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Natural Hormones: Are They A Safe Alternative?

by Amy Allina & Adriane Fugh-Berman

In the wake of the recent news about the risks of estrogen/progestin hormone replacement therapy (HRT), many women are looking to so-called "natural" or "bioidentical" hormone preparations in the hope of finding a safer alternative to the synthetic hormones contained in conventional regimens. "Natural" may refer to hormones made from natural substances; "natural" or "bioidentical" may also refer to hormones that match those in the human body. Manufacturers of these alternative products have leaped into the fray to promote their hormone preparations as better and safer than HRT.

All hormones, whether natural or synthetic, are powerful chemicals that affect many parts of the body. Women should be skeptical of natural hormone products that claim they will extend life, reverse aging, restore youth or prevent disease without causing any adverse effects. Whether a product is recommended by a doctor, a nurse practitioner, or a naturopath, hormones are not wonder drugs or panaceas.

Many people don't realize that just as pharmaceutical companies promote drugs, there is a large industry developing, producing and selling alternative health care products. Alternative health care practitioners are subject to similar influences from these companies as conventional doctors are from drug companies.

It is very important for women to know that products are not necessarily safe just

because they're natural. The same questions that we ask about drugs need to be answered for natural therapies too: What is the specific reason to take it? Are there studies on this treatment showing that it is effective for the recommended purpose? What are the risks associated with it? A natural product is less likely to have been studied than a conventional drug, and some women may decide to take a natural product with less evidence of efficacy than they would expect for a synthetic drug. But

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women still need to investigate what is known about natural products and consider any safety concerns in order to be able to make an informed decision.

Here's what we know so far about the safety and efficacy of the natural hormones most commonly promoted to women at menopause, such as: DHEA (dehydroepiandrosterone), estriol, melatonin, natural progesterone and ipriflavone.

DHEA

DHEA is produced by the adrenal glands and is a precursor of both testosterone and

estrogen. It is promoted for anti-aging, anti-cancer and anticardiovascular disease properties, as well as for relieving vaginal dryness, increasing libido and increasing bone mineral density.

Proponents of DHEA point to its anticancer and anticardiovascular disease effects in animals as evidence of its great potential. However, most animals used in experiments have low to no circulating DHEA to start with, so even dramatic effects in animals have limited implications for humans who have plenty of DHEA to begin with.

DHEA also has different effects in women than it does in men. For example, it increases testosterone levels in women but not men.¹ It can also cause acne and increase facial and body hair in women. And rather than preventing cancer and heart disease, some research indicates that taking DHEA may increase women's risks for these illnesses. Unlike men, in women, high levels seem to correlate with increased risk for cardiovascular disease.² One study found that DHEA supplementation in women decreases sex-hormone-binding-globulin (SHBG) levels. Since high levels of SHBG are associated with lower risks of breast cancer, this effect is just the opposite of what women need.³

Research has shown that DHEA may help reduce the vaginal thinning that occurs after

(continued on page 6)

INSIDE THIS ISSUE

Natural Hormones: Are They A Safe Alternative?.....	1
Newly Developed Drugs.....	2
The Exchange.....	4
Subscription.....	7
Hot Flashes.....	8

Natural Hormones

(continued from page 1)

menopause and may also help maintain or even increase bone mineral density. Studies of its effect on mood and depression are contradictory, and most studies have involved very small numbers of women.

Because of the possibility that DHEA may increase women's risk of cardiovascular disease and cancer, it can't be considered a safe alternative for women seeking menopause

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relief, even for those indications for which some efficacy has been demonstrated.

Estriol and Tri-Est(rogen)

Estriol is a weak estrogen that can be used in high doses to treat hot flashes and other menopausal symptoms.⁴ It also seems to be beneficial in maintaining bone mineral density.⁵ Some alternative medicine practitioners promote the mixture tri-estrogen or tri-est which contains estrone, estradiol and estriol. Natural progesterone cream is often pre-

scribed with this regimen to protect the uterus from the effects of the estrogen, but progesterone creams are not absorbed well enough to provide this protection, so if a woman using estriol has a uterus, she should take an oral form of progestin to protect herself from endometrial cancer.

Estriol is touted as an estrogen that doesn't cause cancer, and some even claim that it prevents breast cancer. These claims are based on a handful of poor studies. There is no reasonable scientific evidence that estriol has anticancer effects or that it is safer than estradiol or conjugated estrogens.

Melatonin

Melatonin is a hormone that regulates daily wake-sleep cycles. It is produced mostly by the pineal gland (at the base of the brain) and in the intestines. Melatonin levels increase during sleep, but the increase is lessened by the presence of even small amounts of light.

There is evidence that melatonin helps jet lag, sleep quality and tolerance for working night shifts or varying shifts. Some scientists think that nightly surges in melatonin may reduce the risk of certain cancers, but this has not been proven. There's no evidence that melatonin retards aging, which is a claim often made in promoting it to menopausal women.

There's no information available about the long-term effects of taking melatonin supplements every night. For those who want to stimulate their natural melatonin, there's

probably no harm in trying to increase levels by sleeping in a completely dark room or using a sleep mask.

Natural Progesterone

Natural progesterone is manufactured from plant compounds (diosgenin or beta-sitosterol), and is promoted in creams and in under-the-tongue forms to prevent hot flashes, osteoporosis, premenstrual syndrome, fibrocystic breasts and even breast cancer. Natural progesterone proponents distinguish it from synthetic progestins, claiming that progesterone is natural, has different effects and is safe. But this is unproven.

Soybeans, Mexican wild yams and other plants contain diosgenin, the chemical compound from which progesterone is derived.

There's no evidence that melatonin retards aging which is a claim often made when promoting it to menopausal women

But these plants are put through a lengthy conversion process in a chemistry lab to manufacture progesterone, and the human body cannot accomplish the conversion on its own. Although derived from a plant, it is a stretch to consider natural progesterone an herbal product. If a product claims to contain only wild yam extract or diosgenin but causes progestin-like effects, then it is mislabeled and actually contains progesterone; however, it is impossible to know how much progesterone it contains, and how much will be absorbed.

The only claim for natural progesterone that's supported by evidence is that it can help hot flashes. There is no credible evidence that it improves bone mass.⁶

The cancer prevention claims for natural progesterone are perhaps the most dangerous. While oral progestins protect the endometrium from estrogen-induced cancer, progesterone cream should not be used by women taking estrogen to prevent endometrial cancer because it is not well enough absorbed to offer this protection. Progestins do not protect the breast. In fact, the estrogen/progestin combination in HRT has now been shown to increase the risk for breast cancer. The effect of progesterone (natural or synthetic) on the development of breast cancer is unknown.

(continued on page 7)

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Natural Hormones

(continued from page 6)

Ipriflavone

Ipriflavone is heavily promoted for preventing and treating osteoporosis, but there is little reliable evidence supporting the use of ipriflavone to reduce fractures. And, while it is relatively benign, ipriflavone is not without risk.

Ipriflavone alone is not an effective treatment for bone loss in women without ovaries. Several trials have found that it increases spine and wrist bone density, but no trials have looked at its effect on bone density at the hip where the most serious fractures occur. The most recent and largest trial of ipriflavone showed no benefit in maintaining bone density or reducing fractures in the spines of postmenopausal women.⁷ Also, a

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type of white blood cell decreased in a significant number of women, which may indicate decreased immune function and increased susceptibility to infections.

Conclusion

More time and money need to be spent on assessing the value and risks of natural hormones. Unfortunately, the industry is reluctant to do so on products and therapies that can't be patented, and therefore, have lower profit potential.

In the end, no one has found a magic bullet that will safely treat the varied health concerns of women at menopause. Natural hormones, like their synthetic counterparts (HRT), are powerful substances that may offer health benefits, but also come with risks. Women and their health practitioners need to evaluate the scientific evidence available when considering natural hormonal solutions for their menopausal health — anecdotal “proofs” alone are not enough to guarantee safety and efficacy. Just because the label says “natural” does not mean that it is necessarily “safer” or “better”.

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Notes

¹ Kroboth PD, et al. DHEA and DHEA-S: a review. *J Clin Pharmacol* 39(4): 327-348, 1999.

² Mitchell LE, et al. Evidence for an association between dehydroepiandrosterone sulfate and nonfatal, premature myocardial infarction in males. *Circulation* 89(1): 89-93, 1994; Barrett-Connor E, et al. A prospective study of dehydroepiandrosterone sulfate and cardiovascular disease. *NEJM* 315: 1519-1524, 1986; Barrett-Connor E, et al. Absence of an inverse relation of dehydroepiandrosterone sulfate with cardiovascular disease mortality in post-

menopausal women. *NEJM* 317: 711, 1987.

³ Labrie F, et al. Effect of 12-month dehydroepiandrosterone replacement therapy on bone, vagina and endometrium in postmenopausal women. *J Endocrinol Metab* 82: 3498-3505, 1997.

⁴ Cardozo L, et al. Meta-analysis of estrogen therapy in the management of urogenital atrophy in postmenopausal women: second report of the Hormones and Urogenital Therapy Committee. *Obstet Gynecol* 92(4 Pt. 2): 722-727, 1998; Tzingounis VA, et al. Estriol in the management of menopause. *JAMA* 239: 1638-1641, 1978.

⁵ Minaguchi H, et al. Effect of estriol on bone loss in postmenopausal Japanese women: a multicenter prospective open study. *J Obstet Gynaecol Res* 22:259-265, 1996; Itoi H, et al. Comparison of the long-term effects of oral estriol with the effects of conjugated estrogens on serum lipid profile in early menopausal women. *Maturitas* 36(3): 271-222, 2000.



⁶ Lee JR. Osteoporosis reversal with transdermal progesterone. *Lancet* 336: 1327, 1990; Leonetti HB, et al. Transdermal progesterone cream for vasomotor symptoms and postmenopausal bone loss. *Obstet Gynecol* 94: 225-228, 1999.

⁷ Alexanderson, P, et al. Ipriflavone in the treatment of postmenopausal osteoporosis: a randomized controlled trial. *JAMA*. 2001 Mar 21;285(11):1482-8.

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