

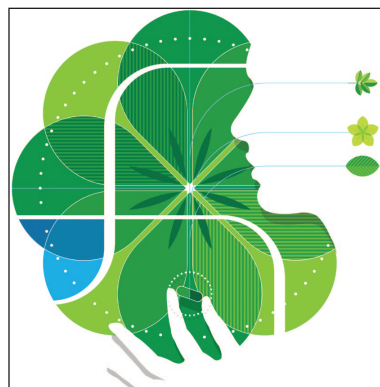
Is Bio-Identical Hormone Therapy Fact or Fairy Tale?

Laura Francisco, ARNP

Bio-identical hormone replacement therapy (BHRT), sometimes referred to as “natural” hormone therapy, is only a slightly familiar term to most primary care providers (PCPs). As BHRT gains in popularity, however, PCPs should become more informed of its benefits and risks compared to conventional hormone replacement therapy (HRT).

Bio-identical hormones are substances derived from plant oils (such as diosgenin in the Mexican yam), and are similar in structure to human steroid hormones. The human body alone cannot alter these plant substances to match the normal function of the hormone, so a chemical conversion process is applied to the plant substance, producing pharmaceutical-grade hormones. The result of this process is a direct match to the structure and function of endogenous hormones, which is then made available for professional compounding.¹ Bio-identical hormones are available commercially as well.

The term “bio-identical” indicates an identical chemical structure to the substance found in the human body, whether it is progesterone, estrogen, or an androgen. “Natural” means found in nature, and “synthetic” indicates a unique structure not found in nature. Conjugated estrogen products such as Premarin can be thought of as “natural” because they are made from pregnant horse urine, but since they are physiologically different from human serum estrogen content, they are not bio-identical.²



Bio-identical hormone replacement therapy (BHRT) is becoming more popular among women, and providers should have adequate knowledge regarding this treatment. This article reviews traditional hormone replacement therapy, BHRT, its premise, treatment options, and its overall strengths and weaknesses.

Over-the-counter progesterone creams are another example. These are “natural” because they are produced from wild yams and plants, but they lack the process that makes them “bio-identical”; therefore, little progesterone is absorbed from the product.³ Medroxyprogesterone is entirely synthetic. It is a progestin and quite unlike the chemical structure of human progesterone. The goal of BHRT is to restore a balance between hormone levels, utilizing compounds that mimic endogenous hormones.

■ The Progression of HRT

In the 1930's, natural hormones were available, but when given orally, they were rapidly destroyed in the gastrointestinal tract. Technology was not available to protect the substance from rapid degradation. More effective means of replacing the hormones (other than painful oil-based injections) were necessary.

Equine estrogens were developed in the 1940's and researched over several decades with better absorbency results.⁴

These had widespread success in managing menopausal symptoms, were well-researched, and heavily marketed over a period of time.

Initially, unopposed estrogen increased the risk of uterine cancer in women who had not undergone a hysterectomy, and in the 1970's, progestin was added,⁵ setting the stage for current therapy. But despite traditional therapy's reported success, more women began looking for an alternative.

In the 1980's, a process was discovered that slowed the

release of bio-identical hormones, allowing effective absorption and increases in serum levels of hormone.¹ Because these products are 1) found in nature, 2) lacking a unique extraction process, and 3) dosed so that therapy is completely individualized, an approval from the FDA has not been sought commercially.⁶

■ Why Advocate HRT?

Traditional therapy includes the use of daily conjugated equine estrogen combined with medroxyprogesterone for a woman with an intact uterus. Studies have indicated relief of the vasomotor and genitourinary symptoms resulting from menopause, as well as the prevention of osteoporosis.

Hot flashes, sweats, genitourinary atrophy, sexual dysfunction, skin changes, and the psychological and somatic symptoms of menopause are distressing and disrupting to a woman's lifestyle, and are often the main reasons women seek HRT. HRT generally is quite effective in relieving the majority of these complaints.⁷

Osteoporosis benefits were substantiated in the Postmenopausal Estrogen and Progestin Interventions (PEPI) Trial, which demonstrated increases in bone density among hormone therapy users.⁸

Recent meta-analyses of several studies over the past 3 decades demonstrated that HRT made significant improvements in bone mineral density, but data was inconclusive on whether actual reduction in vertebral fracture rates occurred. Nonvertebral fractures were significantly reduced.^{9,10}

The cardiovascular benefits of HRT came to light as a secondary gain of estrogen therapy, despite the increased risk of thromboembolic events. However, the American Heart Association (AHA) recently changed its position on the use of HRT in women with cardiovascular disease, as evidence mounts against the use of estrogen/progestin therapy in regard to heart and vascular health.

The Heart and Estrogen/Progestin Replacement Study (HERS) trial did not meet expectations that heart disease is reduced with HRT. HRT mortality did not decrease, and women were more at risk during the first year of therapy for cardiovascular events. Lipid levels were also not favorably decreased with HRT. In general, the AHA's stance is that HRT should not be started for the sole purpose of cardiovascular protection, but individually prescribed for its other



The major sex hormones are estrogen, progesterone, and androgens, primarily testosterone and dehydroepiandrosterone (DHEA). The estrogen portion is actually composed of three estrogens: estrone (E₁), estradiol (E₂), and estriol (E₃). These exist in a balance of about 10% estrone, 10% to 20% estradiol, and 70% to 80% estriol. Estrone is the most potent and estriol has the weakest activity. These three estrogens are highest in activity during the first half of the menstrual cycle. Estrone is abundantly converted in subcutaneous fat, and heavier women may have an overall higher estrogen level than thinner women because of this. Ten to 20% of women may have enough endogenous estrogen after menopause to build the endometrial lining just through conversion via the fat cells.

documented benefits.¹¹

Moreover, the Women's Health Initiative halted their study of combined estrogen and progestin use in postmenopausal women after a little more than 5 years. The safety board concluded that the risk of cardiovascular disease and breast cancer, although small, was significant enough to outweigh the benefits.²⁸ The link to these increased risks appears to be progestin. The estrogen arm of the study continues.

■ The Setting for HRT

The major sex hormones are estrogen, progesterone, and androgens, primarily testosterone and dehydroepiandrosterone (DHEA). The estrogen portion is actually composed of three estrogens: estrone (E₁), estradiol (E₂), and estriol (E₃). These exist in a balance of about 10% estrone, 10% to 20% estradiol, and 70% to 80% estriol. Estrone is the most potent and estriol has the weakest activity. These three estrogens are highest in activity during the first half of the menstrual cycle.

Estradiol is primarily produced by the ovary, whereas estrone is converted from androstenedione in body tissue, and estriol is converted from precursors in the liver.¹² Once the ovaries fail, overall

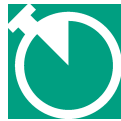
estrogen levels fall. Then estrone becomes the primary estrogen, and estradiol is deficient. Estrone is abundantly converted in subcutaneous fat, and heavier women may have an overall higher estrogen level than thinner women because of this.¹² Ten to 20% of women may have enough endogenous estrogen after menopause to build the endometrial lining just through conversion via the fat cells.⁴

The last half of the menstrual cycle, known as the luteal phase, is dominated by progesterone. Progesterone begins to decrease after age 35 when the ovaries begin to deteriorate, causing a luteal phase deficiency and potentially resulting in irregular or heavy periods, spotting, and increased symptoms of premenstrual syndrome. Levels of progesterone fall substantially after menopause.⁴ Testosterone levels decline gradually with age, generally to less than half of premenopausal levels. Oophorectomized women may see a more dramatic decrease.¹³ Patients who are extremely stressed, both physically and psychologically, may note a decrease in DHEA. In addition, there is an age-related decline in DHEA levels marked in the fifth and sixth decades.¹³ There is also a suggestion that

the decrease in androgens may be related to diseases associated with aging, but not necessarily menopause.²⁹

Deficiencies can be detected by serum or saliva levels of hormones.¹ Serum levels are most available to practitioners, while saliva levels are obtained through a variety of commercial labs. Saliva testing is popular with those who specialize in BHRT because it is easy to use and inexpensive to obtain. There is evidence that saliva accurately correlates with serum levels. Steroid hormones readily diffuse into saliva and are an accurate reflection of free hormone levels (those hormone molecules that are not protein-bound).¹⁴ Saliva samples are stable for a prolonged period of time. Several mail-order companies will do hormone testing without a health care provider's order and include an explanation of the lab tests in correlation with a patient's symptoms. Providers and patients should make sure that the labs are federally certified (CLIA or COLA), which guarantees they are reliable and routinely inspected.

There is no standard practice protocol for measuring hormone levels. Current practice does not routinely check progesterone or estradiol levels in the treatment of perimenopausal or postmenopausal women. Often, follicle stimulating hormone (FSH) is checked to determine if a woman is in menopause.³⁰ However, other hormone levels can be reliably tested and utilized to map a treatment plan.^{2, 16} The goal of BHRT is to regain the balance of the hormones in the body. Without knowing what imbalance exists, the plan is hard to produce (see Tables: "Hormone Levels and Possible Corresponding Symptoms" and "Checking Hormone Levels"). The results of these laboratory tests, accompanied by clinical symptoms, can guide the practitioner in prescribing the bio-identical hormone regimen that is best for the patient. Therapy should be reviewed and revised as symptoms warrant.



Steroid hormones readily diffuse into saliva and are an accurate reflection of

free hormone levels (those hormone molecules that are not protein-bound). Saliva samples are stable for a prolonged period of time. Several mail-order companies will do hormone testing without a health care provider's order and include an explanation of the lab tests in correlation with a patient's symptoms.

■ BHRT Vs. Conventional HRT:

A common question regarding BHRT is what makes this a reasonable alternative to conventional therapy? The answer is complex. After all, traditional HRT has a great deal of research in support of its benefits with regard to symptom relief and bone health. Yet, only 10-25% of menopausal women are taking hormones, only half of the prescriptions written for HRT are filled, and only 40% of women who begin therapy are still on it after a year.³ Fear of breast cancer, lack of knowledge regarding HRT, and troublesome side effects are common reasons why therapy is never started or is discontinued prematurely.³ Side effects such as weight gain, uterine bleeding, breast ten-

Hormone Levels and Possible Corresponding Symptoms

Estrogen Dominance

(Low/normal progesterone with normal/elevated estrogen levels)
PMS

- Mood swings
- Weight gain in hips
- Fibrocystic breasts
- Water retention
- Heavy menses
- Hypothyroid symptoms
- Nervousness
- Irritability
- Anxiousness
- Sweet cravings
- Decreased libido
- Loss of scalp hair

Estrogen Deficiency

- (Low estrogen levels)
- Hot flashes
 - Night sweats
 - Irritability
 - Depression
 - Nervousness
 - Decreased libido
 - Urinary incontinence
 - Heart palpitations
 - Foggy thinking
 - Sleep disturbances
 - Memory lapses
 - Hair loss
 - Dry skin
 - Vaginal atrophy
 - Vaginal dryness

Androgen Dominance

(High testosterone, DHEA levels in comparison to estrogen a/o progesterone)

- Loss of scalp hair
- Acne
- Increased facial a/o body hair

Androgen Deficiency

(Decreased testosterone, DHEA levels)

- Low libido
- Depression
- Heart palpitations
- Thinning skin
- Bone loss
- Memory problems
- Low energy
- General aches
- Fibromyalgia
- Vaginal dryness
- Incontinence

Progesterone Dominance

(Progesterone levels high, estrogen levels normal or low)

- Excessive sleepiness
- GI bloating
- Mild depression
- Candida
- Breast swelling
- Exacerbated lack of estrogen

Progesterone Deficiency

(Low progesterone level)

- Same as estrogen dominance

ness, and bloating are most common, and usually associated with the progestin component of the drugs.⁴

BHRT reportedly gives similar protection against bone loss and endometrial cancer as conventional therapy, with increased compliance and satisfaction. One retrospective study of 100 patients in a particular practice revealed a 96% compliance rate with BHRT and statistically significant improvement for 24 of 37 symptoms of hormonal imbalance. This far outweighs the compliance rate with traditional therapy.¹ A reason for this could be that these women may be more involved in their health care than average patients.

However, supporters of BHRT often quote the beneficial results of traditional therapy studies, and claim the conventional products are unsafe or lacking in full efficacy.³ In view of side effects and low long-term compliance, the supporters are correct, but raw data in sufficient quantities has yet to support BHRT's claims of efficacy and safety.

BHRT does not have double blind, random, placebo controlled trials to back up its claims. However, there are several studies with small sample sizes that do show encouraging conclusions. For example, a study by Hargrove et al detailed a comparison of BHRT with synthetic replacement. The results were promising in regard to symptom relief, spotting, and hormone levels, but the sample size was less than fifty.¹⁷ A Japanese study in 1996 featured 75 women with decreased bone density tests using estriol for nearly a year with prevention of further bone loss and improved climateric symptoms.¹⁸ Estriol is very popular in Europe for HRT, and several large, controlled studies have shown decreased urinary tract infections in postmenopausal women as well as improved lipid panels and menopausal symptoms.^{19,20,21} These studies are somewhat old, however, and have not been reproduced in current practice.

Oral micronized progesterone compared to medroxyprogesterone did receive a favorable report in the PEPI trial, a large and well-controlled study.¹ Additionally, a recent study of 58 women revealed that the topical application of progesterone did have an anti-proliferative effect on the endometrium without significant side effects.²² Vasomotor symptoms treated with topical progesterone were improved in a controlled study of 100 women, though no improvement in bone density was noted with progesterone alone.²³

DHEA was shown to be effective in a 12-month study,



There is no standard practice protocol for measuring hormone levels. Current practice does not routinely check progesterone or estradiol levels in the treatment of perimenopausal or postmenopausal women. The goal of BHRT is to regain the balance of the hormones in the body. The results of these laboratory tests, accompanied by clinical symptoms, can guide the practitioner in prescribing the bio-identical hormone regimen that is best for the patient. Therapy should be reviewed and revised as symptoms warrant.

with positive outcomes on bones, menopausal symptoms, and the endometrium. Although the p values were significant, there were no controls or randomization.²⁴ Anecdotally, there appears to be a positive correlation to DHEA-S levels and longevity, but there are few studies to prove a safe use for supplementation. It is sometimes used for treatment of depression, dysthymia, lupus, and adrenal insufficiency, and has shown promising results. Independent validation of risk/benefit ratio has yet to be determined.¹³

In a study, 75 oophorectomized women were evaluated for testosterone replacement for a period of three months. Researchers concluded that transdermal testosterone improved sexual function and psychological well-being. This study had a placebo group and subjects were randomly assigned.²⁵ Testosterone levels did rise in serum as well. Estrogen ther-

apy itself, as well as oophorectomy and menopause, can drive testosterone levels down. This gives an opportunity to rebalance with supplementation.²⁶

Although the theories are logical and preliminary results promising, a large, well-controlled study should be designed,

Checking Hormone Levels

- Hormone levels should be checked in the midluteal phase in premenopausal or perimenopausal women for best results.
- Remember this is a tool in the total assessment picture to validate symptoms and diagnosis.
- Utilize the reference ranges given by the laboratory. If a particular lab is at an extreme in the normal range, but symptoms fit, treatment with follow up is appropriate.
- An estrone level could be warranted in heavier women who may have a lot of stored estrogen.
- Look at the balance of progesterone and estrogen—is the estrogen high normal, where the progesterone is low normal or low? If symptoms also fit, you could use a progesterone compound to treat estrogen dominance.
- If women are already on hormone replacement of any type, draw labs 8 hours post dosing for accuracy.

submitted, funded and completed to verify the claims made by those who support compounded BHRT. However, the observations of those who prescribe these regimens and individualize treatment for both premenopausal and postmenopausal women, give practitioners an alternative when conventional therapy has not worked or is initially unacceptable to the patient.

■ Replacement Options

Traditional hormone replacement includes products such as Premarin, Premphase, and Prempro, which are conjugated equine estrogen products. The progesterone component that is most frequently prescribed is medroxyprogesterone, such as Provera, which is not actually progesterone, but a progestin. Progestin versus progesterone creates a significant difference in side effects, and is often the reason why conventional therapy is prematurely discontinued.⁴

Commercially prepared bio-identical hormones are available. Estradiol, one of the estrogen triad, is available in both oral forms, such as Activella, and patches including Climara, Vivelle, and other products. These are often covered under prescription plans. Prometrium is a bio-identical progesterone in a peanut oil (beware of allergies) that is commercially avail-



Raw data in sufficient quantities has yet to support BHRT's claims of efficacy and safety. BHRT does not have double blind, random, placebo controlled trials to back up its claims. However, there are several studies with small sample sizes that do show encouraging conclusions. Although the theories are logical and preliminary results promising, a large, well-controlled study should be designed, submitted, funded and completed to verify the claims made by those who support compounded BHRT.

able, though frequent dosing is necessary.

Alternatively, compounded BHRT has endless combinations that can be individually determined and prescribed. A compounding pharmacist trained in BHRT is an invaluable asset when beginning this type of treatment² (see Table: "Examples of BHRT Dosing"). Remember, there are no trade names for these products and they are only available at compounding pharmacies. Reliable compounding pharmacies can be found by checking with Professional Compounding Centers of America (PCCA) or the International Academy of Compounding Pharmacists (IACP). Comparing symptoms and serum levels, one can determine what hormones should be balanced. Usually, it is advisable to start conservatively and have the patient reevaluated regularly to adjust dosages

for symptoms relief. It is important to remember that these drugs are just like the commercially-prepared products, and have similar side effects (see Table: "Side Effects of BHRT"). Women who are not eligible for traditional HRT, and those with a history of breast cancer or thromboembolic events should not use BHRT.

Of course, besides pharmaceutical treatment options, the primary care provider should provide education and support. HRT, whether traditional or bio-identical, is not a magic bullet. Recommendations should include stress relief, proper nutrition and sleep, weight reduction, and smoking cessation. These interventions are most important to overall health and

Examples of BHRT dosing

Tri-est (80% Estriol, 10% estradiol, 10% estrone): 1.25-5 mg daily (po), these percentages can be adjusted for symptoms. For example, if ineffective for hot flashes, may try a 70-20-10 to increase the estradiol component.

Progesterone SR 100-200mg 1-2x/d or 2-4% cream 10-20mg 1-2x/d, usually cycled 12-25 days of a cycle.

Testosterone cream 10mg/ml, 1-2mg per day (this is available as an oral sustained release, but better results are obtained when given topically without harmful liver effects).

All of the above are available in an oral, transdermal, sublingual, or vaginal route. These are customized to each patient preference, history of GI disturbance, and level of compliance. A good, compounding pharmacist will assist with delivery routes and dosing.

DHEA-S 2.5-10mg per day (po)
Avoid a late day dose to prevent insomnia^{1,2}

Side Effects of BHRT

Estrogen: nausea, loss of appetite, breast tenderness, headaches, possible increased risk of breast cancer, breakthrough bleeding, fluid retention, mood swings, increased risk of thromboembolic disorder, migraines (mediated by dose and counter-balance of progesterone)

Progesterone: drowsiness-(reduced if used at bedtime), nausea, edema, breakthrough bleeding

Testosterone: acne, hirsutism, nausea, vomiting, edema, deepening of voice, impaired liver function, increased cholesterol levels, loss of scalp hair

DHEA: jaundice, elevated LFTs, virilization, adverse effects on lipids, insomnia


Note: Symptoms are generally dose-related.

are often overlooked when completing an assessment and treatment plan of the premenopausal, perimenopausal, and postmenopausal woman.²⁷

Conclusion

Each woman should be evaluated individually to meet her particular needs and become fully informed of her options. BHRT is not the answer for every woman, just as traditional therapy does not fit every patient.

BHRT's are at a disadvantage because they lack long-term, controlled studies, making acceptance difficult to earn. Patients should be aware of this before starting this regimen. Observationally, there are a number of success stories, and research continues to provide an evidence-based approach to this treatment. The PEPI trial was a giant step in affirming the benefits of oral micronized progesterone therapy.

Hopefully, in time, more results will become available regarding other BHRT options. Currently, guidelines state that HRT should be used as a short-term relief for menopausal symptoms, with a full understanding of the risks and benefits.³⁰ Acquiring a knowledge base regarding all types of therapy will benefit both providers and patients. 

REFERENCES

- Walker C. BHRT: A natural option for perimenopause and beyond. *Advance for Nurse Practitioners* 2001; 9(5): 39-45.
- Lorentzen J. Clinical consideration of HRT. Lecture: Professional Compounding Centers of America. 2001: Houston.
- Taylor M. Alternatives to conventional HRT. *Compr Ther* 1997; 23(8): 514-32.
- Moskowitz D. Changing views: the emergence and efficacy of natural hormones in the treatment of menopause. *JAMA* 2000; 3(3): 36-44.
- DeLignieres B, MacGregor E. Risks and benefits of HRT. *Cephalgia* 2000; 20: 164-9.
- Lorentzen J. The Evolution of Hormone Treatment. *International Journal of Pharmaceutical Compounding* 2001; 5(5): 336-8.
- Hargrove J, Eisenborg E. Menopause. *Office Gynecology* 1995; 79(6): 1337-56.
- The writing group for the PEPI trial: Effects of hormone therapy on bone mineral density. Results from the Postmenopausal Estrogen/Progestin Interventions (PEPI) trial. *JAMA* 1996; 276(17): 1389-96.
- Craven R. Meta-analysis of randomized controlled trials of oestrogen replacement therapy for osteoporosis. *Australian and New Zealand Journal of Medicine* 2000; 30 (4): 545.
- Torgeson DJ, Bell-Syer S. Hormone replacement therapy and prevention of non-vertebral fractures: a meta analysis of randomized trials. *JAMA* 1998; 28 (7): 605-13.



Compounded BHRT has endless combinations that can be individually determined and prescribed. A compounding pharmacist trained in BHRT is an invaluable asset when beginning this type of treatment. Remember, there are no trade names for these products and they are only available at compounding pharmacies. Reliable compounding pharmacies can be found by checking with Professional Compounding Centers of America (PCCA) or the International Academy of Compounding Pharmacists (IACP). Comparing symptoms and serum levels, one can determine what hormones should be balanced. Usually, it is advisable to start conservatively and have the patient reevaluated regularly to adjust dosages for symptoms relief.

- Mosca L, Collins P, Herrington DM et al. AHA science advisory: hormone replacement and cardiovascular disease. A statement for healthcare professionals from the AHA. *Circulation* 2001; 104 (4): 499-503.
- Follingstad A. Estriol, the forgotten estrogen. *JAMA* 1978; 239 (1): 29-30.
- Davis S. The clinical use of androgens in female sexual disorders. *Journal of Sex and Marital Therapy* 1998; 24: 153-63.
- Read G, Walker R, Wilson D, Griffiths K. Steroid analysis in the saliva for the assessment of endocrine function. *Ann NY Acad Sci* 1993: 260-274.
- Smith K, Judd H. Menopause and postmenopause. In: de Cherney, A. and Pernoll, M. ed. *Current Obstetric & Gynecologic Diagnosis & Treatment*, 8th edition. New York, NY: McGraw Hill, 1994; 1030-49.
- Hargrove J, Osteen K. An alternative method of hormone replacement therapy using the natural sex steroids. *Infertility and Reproductive Medicine Clinics of North America* 1995; 6(4): 653-74.
- Hargrove J, Maxson W, Wentz A, Bunnett L. Menopausal HRT with continuous daily oral micronized estradiol and progesterone. *Obstetrics and Gynecology* 1989; 73 (4): 606-12.
- Minaguichi H et al. Effects of estriol on bone loss in postmenopausal Japanese women: A multicenter prospective open study. *J Obst Gynecol Res* 1996; 22 (3): 259-65.
- Raz R, Stamm WE. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. *N Engl J Med* 1993 Sep 9; 329 (11):802-3.
- Kirkengen A, Andersen P, Gjersoe E et al. Oestriol in the prophylactic treatment of recurrent urinary tract infections in postmenopausal women. *Scand J Prim Health Car* 1992 Jun; 10(2): 139-42.
- Karjalainen A., Heikkinen J, Savolainen M, et al. Metabolic changes induced by peroral oestrogen and transdermal oestradiol gel therapy. *British Journal of Obstetrics and Gynecology* 1997; 104 (16): 38-43.
- Anasti J, Leonetti H, Wilson K. Topical progesterone cream has antiproliferative effect on estrogen-stimulated endometrium. *Obstet Gynecol* 2001 Apr; 97 (4 suppl 1): S10.
- Leonetti H, Longo S, & Anasti J. Transdermal progesterone cream for vasomotor symptoms and postmenopausal bone loss. *Obstet Gynecol* 1999; 94(2): 225-8.
- Labrie F, Diamond P, Cusan L et al. Effect of 12 month dehydroepiandrosterone replacement therapy on bone, vagina, and endometrium in postmenopausal women. *J of Clinical Endocrinology and Metabolism* 1997; 82 (10): 3498-3505.
- Shifren J, Braunstein G, Simon J et al. Transdermal testosterone treatment in women with impaired sexual function after oophorectomy. *N Engl J Med* 2000 Sep 7; 343(10): 682-8.
- Casson P, Elking-Hirsch K., Buster J. et al. Effect of postmenopausal estrogen replacement on circulating androgens (abstract). *Obstetrics and Gynecology* 1997; 90 (6): 995-8.
- Algrim M. Natural hormone replacement: individualized vs one size fits all therapy. *Am J Natural Med* 1997; 4(7): 6-7.
- Ouhilal S, Santoro N. Update: Weighing the merits of hormone replacement. *Emergency Medicine* 2002; V34 (10): 30-44.
- Burger H, Dudley E, Jesheng C et al. A prospective longitudinal study of serum testosterone, DHEA, sex hormone binding globulin levels through the menopause transition. *J Clin Endocrinol and Metab* 2000; 85(8): 2832-38.
- Hormone replacement therapy: collaborative decision making and management. Institute for Clinical Systems Improvement (ICSI), Bloomington, MN. Found at www.icsi.org. 10/21/02.

ABOUT THE AUTHOR

Laura Francisco is a NP at Penn Avenue Internal Medicine, Des Moines, Ia.

