



Bio-Identical HRT for Women

What is different about this?

As most of you know, there has been a lot of bad press in the past months concerning the use of hormones for menopausal and postmenopausal women. Tom Bader, R.Ph, is the owner of College Pharmacy and he stated on his website¹ the following: [The Women's Health Initiative (WHI)²] "study was initiated to determine any relationship between [Hormone Replacement Therapy] HRT and other health risks such as breast cancer, cardiovascular disease, and osteoporosis to name but a few. The protocol involved thousands of women aged 50 to late 70's and were given a *single dosage* [emphasis mine] regardless of their physical and physiological differences. For instance, there was no distinction made between participants with intact uteruses and ovaries and those without. This is an extraordinary assumption as it is widely held that hormonal requirements, and therefore dosages, vary substantially based on the specific patient's unique chemistry. One dose does not fit all."

Healthcare providers and their patients have been left wondering where to turn next in the wake of the WHI decision to stop their study regarding HRT. Unfairly, the WHI has left the impression that all HRT is the same and poses the same health risks identified in the study. This is simply not the case. There are alternatives to the one-size-fits-all dosage and single product focus of WHI. They are also safe and efficacious."

For more than 25 years, College Pharmacy has advocated the use of Biologically Identical Hormones (BHRT) individualized to the patients' unique requirements. The distinction between the synthetic hormones used in the WHI study and BHRT is the molecular structure of the hormones. BHRT provides the patient with medications that are exactly the same chemically as that produced by the body. Additionally, the route of administration used in the study (oral) could increase risk to the patient due to the production of known high-risk metabolites caused by interaction of the medications with the liver [*i.e.*, estrone]. Non-oral routes of administration such as trans-dermal, sublingual, and pellet implants were not studied by the WHI. These alternative routes of administration are widely

known to provide a more consistent and natural way to introduce medications into the body."

Let's take a look at some of the fears that women have with HRT. Some of them are real but avoidable.

1. **HRT causes breast cancer.** This is the "biggie" for the termination of HRT. The actual number of breast cancer patients that appeared in the WHI was small but it was statistically significant. So why is BHRT better and is not as scary has mainstream HRT? As mentioned previously, it avoids the liver and therefore the formation of estrone is greatly reduced. Estrone is one of the estrogens that are produced in a woman's body and the level increases with age. Unfortunately, when the liver metabolizes it, it can go either the 16- α hydroxylated estrogen metabolite pathway or the 2-hydroxylated metabolite pathway, with lower estrogenic activity. The latter pathway is associated with a lower rate of breast cancer in women³. One of the natural ways to steer the liver into the 2-hydroxylated pathway is to eat cruciferous vegetables, *e.g.*, broccoli, cauliflower, and cabbage^{4,5}. These contain indole-3-carbinol which converts to diindolylmethane (DIM) and indolylcarbazole (ICZ) when exposed to stomach acid. Both of these are inducers of the liver in the 2-hydroxylated pathway.
2. **BHRT isn't natural, menopause is.** This is probably the biggest argument made by health care providers who do not believe in the use of BHRT or any type of HRT. They believe that menopause and andropause are just the inevitable results of aging and we should just enter it as gracefully as we can. *That is hogwash and is illogical.* For example, heart disease is part of the aging process with long time exposure to oxidative stress, advanced glycation endproducts, and lifestyle habits (to name but just a few) and essentially we all have or will have heart disease. If so, then why bother treating it? Just let the disease take its "natural course" and hold your head up high until you die of a massive heart at-

¹ www.collegepharmacy.com

² Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results From the Women's Health Initiative Randomized Controlled Trial. JAMA 2002;288:321-33

³ Muti P, Bradlow HL, Micheli A, et.al. Estrogen metabolism and risk of breast cancer: a prospective study of the 2:16 α -hydroxyestrone ratio in premenopausal and postmenopausal women. Epidemiology. 2000 Nov; 11(6):635-40.

⁴ Fowke JH, Longcope C, Hebert JR. Brassica vegetable consumption shifts estrogen metabolism in healthy postmenopausal women. Cancer Epidemiol Biomarkers Prev. 2000 Aug;9(8):773-9.

⁵ Jay H, Fowke, JH, Chung, FL, et.al. Urinary Isothiocyanate Levels, Brassica, and Human Breast Cancer. Cancer Res. 2003 Jul 15;63(14):3980-6.

tack or a stroke. Don't take any cholesterol drugs or blood pressure drugs, since that would alter the course of this "natural" disease. So if we perform interventional therapy to treat heart disease, then we should perform interventional therapy to treat menopause and andropause.

So which hormones should you take? That's a pretty easy choice...how many did you have when you were younger? What were your ovaries producing? They were mostly producing estradiol, estriol, progesterone, and testosterone. So if you were producing these, then why do physicians only give you one or two of them *IF* they treat you with HRT? Frankly, I have no idea except to consider that mainstream medicine likes to treat minimally. Women who have had hysterectomies tell me that they don't need progesterone because their prior physicians have told them so. If that is true, why are there receptors for progesterone in the brain? Isn't it amazing that we physicians know exactly why God gave women progesterone? But then, why do men have progesterone receptors too?

The idea behind BHRT is that we should attempt to mimic, as much as possible, the hormones that were secreted when you had functioning ovaries. The hormones should never be given orally (except for micronized progesterone {Prometrium®}) so as to avoid the liver in high doses. Therefore, you will need to get your hormones either transdermally, sublingually, or subcutaneously (pellets).

Transdermal products are compounded for you at a special pharmacy (I like to use *College Pharmacy* in Colorado Springs, CO, or *Medical Dental Pharmacy*, which is located locally at First and Nees.) You will need to apply this to your inner forearms every morning. You can receive all four hormones in this fashion.

Sublingual preparations are compounded at *College Pharmacy* (I don't believe that *Medical Dental* can do this one) and consist of estradiol, progesterone and testosterone. These pills are put under the tongue twice a day and do require some oral preparation before you take the dose and some restrictions on drinking/eating for a period of time after you take the medication.

The one that is probably the most popular here in this practice is pellet therapy. Unfortunately, progesterone cannot be put into pellet form yet, so Prometrium® is used as the progesterone replacement. The pellets of estradiol and testosterone are implanted under the skin at your hip height and put into a fat pad just back of your hip. This procedure is very short, relatively painless and is covered under your insurance except for the cost of the pellets. Each pellet costs \$15 so it can range between \$30 and \$45 per procedure. Each implant will last between 2 ½ months to 3 ½ months.

Blood work is done periodically to ensure that your blood levels for each hormone are at the right level. Saliva tests are not very accurate, so do not waste your money (or spit) on them. If you want a "snapshot" of your levels, then blood is the best. If you need a metabolic picture instead, a 24-hour urine for the hormone and/or hormone metabolites is needed.

What are the contraindications for BHRT, *i.e.*, who can't take it? First and foremost are women with a history of breast cancer. Breast cancer is stimulated by estrogens and so even the bio-identical form will stimulate the cancer receptors. Second are women with a history of blood clots in their legs. While the research is still out on whether BHRT will cause the clots like the standard horse/artificial ones, this is a relative contraindication. A relative contraindication means that once everything is considered, including the risks versus the benefits, if you decide to take that chance on the BHRT, then you can.

A third relative contraindication is a first-degree relative with breast cancer, e.g., mother, sister, or daughter. This may be an indication of an inheritance of breast cancer genes, which means that perhaps you are more prone to breast cancer.

Please understand that there is no such thing as a guarantee for anything that you do. You take risks getting into your car to go to work or to come see a doctor. The bathroom is the most dangerous place in your home, but we don't consider that to be "scary". So if you decide to start therapy, you already understand the benefit (which is why you want to start) and you must know the risks for the treatment as well. We have covered the benefits in depth and also the differences in delivery systems and chemical structures from BHRT versus standard HRT. The risks, in my medical opinion, are less but are not absent. You must be the final judge. Also remember another option, if you decide that estradiol, estriol, and progesterone are too much for you, you may want to consider just taking testosterone for the health benefits noted in the previous article.

If you still have a uterus, while we are adjusting your doses of the different hormones, you may get some bleeding/spotting. Some have even restarted their menses. While this is more of an annoyance than anything else, it will be monitored closely and if it continues then to ease everyone's mind, we may decide to perform an endometrial biopsy in the office.