

SOY

& HEALTH

Women's Health and Disease Prevention



Changes Occurring with Menopause

The hormonal changes which occur during menopause can cause a variety of symptoms and increase risk for heart disease and osteoporosis.^{1,2,3} Soyfoods, which contain phytoestrogens, are being studied for possible efficacy in decreasing the negative effects of menopause.

During peri-menopause women experience fluctuations in estrogen levels. This can cause uncomfortable symptoms like hot flashes, night sweats, insomnia, vaginal dryness, or headaches. Changes in estrogen levels have surprisingly wide-ranging effects throughout the body. At first it was not understood why estrogen should affect so many parts of the body which are outside the reproductive system. Now we know that there are two kinds of estrogen receptors, alpha (ER α) and beta (ER β), and that they are found in almost every organ of the body.⁴ Men also have estrogen receptors. Some organs have predominantly ER α , such as kidney, uterus, pituitary, and epididymis. Others have equal or greater amounts of ER, including ovary, prostate, and brain.⁴ We know that estrogen receptors are present in the cardiovascular system and bone, and that estrogen plays an important role in the health of these tissues. The ultimate decline in estrogen production which occurs with menopause leads to an increased risk for cardiovascular disease² and osteoporosis.³

Hormone replacement therapy (HRT) is commonly prescribed to help prevent the negative health effects of menopause. However, many women do not want to take HRT because of the possible increased risk for breast cancer. Can soyfoods provide the same kinds of health benefits as HRT, without the risks? We don't have the answer yet, but evidence is accumulating for several health benefits of soy.

Soy Phytoestrogens

Soy contains phytoestrogens in the form of the isoflavones, genistein and daidzein. These are known to have weak estrogenic effects when consumed by animals and humans.⁵ Researchers are studying the physiological effects of the isoflavones to find out whether they can serve some of the same functions as physiological estrogens, and thereby decrease the health risks associated with menopause.

Soyfoods are commonly consumed in the Asian countries, providing an estimated 25 to 45 mg of isoflavones per day for the average person.⁵ Japan has the highest consumption of soy, and an estimated 200 mg per day intake of isoflavones. In the US and Canada, average isoflavone consumption is less than 5 mg per day.⁵ A cross-cultural study of menopause found that women in Japan rarely reported the symptoms of peri-menopause which are common in the West.¹ Post-menopausal Japanese women also have lower rates of osteoporosis and heart disease, and a longer life-expectancy.¹ These facts have fueled an interest in research designed to clarify the relationship between soy consumption and health.

Research on the effects of soy isoflavones on the human reproductive system has been inconclusive. In premenopausal women, dietary soy isoflavones were found to delay menstruation, and to have antiestrogenic effects.⁶ A study compared the incidence of hot flashes in menopausal women consuming either soy flour or wheat flour. In the first half of the study, the soy group had a 40% lower incidence, but by the end of the study there was no significant difference between the two groups.⁷ Postmenopausal women fed a high soy diet showed no significant effects on blood hormone levels, and only a small estrogenic effect on vaginal cells.⁸ Apparently soy isoflavones behave as weak estrogen agonists or antagonists, depending on the amount of competition there is for estrogen receptors.

Soy and Cardiovascular Disease Women of childbearing age have a lower risk for heart disease than men, but after menopause the risk is the same for both genders in that age group.² We know



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that estrogen replacement therapy helps older women keep down their blood levels of LDL cholesterol, thus decreasing their risk. There is a large body of research which shows that consumption of soy protein also has a cholesterol-lowering effect.⁹ Some research with rhesus monkeys indicates that the combination of soy protein plus isoflavones may have an enhanced beneficial effect on cholesterol.¹⁰ Soy protein products have varying amounts of isoflavones associated with them, depending on how they have been processed.

Besides the cholesterol-lowering effects, soy appears to have other cardiovascular benefits. A recent human study found that consumption of soy protein inhibited oxidation of LDL cholesterol.¹¹ Genistein from soy was shown to inhibit smooth muscle cell proliferation in vitro.¹² Both the decrease in oxidized LDL and the smooth muscle cell effects would help reduce the risk of atherosclerosis. Furthermore, another in vitro study found that genistein inhibits platelet aggregation.¹³ Thus, by interfering with clot formation, soy may reduce the risk for stroke and heart attack.

Soyfoods can be an important part of a heart-healthy diet. Soybeans have no cholesterol and are low in saturated fat.¹⁴ They offer high quality protein equivalent to that found in animal foods.¹⁴

Soy and Osteoporosis About 10 million Americans have osteoporosis, 80% of whom are women.³ The disease is much more common in women because they have a smaller peak bone mass than men. Incidence of osteoporosis increases dramatically following menopause. By age 65, 20% of American women have experienced a bone fracture because of osteoporosis.³

Circulating estrogen helps protect young women from osteoporosis. In postmenopausal women, HRT reduces bone loss by about 50%.¹⁵ Researchers are now trying to find out whether phytoestrogens, such as the soy isoflavones, have a similar benefit. In a rat model of osteoporosis, dietary soy protein containing isoflavones was found to prevent bone loss.¹⁶ The same effect was seen in another rat study using genistein alone.¹⁷ In postmenopausal women ipriflavone, a drug which is metabolized to daidzein, inhibits bone resorption.¹⁸

We now know that genistein has a fairly weak affinity for ER α , but a strong affinity for ER β .⁴ Before the ER was characterized as a separate type of estrogen receptor, researchers noticed that the receptors in bone behaved differently.¹⁹ It is likely that the estrogen receptors in bone are largely of the beta type, which would help to explain the bone protective effects of soy isoflavones.

Calcium balance is also an important factor in osteoporosis prevention. Many girls and women do not consume enough calcium to meet their requirements.²⁰ As a result, their peak bone mass is smaller than it should be, putting them at risk for osteoporosis later in life.

Americans typically think of dairy products as the best source of calcium, but many plant foods are also good sources.²¹ It is true that calcium is less bioavailable from some plants because of the presence of large amounts of oxalates and phytates, which block absorption of minerals. The bioavailability of calcium from soybeans is equivalent to that of milk,²¹ despite the presence of phytates. Soyfoods contain varying amounts of calcium. A cup of cooked whole soybeans contains 175 mg of calcium.¹⁴ A half cup of firm tofu contains about 258 mg of calcium,¹⁴ but tofu processed with calcium salts contains up to 750 mg in a serving.

Calcium intake is only part of the story. Urinary calcium loss is often the factor which creates a negative calcium balance.²² Excessive consumption of sodium and/or protein increases urinary calcium losses.^{22,23} This is especially true with animal proteins because they are high in the sulfur amino acids, which are apparently responsible for this effect.^{22,23} Epidemiological studies show that countries with the greatest consumption of animal protein have the highest rates of hip fractures.²⁴ Of all the high quality protein foods, soyfoods cause the least urinary calcium loss.²³

Including soyfoods in the diet can help promote bone health in several ways. Soy provides bioavailable calcium and high quality protein, with a minimum of urinary calcium loss. Soy isoflavones may also act directly on bone to inhibit calcium resorption.

Conclusion Further studies are needed to clarify the role of soy in the treatment of menopause and its accompanying risks for disease. Research on the interaction of soy isoflavones with estrogen receptor should be particularly interesting to those concerned about women's health.

For more information, call 1-800-TALK SOY, or visit our Web site at www.talksoy.com

References

1. Lock, M. Menopause in cultural context. *Exp Gerontol.* 1994; 29(3-4): 307-317
2. American Heart Association. 1997 Heart and Stroke Statistical Update. Dallas, TX: 1997
3. National Osteoporosis Foundation. Fast Facts on Osteoporosis. Washington, DC: 1997
4. Kuiper, GGJM, Carlsson, B, et al. Comparison of the ligand binding specificity and transcript tissue distribution of estrogen receptors α and β . *Endocrinology.* 1997; 138: 863-870
5. Knight, DC, Eden, JA. A review of the clinical effects of phytoestrogens. *Obstet Gynecol.* 1996; 87: 897-904
6. Cassidy, A, Bingham, S, Setchell, KDR. Biological effects of a diet of soy protein rich in isoflavones on the menstrual cycle of premenopausal women. *Am J Clin Nutr.* 1994;60:333-40
7. Murkies, AL, Lombard, C, et al. Dietary flour supplementation decreases post-menopausal hot flushes: effect of soy and wheat. *Maturitas.* 1995; 21: 189-195
8. Baird, DD, Umbach, DM, et al. Dietary intervention study to assess estrogenicity of dietary soy among postmenopausal women. *J Clin Endocrinol Metab.* 1995; 80(5):1685-90
9. Anderson, JW, Johnstone, BM, Cook-Newell, ME. Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med.* 1995; 333: 276-282
10. Anthony, MS, Clarkson, TB, et al. Soybean isoflavones improve cardiovascular risk factors without affecting the reproductive system of peripubertal rhesus monkeys. *J Nutr.* 1996; 126: 43-50
11. Kanazawa, T, Osanai, T, et al. Protective effects of soy protein on the peroxidizability of lipoproteins in cerebrovascular diseases. *J Nutr.* 1995; 125: 639S-646S
12. Hollenberg, MD. Tyrosine kinase pathways and the regulation of smooth muscle contractility. *TIPS.* 1994; 15: 108-114
13. Murphy, CT, Kellie, S, Westwick, J. Tyrosine-kinase activity in rabbit platelets stimulated with platelet-activating factor. *Eur J Biochem.* 1993; 216: 639-651
14. United States Department of Agriculture. Composition of Foods: Legumes and Legume Products. Washington, DC: USDA, 1986. (USDA handbook 8-16)
15. Committee on Diet and Health, Food and Nutrition Board, NRC. Osteoporosis in Diet and Health: Implications for Reducing Chronic Disease Risk. Washington, DC: National Academy Press, 1989; 615-626
16. Arjmandi, BH, Alekel, L, et al. Dietary soybean protein prevents bone loss in an ovariectomized rat model of osteoporosis. *J Nutr.* 1996; 126: 161-167
17. Blair, HC, Jordan, SE, Peterson, TG, Barnes, S. Variable effect of tyrosine kinase inhibitors on avian osteoclastic activity and reduction of bone loss in ovariectomized rats. *J Cell Biochem.* 1996; 60: 1761-1769
18. Valente, M, Bufalino, L, et al. Effects of 1-year treatment with ipriflavone on bone in postmenopausal women with low bone mass. *Calcif Tissue Int.* 1994; 54: 377-380
19. Grandien, K. Determination of transcription start sites in the human estrogen receptor gene and identification of a novel, tissue-specific, estrogen receptor-mRNA isoform. *Mol Cell Endocrinol.* 1996; 116(2): 207-212
20. USDA. Nationwide Food Consumption Survey: Continuing Survey of Food Intakes by Individuals. 1985 Hyattsville, Maryland: USDA, 1987 (Report No. 85-4)
21. Weaver, CM, Plawecki, KL. Dietary calcium: adequacy of a vegetarian diet. *Am J Clin Nutr.* 1994; 59(suppl): 1238S-1241S
22. Heaney, RP. Cofactors Influencing the Calcium Requirement – Other Nutrients. In NIH Consensus Development Conference on Optimal Calcium Intake. Bethesda, Maryland: NIH, 1994
23. Breslau, NA, Brinkley, L, Hill, KD, Pak, CYC. Relationship of animal protein-rich diet to kidney stone formation and calcium metabolism. *J Clin Endocrinol Metab.* 1988; 66: 140-146
24. Abelow, BJ, Holford, TR, Insogna, KL. Cross-cultural association between dietary animal protein and hip fracture: a hypothesis. *Calcif Tissue Int.* 1992; 50: 14-18