow)	Cake (angel food, white, gingerbread)
Cookies	Graham crackers, ginger snaps
<i>Snacks and Sweets</i>	
Nuts	Air popped popcorn, fruits
Ice cream	Frozen yogurt
Custards or puddings (with whole milk)	Puddings (made with skim milk)
For more ideas, see: www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/lcal_fat.htm .	

Gerald T. Keegan, MD is Emeritus Staff, Scott & White Clinic and Hospital, and former Professor of Surgery (Urology), Texas A&M University School of Medicine.

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Can a Cup of Green Tea Keep the Doctor Away?

Source: Ahn WS, et al. Protective effects of green tea extracts (polyphenon E and EGCG) on human cervical lesions. *Eur J Cancer Prev* 2003;12:383-390.

Abstract: The authors investigated clinical efficacy of green tea extracts (polyphenon E; poly E and (-)-epigallocatechin-3-gallate [EGCG]) delivered in a form of ointment or capsule in patients with human papilloma virus (HPV)-infected cervical lesions. Fifty-one patients with cervical lesions (chronic cervicitis, mild dysplasia, moderate dysplasia, and severe dysplasia) were divided into four groups, as compared with 39 untreated patients as a control. Poly E ointment was applied locally to 27 patients twice a week. For oral delivery, a 200 mg of poly E or EGCG capsule was taken orally every day for eight to 12 weeks. In the study, 20 out of 27 patients (74%) under poly E ointment therapy showed a response. Six out of eight patients under poly E ointment plus poly E capsule therapy (75%) showed a

response, and three out of six patients (50%) under poly E capsule therapy showed a response. Six out of 10 patients (60%) under EGCG capsule therapy showed a response. Overall, a 69% response rate (35/51) was noted for treatment with green tea extracts, as compared with a 10% response rate (4/39) in untreated controls ($P < 0.05$). Thus, the data collected here demonstrated that green tea extracts in a form of ointment and capsule are effective for treating cervical lesions, suggesting that green tea extracts can be a potential therapy regimen for patients with HPV-infected cervical lesions.

■ COMMENTS BY MARY L. HARDY, MD

Green tea, made from lightly steamed leaves of the *Camellia sinensis* plant, is one of the most popular beverages in the world. Steaming green tea leaves prevents the enzymatic breakdown of the polyphenol components, also known as catechins, which are thought to be responsible for its medicinal effects. The catechins in general account for up to 40% of the dry weight of tea and epigallocatechin gallate (EGCG) is the most prominent catechin.

Epidemiological studies have shown an inverse relationship between amount of tea consumed and rates of a number of cancers including oral-pharyngeal, gastric, esophageal, colorectal, pancreatic, prostate, and some urinary tract carcinomas.¹ The evidence for the protective effects of tea are strongest in Asian populations, who mainly drink green tea. The amount of green tea needed to show a positive preventive effect has been as high as 10-14 cups/d in some studies.¹ Given the high dose needed to show benefit, there has been great interest in developing highly concentrated, generally decaffeinated green tea extracts. An average cup of tea contains 300-400 mg, and many commercial extracts—which contain more than 90% polyphenols, mainly EGCG, and are equivalent to 2-6 cups of green tea—are being prepared.

For women in particular, there has been relatively little evidence that tea decreases cancer risk. The Iowa Women's Health Study showed that tea consumption decreased the rate of rectal cancer, but did not decrease the incidence of any gynecological cancers.² The tea consumed in this study was mainly black tea, which may account for the general lack of effect observed. This possibility is supported by the findings of a case-control study in China that showed a decreased risk in the incidence of developing ovarian carcinoma with increased consumption of green tea.³ Finally, a Japanese observational study showed that a high rate of green tea consumption (≥ 5 cups/d) was associated with an improved prognosis in patients presenting with stage I and II breast cancer.⁴

A common gynecological malignancy, cervical cancer, has become, in the developed world, a generally preventable disease, thanks to effective screening. Incidence in the United States of new cases and death are relatively low compared to more common cancers in women, such as breast or lung.⁵ However, for certain populations (HIV-positive or other immunocompromised women) or those in developing countries, cervical cancer can represent a significant disease burden—80% of the new cervical cancer cases reported worldwide are reported in developing countries.⁶ Therefore, interest would be high in a natural, low-cost, non-toxic treatment that could interrupt the progression from dysplasia to malignancy in women with cervicitis.

Eighty-eight women were enrolled in a randomized study to test the effect of poly E ointment, poly E capsules, and ECGC capsules on morphological changes in patients with documented HPV-related cervical changes.⁷ All women were demonstrated to have either atypical squamous cells of unknown significance (ASCUS), low-grade squamous intraepithelial lesions (LSIL), or high-grade squamous intraepithelial lesions (HSIL) by pap smear. Patients were treated with either active therapy or customary care (observation) for 8-12 weeks. The four active therapy groups included: poly E ointment alone applied topically twice a week directly to abnormal cervical tissue, poly E ointment plus oral poly E capsules (200 mg/d), poly E capsules alone, or another ECGC capsule at the same 200 mg/d dose. Poly E is a high polyphenol content, decaffeinated, proprietary green tea extract. Results of therapy were evaluated by repeat pap smear, biopsy of lesion, HPV testing, and general response to therapy as determined by their change in degree of atypia or dysplasia.

The design of this study was complex (multiple interventions and multiple degrees of dysplasia), and, therefore, the number of patients in any particular group (e.g., ASCUS women who had topical treatment only) was of necessity small. Therefore, it was not generally possible to conduct statistical analysis for all conditions and all interventions. However, overall, the response to therapy was reportedly favorable. A large proportion (74% [20/27]) of the women who received topical poly E ointment responded to therapy. This response is similar to the combination group and the oral treatment only group (75% [6/8] and 60% [6/10], respectively). The overall response to any form of green tea extract was 69% (35/51 patients). None of the treatment regimens appeared to be more effective than the others and the proprietary product was not clearly better than the other ECGC capsule. Green tea extract treatment did not consistently change HPV

status. Extracts generally were well-tolerated. There was only a single case of increased liver function tests which resolved without withdrawal of medication. Very few symptoms were reported with topical use of poly E cream as well.

The main limitation in this study was the complexity of the design, which did not allow for a sufficient number of subjects in any arm of the study to demonstrate differences among therapy or for any given degree of dysplasia. However, the consistent response to all forms of green tea extract intervention was very encouraging. Although ointment was helpful, oral therapy in this study at least, appeared to be as effective, thus decreasing cost of administration and improving compliance with this potentially effective therapy.

Given the outcome of this trial (good response, low toxicity) together with the extensive experimental information available about the chemopreventative effects of green tea, we should consider recommending an 8-12 week trial of a high polyphenol content green tea extract at a dose of 200 mg/d for patients who present with cervical atypia—especially those patients for whom watchful waiting is the recommended conventional course of therapy. This also may be a reasonable supplement to consider using chronically for those patients at high risk of developing aggressive cervical carcinoma, and for HIV-positive and immunocompromised women. Green tea certainly bears further investigation as a primary preventive agent for cervical carcinoma. ❖

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CE Objectives

After reading *Alternative Therapies in Women's Health*, the health care professional will be able to:

1. evaluate alternative medicine and complementary therapies for women's health concerns;
2. identify risks and interactions associated with alternative therapies;
3. discuss alternative medicine options with patients; and
4. offer guidance to patients based on the latest science and clinical studies regarding alternative and complementary therapies.

CE/CME Instructions

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After completing this activity, you must complete the evaluation form provided and return it in the reply envelope provided at the end of the semester to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you.

CE / CME Questions

27. What is the most common cancer in women?
 - a. Lung
 - b. Cervical
 - c. Colon
 - d. Breast
28. A diet containing more than _____ of calories from fat is considered a high-fat diet.
 - a. 50%
 - b. 40%
 - c. 30%
29. The relationship of fat intake to breast cancer risk is not fully established. However, recent data suggest that saturated fats from red meat and dairy products are related to an increased risk of breast cancer.
 - a. True
 - b. False
30. In a recent trial of women with documented human papilloma virus-related cervical changes, green tea extract, administered orally and/or topically, appeared to be effective for treating cervical lesions.
 - a. True
 - b. False
31. What dose of green tea extract was given to study subjects for protection of cervical lesions?
 - a. 20 mg/d
 - b. 200 mg/d
 - c. 2 g/d

Answers: 27. d, 28. c, 29. a, 30. a, 31. b.

News Briefs

More Than One-Third of Americans Use CAM, Says Government Survey

Thirty-six percent of U.S. adults older than 18 years used some form of complementary and alternative medicine (CAM) in 2002, according to a new government survey. When prayer specifically for health reasons is included in the definition of CAM, the number of U.S. adults using some form of CAM in the past year rises to 62%.

The survey, administered to more than 31,000 repre-

sentative U.S. adults, was conducted as part of the Centers for Disease Control and Prevention's (CDC) 2002 National Health Interview Survey. Developed by the National Center for Complementary and Alternative Medicine (NCCAM) and the CDC's National Center for Health Statistics, the survey included questions on 27 types of CAM therapies commonly used in the United States. These included 10 types of provider-based therapies, such as acupuncture and chiropractic,

and 17 other therapies that do not require a provider, such as natural products, special diets, and mega-vitamin therapy.

The results of the survey provide the “most comprehensive data ever obtained about the use of complementary and alternative medicine by the U.S. adult population,” says Stephen E. Straus, MD, director of the Bethesda, MD-based NCCAM. The survey looked at usage rather than safety or effectiveness. It asked why people are using CAM, what practices they are using, and for what health conditions, he says.

It appears that most of the individuals surveyed who have ever used CAM used it within the 12 months that the survey was conducted, says Richard L. Nahin, PhD, MPH, senior advisor for scientific coordination and outreach for NCCAM. The survey revealed that CAM use was greater among a variety of population groups, including women; people with higher education; those who had been hospitalized within the past year; and former smokers, compared to current smokers or those who had never smoked.

CAM approaches most often were used to treat back pain or problems, colds, neck pain or problems, joint pain or stiffness, and anxiety or depression. However, only about 12% of adults sought care from a licensed CAM practitioner, suggesting that most people who use CAM do so without consulting a practitioner. According to the survey, the 10 most commonly used CAM therapies and the approximate percent of U.S. adults using each therapy were:

- Prayer for own health, 43%
- Prayer by others for the respondent’s health, 24%
- Natural products (such as herbs, other botanicals, and enzymes), 19%
- Deep breathing exercises, 12%
- Participation in prayer group for own health, 10%
- Meditation, 8%
- Chiropractic care, 8%
- Yoga, 5%
- Massage, 5%
- Diet-based therapies (such as Atkins, Pritikin, Ornish, and Zone diets), 4%

The 19% use of natural products appears to be an increase from previous surveys done in the 1990s,

Nahin says. The most commonly used natural products were echinacea (40.3%), ginseng (24.1%), *Ginkgo biloba* (21.1%), and garlic supplements (19.9%). The survey data indicate that echinacea probably was used for the relief or prevention of either head colds or chest colds. Clinical trials currently are underway to study this use of echinacea, he notes. Another interesting finding is the continued use of the herbal product kava, which has been linked to liver disease.

In addition to the types of CAM therapies, researchers identified several reasons respondents use CAM. These include:

- 55% of adults said they were most likely to use CAM because they believed that it would help them when combined with conventional medical treatments;
- 50% thought CAM would be interesting to try;
- 26% used CAM because a conventional medical professional suggested they try it;
- 13% used CAM because they felt that conventional medicine was too expensive.

There is a high rate of CAM use for diseases or conditions associated with chronic or recurring pain, Nahin says. “It may be that the public is turning to complementary and alternative medicine because it’s not getting relief [from these conditions] from conventional medicine.” In fact, 28% of the people who responded to the survey said they used CAM because they thought conventional medicine would not help them. “We need to identify further the reasons they thought this and for what conditions they thought conventional medicine was ineffective.”

Although the survey gives important information about the current use of CAM, it also provides a baseline against which future comparisons can be made, Straus says. “We at the national center will be relying heavily on the results of this survey to help guide our research and research training investments. We prioritize those practices and products that are more widely used by the public and for which there is greater suggestion of some benefit in activity. This survey will help us shape our future investments.”

For complete survey results, see www.nccam.nih.gov/

In Future Issues:

St. John’s Wort for Depression
Feverfew for Migraine
Antioxidants for Cervical Cancer
NSAIDs and Calcium with Vitamin D
for Prevention of Colon Cancer