

Bio-Identical Hormone Replacement: risks you should know and how to reduce them

by Dr. Jonathan Wright, MD on June 28, 2010

I've been writing about the benefits of bio-identical hormone replacement therapy (BHRT) for years. Not only does BHRT help alleviate the symptoms associated with menopause (and the male version of hormone decline, called andropause), but it also offers many other significant health benefits as well.

Whether you're a man or a woman, there's excellent scientific evidence that BHRT will substantially reduce your risk of Alzheimer's disease and other cognitive decline. Other research has proven that BHRT significantly lessens risk of heart and blood vessel disease, osteoporosis, and (in non-smoking women) chronic obstructive pulmonary disease (COPD). It has also been proven to significantly reduce deaths from all causes in men (it's very likely it will reduce all-cause mortality for women, too, though it hasn't been proven just yet).

Another "perk" of BHRT is that it slows the progression of aging, including age-related changes in appearance. Women using BHRT for five to 10 years appear significantly younger than women of the same age who haven't used BHRT. Wrinkling is less, and skin elasticity is better for much longer. Both women and men using BHRT frequently report improved libido and sex life, too.

And over the last 25 or more years, I've heard from hundreds of women and men using BHRT that they're feeling better mentally, they're more cheerful, they remember things better, and they have more "get up and go." As helpful as BHRT is, though, there are a few cautions. For maximum safety, it's always best to "Copy Nature," using the exact molecular duplicates of human hormones, in the same quantities normally in bodies, taken into our bodies the right way (for example, swallowing estrogens is actually dangerous), and following Nature's timing. But even that isn't enough: There are still some potential problems with BHRT. Most of them can be easily corrected if you're monitoring your hormone levels regularly and working with a physician skilled and knowledgeable in both natural medicine and BHRT. But it's important to know what to look out for. So this month, let's go over some of the most common BHRT problems, and how you and your doctor can find them and fix them, using entirely natural means.

Why your estrogen treatment "failed" and what you can do about it

You've heard about all of the wonderful benefits of BHRT and how it can help women feel better—sometimes almost immediately. But when you tried it, it didn't work very well for you. So your doctor increased the dose, but it still didn't seem to help. If this situation sounds familiar, it's very likely your body is retaining too little estrogen—"kicking out" most of it right away through your kidneys and bowels. This problem—technically called estrogen "hyperexcretion"—can be confirmed if there are higher than usual amounts of estrogens in a urine specimen collected for 24 hours, while estrogens in the blood (serum estrogens) are low-normal or low, and symptoms of low estrogen continue. Why does this happen? Well, there's no way to know for certain, but there are a few theories. This problem seems to occur more in women who previously took horse urine estrogen (Premarin®), birth control pills, or who have had high exposure to one or more environmental estrogens. Fortunately, there is something you can do about it. A decade or so ago, I found that estrogen hyperexcretion can always be corrected with very low doses—just 500 micrograms (or less) per day—of the essential element cobalt.¹ These low quantities are safe, as diet surveys from around the world have found that dietary cobalt intake ranges from 10 to 600 micrograms daily.

Symptom relief usually starts within two to three weeks, and symptoms are completely corrected within two to four months. Of course, even if you're feeling better, you should confirm that the problem has been solved by doing a follow-up 24 hour urine test. If your urine test comes back showing that your estrogen levels have diminished into the expectable range, you can likely stop taking cobalt (and, in most cases, there's no need to resume taking it). Cobalt also helps normalize hyperexcretion of other hormones, such as testosterone and cortisol, but these situations are much more rare than estrogen hyperexcretion. What is more common with testosterone is the next potential BHRT problem on our list...

Attention men: What you should do if your testosterone “stops working”?

Here's another common scenario—this one for the men: You've seen a doctor familiar with BHRT, had your testosterone and free testosterone tested, and started on a transdermal or (preferably) a transmucosal prescription testosterone crème.

Initially, you could really feel a difference. You felt stronger, and more motivated to get things done. Your libido definitely improved. But in just a few weeks, the effect wore off substantially, maybe even entirely. What happened? Is your body getting rid of (hyper-excreting) too much testosterone? While this is possible, as I mentioned above, testosterone hyperexcretion is rare. Much more likely, this initial response and then decline is due to another problem, called hyper-aromatization. Hyper-aromatization occurs when the body makes too much estrogen out of testosterone. Since this topic was covered in detail in the September 2009 issue of Nutrition & Healing, I'll just re-cap it briefly here (you can download and view the September issue for free by visiting www.wrightnewsletter.com and logging on to the Archives).

You're more likely to have hyper-aromatization of testosterone if you're significantly overweight or if you have

- Type 2 diabetes (or if it runs in your family)
- High cholesterol
- High triglycerides
- Skin tags (little flaps of skin that stick out from the surface, usually on the neck, under the arms, or in the groin area)
- High blood pressure

If any of these conditions apply to you, check with a physician skilled and knowledgeable in nutritional and natural medicine (as well as BHRT), and have insulin resistance testing done.² Insulin resistance is a sign that you're at increased risk for type 2 diabetes, and it's almost always found when hyper-aromatization of testosterone is present.

In other words, if you're a man using testosterone and your body is transforming that testosterone into too much estrogen, it's very likely that you're “on the way” to type 2 diabetes! And though there's no outright proof, it appears very likely that the high insulin levels associated with insulin resistance are at least part of the cause of this problem, and possibly the entire cause. So it makes sense that reversing hyper-aromatization and preventing (or improving) type 2 diabetes go hand-in-hand. Getting insulin resistance under control with diet and exercise will eventually reverse hyper-aromatization of testosterone, but it can take a minimum of several months or even a year or two.

Learn More About Dr. Wright and the Tahoma Clinic - Seattle, WA

In the meantime, there are two safe, natural botanical “Band-Aids” which will slow down the hyper-aromatization in the short term, while you're working on the permanent solution. One is Myomin, a combination of four Chinese botanicals. The other is the flavonoid chrysin. (Chrysin comes in both tablet/capsule form and a liposomal spray—the spray is much more effective.) Both of these supplements are also available from natural food stores, compounding pharmacies, and the Tahoma Clinic Dispensary. Of course, there are patent medicines which suppress hyper-aromatization, too. But they have many possible adverse effects, and should only be used if nothing else works.

4 ways to keep tabs on your cancer risk

There's one more precaution to keep in mind with BHRT, and this one is definitely the biggest. I'm referring to cancer risk. But before you get worried, keep in mind that BHRT can actually help you decrease your risk of this dreaded disease. The key is to keep an eye on some very specific risk factors.

Let's start with the factors women need to know about.

There are four main markers to consider. First on the list is the estrogen quotient, or EQ. The estrogen quotient (EQ) is determined by dividing the total estriol by the sum of estrone and estradiol. (In mathematical terms it looks like this: $EQ = E3 / E1 + E2$). An EQ that is greater than one indicates a lower risk of estrogen-related cancer.³ And in order to have an EQ that's greater than one, your urine test needs to show more estriol than estrone and estradiol.⁴ One thing to keep in mind: The EQ cannot be determined from blood testing, since the half-life of estriol in the blood is very short.⁵ Unfortunately, conventional physicians unaware of this fact often claim that estriol is only secreted and found during pregnancy, which definitely isn't the case. To get an accurate estriol measurement and to determine your EQ, you'll need to do a urine test that measures urine samples collected over a 24-hour period.

The second cancer risk factor is one you may recognize if you've been reading Nutrition & Healing for awhile—the "2/16" ratio. Like the EQ, testing your 2/16 ratio can also be done with a 24-hour urine test. The 2/16 ratio looks at the amount of 2-hydroxyestrogens in your body in relation to the amount of 16-alpha-hydroxyestrogens. "16ahydroxyestrogens" are pro-carcinogens, but the "2" type are not, so it's safer to have significantly more "2" than "16a." However, you don't want too much more "2" than "16a," since that's been shown to be associated with excess osteoporosis risk. As is so often the case, correct balance is the key! The last cancer risk factors women using BHRT need to keep an eye on are estrone and 4-hydroxyestrone.

Estrone and 4-hydroxyestrone are individual estrogen metabolites. If either one is elevated, it is associated with increased cancer risk. So even though every woman has some level of each, you want as little as possible. By contrast, 2-methoxyestradiol is an extremely potent anti-carcinogen, and you want as much of this estrogen as you can get! (For complete details and references concerning 2-methoxyestradiol, see the February 2008 issue of Nutrition & Healing.) Again, a 24-hour urine test can tell you if your levels of estrone or 4-hydroxyestrone are elevated. If they are—or if testing shows any of these markers point to increased risk, there are steps you can take to reverse it.

Easy strategies for keeping cancer risk as low as possible

Let's start with the EQ. If your EQ is less than one, you can almost always boost your estriol production with either iodine or iodide. (For the technically inclined, iodine and iodide induce the pathway from estrone → 16a hydroxyestrone → estriol, $E1 \rightarrow 16aOHE1 \rightarrow E3$). Six to eight drops of Lugol's iodine daily (equivalent to three to four tablets of Iodoral or capsules of i-Throid) or four to six drops of SSKI daily for 30 to 60 days will usually bring an EQ back up to greater than one. After your EQ is normalized, continue taking two drops of Lugol's iodine daily (or one Iodoral or i-Throid tablet or capsule daily), not only to support your EQ, but also to significantly reduce your breast cancer risk. Just make sure to have your thyroid function tested periodically if you exceed this amount of iodine long-term. And it's not a good idea to use SSKI for long-term maintenance, since it's not "balanced" with both iodide and iodine. SSKI is available by prescription (through compounding pharmacies) and over-the-counter as "Tri-Quench" from natural food stores and the [Tahoma Dispensary](#). Lugol's iodine is available only by prescription, but Iodoral tablets and i-Throid capsules contain exactly the same amount of iodine and iodide as Lugol's and both are available from all three sources listed above.

Boost your protection with Brussels sprouts

If your 2/16 ratio is too low, you can often bring it into the normal range simply by eating more vegetables from the Brassica family (also known as cruciferous or mustard family vegetables). Broccoli, cauliflower, cabbage, Brussels sprouts, bok choy, mustard greens, and kale are all

good options. These foods contain natural substances which shift more estrone towards 2-hydroxyestrone and away from 16-alpha-hydroxyestrone. Flaxseed and soy also help this metabolic shift.

Supplemental indole-3-carbinol (I3C) and di-indolylmethane (DIM) can also raise the 2/16 ratio. But it is possible to “overdose” on I3C or DIM. In some people, more than a little of these supplements can shift so much estrone away from 16-alpha-hydroxyestrone that not enough estriol is produced to maintain a healthy EQ. In that case, you need to reduce your dose of DIM or I3C. (And just to put your mind at ease, an abnormally elevated 2/16 ratio is quite rare except in cases of I3C or DIM excess.)

The simple switch that makes a big difference

One of the most common causes of high estrone (E1) is oral supplementation of DHEA: If you’re taking oral DHEA by swallowing a capsule, the DHEA will frequently show up as high E1 on the 24-hour urine test. But if you switch your DHEA supplement to a transdermal or transmucosal crème (which is Nature’s preferred delivery route), this effect almost always vanishes. (And, even better, DHEA is much more effective this way.)

Specific supplements to consider

Since 4-hydroxyestrone is the most potent estrogenic carcinogen (and precursor of carcinogens), you definitely want as little of it as possible. And the best solution for lowering an elevated 4-hydroxyestrone level is to use “methyl-group-donating” supplements to raise levels of the very potent anti-carcinogenic estrogen metabolite, 2-methoxyestradiol. As 2-methoxyestradiol goes up, 4-hydroxyestrone usually goes down. These supplements include the methylcobalamin form of vitamin B12, the methylfolate form of folate/folic acid, S-adenosylmethionine (SAME), betaine, and glutathione.

Follow-up testing—usually in two to three months—will tell you if these or any of the other risk factors have been favorably affected.

Men: The ratios you need to balance for ultimate prostate protection

Now that we’ve covered increased cancer risk factors—and solutions—for women, let’s talk about similar factors for men using BHRT. The most recent “mainstream” research indicates that low testosterone levels increase a man’s risk of prostate cancer. As natural medicine doctors have been pointing out for decades, prostate cancer increases with declining testosterone levels (andropause). And estrogens may increase by up to 40 percent in men’s bodies during andropause. So suspicion is increasing that estrogens may be related to prostate cancer to a significant degree.

One specific area of estrogen-and-prostate-cancer research involves low 2/16 ratios in men. Even when the level of each individual estrogen is within the normal range, if they’re out of balance, there’s increased cancer risk. As noted above, increasing consumption of Brassica vegetables and flaxseed can also increase the male 2/16 ratio (though it’s likely best for men to avoid regular soy consumption because of its plant estrogen content). And research done right here in Seattle found that men who eat Brassica vegetables four times a week have 40 percent less risk of prostate cancer. DIM and I3C can be used if dietary changes aren’t sufficient to do the job.

The second risk factor men taking BHRT need to be aware of is a low androstenediol/DHT ratio (A/D ratio). You’ve probably heard of DHT and the potential problems it can cause. But you may not have heard about androstenediol. This substance is what testosterone eventually metabolizes into, “stopping off” as DHT along the way. But unlike DHT, androstenediol is anti-carcinogenic.

According to one logical (but as yet unproven) theory published in the *New England Journal of Medicine*, the reason there were fewer cancers overall but a higher percentage of significantly more aggressive cancers among men taking finasteride (a patent medicine which suppresses DHT) in the placebo-controlled “Prostate Cancer Prevention Trial” is that finasteride suppresses androstenediol even more than DHT.⁶ This would create an unfavorable A/D ratio, with less of

the anti-carcinogenic androstenediol and more of the pro-carcinogenic DHT—a situation parallel to an unfavorable 2/16 ratio. Because of this relationship, measurement of DHT alone is not as likely to be as accurate an indicator of cancer risk as the androsterone/DHT (A/D) ratio.

I work with many men who've been told that they have "too much DHT" without having their androstenediol measured, which gives them a likely-unnecessary cancer risk scare. Some of these men are told they "must" take finasteride or another similar patent medication, to lower the risk of prostate cancer—again, without any measurement of androstenediol to see what their A/D ratio is. When I ask men to have both these testosterone metabolites measured, the very large majority—with the notable exception of a few men taking the patent medicine finasteride and other patent medications with similar actions—have had an A/D ratio considerably greater than one, which indicates that they actually have less cancer risk, not more. Although the value of the A/D ratio is not "scientifically proven," it's every bit as logical as the 2/16 ratio, and so far there is no argument against this theory.

So what advice can I give for sure about testosterone and DHT? Never take any action based on measurements of just one testosterone metabolite—DHT—alone. Always have androstenediol measured, too, look at the A/D ratio, and discuss the meaning of all of the data with a physician skilled and knowledgeable in bio-identical hormone replacement. – JWV

Thanks to Leah Alvarado-Paz, ND, Terra Sowinski, ND, and Ronald Steriti, ND, PhD for their contributions to this article.

Citations available upon request and on the Nutrition & Healing website:

www.wrightnewsletter.com

[Learn More About Hormone Testing at Meridian Valley Lab](#)

Learn More About Dr. Wright's Tahoma Clinic in Seattle, WA