



# Hormone Replacement Therapy (HRT): *Risks & Natural Alternatives*

©2000 Huntington College of Health Sciences

Literature Education Series On Dietary Supplements

By Gene Bruno, MS, MHS – Dean of Academics, Huntington College of Health Sciences

*Smart Supplementation™ is a free series of educational literature created by Huntington College of Health Sciences (HCHS) as a public service. Although copyrighted, it may be freely photocopied and distributed, but may not be altered in any way. Smart Supplementation™ is not intended as medical advice. For diagnosis and treatment of any medical condition, consult your physician.*

Many physicians routinely prescribe hormone replacement therapy (HRT) to postmenopausal or even perimenopausal women. As a matter of fact, about 17.5 million American women were taking HRT in 1998, according to a national survey. HRT, however, is not without its health risks. Before discussing HRT risks and alternatives, let's first examine the rationale for HRT in association with menopause.

## **Menopause: Physiological Changes**

Menopause refers to the stopping of menstruation and the end of the reproductive capacity of a woman. This event usually occurs around age 50 but may happen prematurely in some individuals before age 45 or artificially by the removal of the ovaries during a hysterectomy. As many as ten years before menopause, the ovaries begin to cease normal function. During this time, many basic physiological changes occur, including failure to ovulate; a decreased number of developing follicles and oocytes; a decreased level of the hormones estrogen and progesterone; and a rapid rise in follicle stimulating hormone (FSH), a pituitary hormone, as well as a gradual rise in luteinizing hormone (LH). These ovarian changes eventually result in the cessation of menstruation (amenorrhea) and infertility. In the years before menopause a woman may have irregular uterine bleeding, heavy enough in some instances to produce anemia. Postmenopausal bleeding indicates a need for immediate medical attention, because the incidence of uterine or cervical cancer after menopause ranges from 15 to 30% of women.

## **Menopause: Symptomology**

Most symptoms that occur during menopause result directly from the estrogen deficiency produced by the failing ovaries. It can be difficult to distinguish these symptoms from those caused by the normal aging process or from the social and domestic pressures faced by middle-aged women. Physical symptoms include hot flashes, night sweating, and tension or migraine headaches. These temporary symptoms contribute to the overall irritability and insomnia that normally occurs during this time. Osteoporosis, caused by severe or prolonged bone loss as a result of estrogen deficiency, affects 35% of women after a natural menopause. Psychological symptoms of menopause may include anxiety, depression, irritability, diminished energy, difficulty with concentration, and tension. Many women experience heightened libido after menopause because they know they can no longer get pregnant. However, emotional problems can cause a decline in sexual activity in some women.

## **The Benefits of HRT**

Conventional medical treatment for menopause often involves HRT pharmaceutical hormones. It has been well documented for several decades that HRT can be an effective remedy for the hot flashes and sleep disturbances that often accompany menopause. Hormone replacement therapy has also consistently been shown to decrease vaginal discomfort by increasing the thickness, elasticity, and lubricating ability of vaginal tissue. Urinary tract tissue also becomes thicker and more elastic, which may reduce the incidence of stress incontinence and urinary tract infections. Furthermore, some physicians and medical agencies have advised that HRT may even decrease the risk for heart disease in postmenopausal women. These potential benefits of HRT are all well and good—and if this were the end of the story, I wouldn't have written this article. Unfortunately, there are health risks associated with HRT.

## **The Risks of HRT**

Heretofore, the main concerns about HRT centered on the risk of endometrial cancer, ovarian cancer, and breast cancer, especially after long-term use (more than 10 years).<sup>1</sup> For example, some studies

suggest that HRT is associated with a 1% to 30% increase in the risk of breast cancer.<sup>2</sup> Another study conducted by the American Cancer Society followed 211,581 postmenopausal women who had no history of cancer at the time of enrollment. Results of followup from 1982 through 1996 showed that women who used HRT for 10 or more years had an increased risk of dying from ovarian cancer, compared with women who had never used HRT or had used it for less than 10 years.<sup>3</sup>

Recently, another potential risk issue regarding HRT and cardiovascular health has emerged. New recommendations by the American Heart Association, released on July 23, 2001, indicate that women who have had a heart attack or stroke do not benefit from HRT and may even increase their risk of suffering another attack.

This is based upon research where researchers randomly assigned women with known heart disease to take either hormones or a placebo. The researchers found no difference between the two groups in fatal or nonfatal heart attacks after four years. In the first year of the study, women taking hormones had 52 percent more heart-related illnesses than the placebo group. Then, a separate study testing estrogen in women with a previous stroke found that those who took the hormone suffered a higher incidence of fatal strokes than those who took a placebo.<sup>4</sup>

This new AHA position removes one of the main reasons many women take hormones—to reduce their risk of heart disease, which kills more than 226,000 American women a year, making it the No. 1 cause of death in U.S. women.

Finally, a landmark study was published in the July 2002 issue of *JAMA*, which included 16608 postmenopausal women aged 50-79 who were using HRT as Estrogen plus progestin. The researchers found a significantly increased their risk of a heart attack or stroke beginning in women's first year of HRT use. In addition, the risk of breast cancer jumped after four years of HRT use. The researchers concluded that overall health risks exceeded benefits from use of combined estrogen plus progestin, and that “the results indicate that this regimen should not be initiated or continued for primary prevention of CHD [coronary heart disease].”<sup>5</sup>

Does all this mean that women who are currently using HRT should discontinue their medication; or that women who are not yet using HRT should not do so? After the aforementioned *JAMA* study was published, the position of the National Institutes of Health (who sponsored the study) was to urge women who currently use HRT to talk with their doctors about what to do.<sup>6</sup> Certainly this is a personal decision which can only be made by a woman and her doctor. Nonetheless, some women who are

concerned about conventional HRT have turned to natural HRT alternatives.

### **Phytoestrogens: Natural Alternatives to HRT**

Natural alternatives to HRT include the use of phytoestrogens. Phytoestrogens are natural components from plants which bind to estrogen receptors in the body. Make no mistake, phytoestrogens are not actually estrogen, but since they are capable of binding to estrogen receptors, they can “fool” the body into thinking and reacting as though there were more estrogen present. Furthermore, since they are not actually estrogen, phytoestrogens are not a risk factor in the development of breast or female reproductive system cancers. As a matter of fact, research suggests that certain phytoestrogens may even help to reduce the risk of these cancers, and promote a healthy cardiovascular system. Some of the most effective phytoestrogens can be found in Soy, Black Cohosh, Red Clover Leaf, Licorice Root, and Wild Yam. In addition, certain nutrients may also play a valuable role during menopause.

In fact, The American College of Obstetricians and Gynecologists (ACOG) now recommends three botanicals for management of menopausal symptoms. These are Black Cohosh, Soy bean (isoflavones) and St. John's Wort (SJW for symptoms of depression, not for any direct impact on female hormonal biochemistry).<sup>7</sup>

### **Soy**

The protein fractions of soybeans contain an interesting group of substances called isoflavones. The ACOG suggests that short-term use of the phytoestrogens in soy may be helpful for relieving hot flashes and night sweats.<sup>8</sup> In addition, research also indicates that these isoflavones may provide some very specific benefits, including cancer prevention, cholesterol reduction, and building bone density.

### Cancer prevention

The isoflavones in soybeans have been shown to have anti-cancer effects. Apparently, the isoflavones have phytoestrogenic and antioxidant properties. One particular isoflavone called genistein (and possibly another called daidzein) has been proposed to contribute an important part of the anti-cancer effect of soy isoflavones. As a matter of fact, genistein in soy is considered by some researchers to be responsible for the lower rate of breast cancer observed in Asian women consuming soy.

The effect of genistein was tested in one study in five human breast cancer cell lines. Genistein inhibited the growth of each of these cancer cells.<sup>9</sup> Similar studies using genistein also showed significant inhibitory effects on breast cancer cells. It seems that genistein effects estrogen receptors in such a way as

to prevent breast cancer growth<sup>10</sup>. This estrogen altering response was also apparent in another study which examined the influence of total soy isoflavones in six premenopausal women for one month. The result was that menstruation was delayed and cholesterol concentrations decreased 9.6%.<sup>11</sup>

Furthermore, soy's anti-cancer effects are not limited to breast cancer. Researchers conducted test-tube research on human and animal bladder cancer cell lines, using pure soy isoflavones and soy phytochemical concentrate. The results were that both the pure soy isoflavones (genistein, genistin, daidzein, and biochanin A) and soy phytochemical concentrate inhibited growth of human and animal bladder cancer cell lines. Animal research also demonstrated that the ability of genistein, soy phytochemical concentrate, and soy protein isolate to inhibit the growth of bladder cancer in the animal (not in the test-tube). Genistein, dietary soy phytochemical concentrate, and dietary soy protein isolate reduced tumor size by 40%, 48%, and 37%, respectively, as compared with controls.<sup>12</sup>

#### Cholesterol reduction

Research indicates that substituting soy protein for animal protein may lead to reductions in plasma cholesterol. Three separate studies investigated the effect of soy products and isoflavones on the blood lipid levels of 74 postmenopausal women over a 6 month program.. Forty grams of test protein were incorporated into the subjects diets. The test protein was either isolated soy protein containing moderate amounts of isoflavones (ISP56), isolated soy protein containing higher amounts of isoflavones (ISP90), or casein and nonfat dry milk. The results were that both groups consuming the isolated soy protein diets had increased HDL levels (the "good" cholesterol). A significant lowering of non-HDL cholesterol (the "bad" cholesterol) was found in the groups consuming either of the isolated soy proteins in comparison to the group consuming casein dry milk protein. The results indicate that a low cholesterol, low saturated fat diet, combined with soy protein therapy may be effective in positively changing the ratio of HDL to non-HDL in postmenopausal women with high cholesterol levels.<sup>13</sup> Although this research is very good, there is even more impressive research regarding soy and cholesterol reduction.

A meta-analysis (an analysis of many studies that examine the same topic) published in The New England Journal of Medicine clearly demonstrated that soybean protein (which contain isoflavones) has significant cholesterol lowering properties.<sup>14</sup> This meta-analysis examined 38 controlled clinical trials. The average soy protein intake was 47 grams per day. The following net changes were associated with the soy intake: total cholesterol decrease of 9.3%, LDL cholesterol decrease of 12.9%, and triglyceride decrease of 10.5%.

#### Building bone density

A review of interventional trials examining isoflavones and bone in animals and humans suggest that including them in the diet results in reduction in bone resorption caused by estrogen deficiency.<sup>15</sup> For example, researchers at the University of Illinois at Urbana-Champaign decided to examine the effects of soy protein and its isoflavones on bone density in postmenopausal women. Sixty-six, postmenopausal women were randomly assigned to one of three dietary treatment groups for 24 weeks. One group consumed 40 grams of protein per day obtained from casein and nonfat dry milk. Another group obtained their 40 grams of protein from isolated soy protein containing 1.39 isoflavones per gram of protein (providing a total of 56 mg of isoflavones). The last group consumed their protein from isolated soy protein containing 2.25 mg isoflavones per gram of protein (providing a total of 90 mg of isoflavones). Bone density was measured twice during the study. The results showed that significant increases occurred in both bone mineral content and density in the soy group that received 90 mg of isoflavones. No other effects on bone density were seen in the other soy protein group or the casein group. This study successfully showed that soy protein providing 90 mg of isoflavones daily is effective in decreasing the risks of osteoporosis in postmenopausal women. The authors of this study pointed out that this discovery about the benefits of soy are important for postmenopausal women who cannot or choose not to undergo hormone replacement therapy, which is usually used for prevention and treatment of these two diseases.<sup>16</sup>

#### **Black Cohosh**

Black Cohosh has a long and successful history as a support herb used by menopausal women. An extract of Black Cohosh contains phytoestrogens that can reduce luteinizing hormone (LH) secretion.<sup>17 18</sup> Surges of LH are associated with hot flashes in menopausal women.

A newer, highly standardized extract of Black Cohosh has created a great deal of excitement internationally due to the results of a large open study employing 131 doctors and 629 patients. The type of extract used standardized for its triterpene glycosides, calculated as 27-deoxyacteine. Within six to eight weeks, over 80% of the patients experienced improvements in both physical and psychological symptoms. These symptoms included hot flashes, profuse perspiration, headache, vertigo, heart palpitation, ringing in the ears, nervousness/irritability, sleep disturbances, and depressive moods. Most patients reported noticeable benefits within four weeks. After six to eight weeks complete resolution of symptoms were achieved in a high number of patients.<sup>19</sup>

### Red Clover

Finnish investigations of the phytoestrogen content of various plants, revealed that Red Clover contained biologically active estrogenic isoflavones, especially biochanin.<sup>20</sup> Furthermore, Red Clover has been shown to improve the elasticity of arteries in menopausal women, which is important given the increased cardiovascular risk associated with menopause.<sup>21</sup> Ethnobotanist Steven Foster has described some research which even shows that the phytoestrogens in Red Clover was found to inhibit the activation of cancer cells.<sup>22</sup>

### Licorice root

Although often used for its gastrointestinal benefits / anti-ulcer benefits,<sup>23</sup> Licorice root also contains phytoestrogens, which have been shown to induce ovulation in women with irregular periods.<sup>24</sup> In addition, the journal *Alternative and Complementary Therapies* has indicated that Licorice root helps to balance estrogen and progesterone levels;<sup>25</sup> clearly a benefit for the menopausal woman.

### Wild Yam

Wild Yam contains diosgenin which has phytoestrogenic properties.<sup>26</sup> One of the reported uses of this botanical is in the treatment of menopausal symptoms.<sup>27</sup>

### Pantothenic acid

Since menopause can be a very stressful state of being for many women, it can potentially affect the adrenal glands which are often considered to be the “stress glands”. This is somewhat problematic, since the adrenal glands produce the hormone DHEA, which can be converted into estrogen to help take over the production of estrogen when the ovaries cease to produce it. When the adrenals are stressed, however, this production of DHEA may be somewhat impaired. Pantothenic acid may be able to help. Pantothenic acid is intimately involved in adrenal function, and the production of adrenal hormones associated with stress.<sup>28</sup> Administration of pantothenic acid has been shown to significantly increase the production of adrenal hormones in both animal and human studies.<sup>29 30</sup>

### Magnesium

Some researchers have suggested that women who are not using HRT should consider the use of certain natural substances as an alternative—including magnesium which may prove to be effective in prevention and treatment of menopausal-related symptoms.<sup>31</sup> Of course magnesium supplementation during menopause makes sense for other reasons as well. For example, research overwhelmingly supports the use of calcium supplementation, alone or in combination with other therapies for slowing or stopping the progression of osteoporosis<sup>32</sup>—a disease which is common postmenopausally. One potential problem with calcium supplementation, however, is

an increased risk of calcium stone formation. Concomitant supplementation with magnesium may reduce this risk and improve mineralization in the bone.<sup>33</sup> This is really no surprise when you consider that magnesium regulates active calcium transport. In fact, at the end of a 2-year study on menopausal women, magnesium supplementation appeared to have prevented fractures and resulted in a significant increase in bone density.<sup>34</sup>

### Boron

Speaking of osteoporosis, research shows that chronically low intakes of the trace mineral boron may pre-dispose people to osteoporosis.<sup>35</sup> Changes caused by boron deprivation include reduced blood levels of calcium, as well as an increase in urinary excretion of calcium. Boron deprivation causes changes similar to those seen in women with postmenopausal osteoporosis, and this mineral is needed to prevent the excessive bone loss which often occurs in postmenopausal women and older men.<sup>36</sup> In addition, studies have reported possible improvements in bone mineral density in women who were supplemented with boron.<sup>37</sup> For example, research has found that supplementation with 3 mg daily of the boron reduced urinary loss of both calcium and magnesium.<sup>38</sup>

### Conclusion

Given the recent and ongoing concerns about health risks associated with HRT, the use of phytoestrogen supplements and other key nutrients may be a wise alternative. I encourage women to discuss this option with their physicians.

### References

1. National Cancer Institute: Cancer Facts “Menopausal Hormone Replacement Therapy” [http://cis.nci.nih.gov/fact/3\\_10.htm](http://cis.nci.nih.gov/fact/3_10.htm)
2. Anonymous, *Am J Nat Med*, (1996) 3(4) p 7-10.
3. National Cancer Institute: Cancer Facts “Menopausal Hormone Replacement Therapy” [http://cis.nci.nih.gov/fact/3\\_10.htm](http://cis.nci.nih.gov/fact/3_10.htm)
4. Okie S. Study: Hormones Don't Protect Women From Heart Disease. *Washington Post* (2001) Tuesday, July 24. Page A1
5. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results From the Women's Health Initiative Randomized Controlled Trial. *JAMA*. 2002;288(3):321-333.
6. Study On Risks Of Estrogen-Progestin Combination To Treat Symptoms Of Menopause Prompts Many Questions. Associated Press. July 10, 2002.
7. The American College of Obstetricians and Gynecologists. ACOG Practice bulletin: Use of botanicals for management of menopausal symptoms. 2001 June 20: <[http://www.acog.org/ from\\_home/publications/misc/pb028.htm](http://www.acog.org/from_home/publications/misc/pb028.htm)>
8. National Cancer Institute: Cancer Facts “Menopausal Hormone Replacement Therapy” [http://cis.nci.nih.gov/fact/3\\_10.htm](http://cis.nci.nih.gov/fact/3_10.htm)
9. Pagliacci, M., et al, *Eur J Cancer*, (1994) 30A(11) p 1675-82.
10. Wang, T., et al, *Carcinogenesis*, (1996) 17(2) p 271-5
11. Cassidy, A., et al, *Am J Clin Nutr*, (1995) 62(1) p 151-

- 3.
12. Zhou JR, et al, *Cancer Research* (1998) 58:5231-5238.
13. Baum J, et al, *American Journal of Clinical Nutrition* (1998) 68:545-551.
14. Anderson, J., et al, *New Eng J Med*, (1995) 333, p 276-82.
15. Scheiber MD, Rebar RW, *Menopause* (1999) 6(3):233-41.
16. Potter SM, et al, *Am J Clin Nutr* (1998) 68(suppl):1375S -1379S
17. Brinker, F., *The Eclectic Medical Journals*, (1996) 2(1) p 2-4.
18. Duker, E., et al, *Planta Med* (1991) 57(5) p 420-7.
19. Anonymous, *ibid*.
20. Saloniemi, H., et al, *Proc Soc Exp Biol Med* (1995) 208(1) p 13-7.
21. Nestel, PJ, et al, *J Clin Endocrinol Metab* (1999) 84(3):895-8.
22. Foster, S., *101 Medicinal Herbs: An Illustrated Guide* (1998), Interweave Press, Loveland, Colorado, pp. 168-9.
23. Foster, S., pp. 132-3.
24. Reichert, R., *Quarterly Review of Natural Medicine* (1994) Spring, p 27-33.
25. Kelly, J. *Alternative and Complementary Therapies* (1996) November/December, pp. 348-353.
26. Mirkin, G., *JAMA* (1991) 265(7) p 912.
27. Fetrow C, Availa J, *Professional's Handbook of Complementary & Alternative edicines* (1999) Springhouse Corp., Springhouse, Pennsylvania, p. 666-668.
28. Kutsky R, *Handbook of Vitamins and Hormones* (1973) Van Nostrand Reinhold Company, New York. pp. 208.
29. Tarasov IuA, Sheibak VM, Moiseenok AG, *Vopr* (1985) 4
30. Fidanaza A, Floridi S, Lenti L, *Boll Soc Ital Biol Sper* (1981) 57(18):1869-72.
31. Kass-Annese B. Alternative therapies for menopause. *Clinical obstetrics and gynecology* (2000) 43(1):162-83.
32. Laulert L, et al, *Revista brasileira de enfermagem* (1995) 48(2):161-7.
33. Celotti F; Bignamini A. Dietary calcium and mineral/vitamin supplementation: a controversial problem. *Journal of international medical research* (1999) 27(1):1-14.
34. Sojka JE; Weaver CM. Magnesium supplementation and osteoporosis. *Nutrition reviews* (1995) 53(3):71-4.
35. Bunker VW, *British journal of biomedical science* (1994) 51(3):228-40.
36. Nielsen FH, *Magnesium and trace elements* (1990) 9(2):61-9.
37. Volpe SL, Taper LJ, Meacham S, *Magnesium research* (1993) 6(3):291-6.
38. Nielson FH, et al, *FASEB J* (1987) 1:394-97.



For more than two decades, Huntington College of Health Sciences (HCHS) has offered more than a conventional undergraduate or graduate education. Our accredited\*, distance learning degrees and diploma programs also include the breadth of responsible complementary and alternative medicine viewpoints, providing our students with a well-rounded and comprehensive approach to nutrition and the health sciences:

- Master of Science in Nutrition
- Bachelor of Health Science in Nutrition
- Associate of Science in Applied Nutrition
- Diploma in Comprehensive Nutrition
- Diploma in Dietary Supplement Science
- Diploma in Sports Nutrition
- Diploma in Women's Nutrition
- Diploma in Natural Sciences
- Diploma in Small Business Management

1204D Kenesaw  
 Knoxville, TN 37919  
 865-524-8079 • 800-290-4226  
 E-Mail: [studentservices@hchs.edu](mailto:studentservices@hchs.edu)  
[www.hchs.edu.com](http://www.hchs.edu.com)

\*Accredited member Distance Education & Training Council.