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# The 6 + 1 Principles of Hormone Replacement

Lisa Everett Andersen, B.Sc. Pharm, CCN, FIACP, FACA

*Note: This is a synopsis of these principles that does not include the detailed explanations and significant physiologic nuances enumerated in my book, *Learning to Thrive in a Toxic World and the Impact of Clinical Endocrinology and BHRT*, available by calling the pharmacy at 913-322-0001 and at [lisaeverettandersen.com](http://lisaeverettandersen.com).*

Whether in writing my book or developing a talk on hormones, I discuss what I used to call the 6 Principles of Hormone Replacement to improve the safety and efficacy of HRT over what has been prescribed for decades. Upon further analysis, however, I realized a very important factor: laboratory monitoring was left off my original list! So lately I have been presenting the 6 + 1 Principles of Hormone Replacement.

## **6 + 1 Principles of Bio-Identical Hormone Replacement Therapy (BHRT)**

### **1. Use only bio-identical (natural) molecules, duplicating the structure of the body's hormones.**

In every species, hormones have different molecular structures and perform different functions. Therefore, the first principle is to replace hormones with their molecular match. Bio-identical hormone replacement utilizes the exact molecules, made from plant sterol precursors, for our human specific biosystem, which is one of the ways they achieve hormone balance without many of the untoward reactions seen with synthetic molecules. Only bio-identical human hormones follow our normal metabolic pathways and can be broken down into other hormones and derivatives our bodies need. Synthetic hormones cannot be converted into those other vital steroids.

Synthetic hormone analogs, such as those found in

birth control pills, ethinyl-estradiol, and medroxyprogesterone acetate, do not naturally occur in humans. Neither does the ground up horse urine found in conjugated estrogens, like Premarin®. Hormone analogs usually are not as effective and can even have opposite effects from the bio-identical hormones. They have side effects such as high cholesterol, facial hair, acne, hair loss, migraine headaches, depression, anxiety, panic attacks, breast cancer, allergies or reactions to physiologic hormones, and heart issues. They also interfere with our natural immune system, resulting in stress-related diseases such as chronic fatigue, fibromyalgia, stomach disorders, and cardiovascular disease. Contrarily, these conditions can be favorably influenced by the functions of our own hormones.

Synthetic analogs often trigger the formation of antibodies, not only to those synthetic molecules, but can produce allergic reactions to other synthetic hormones, such as prednisone or methylprednisolone, as well as to our own steroid molecules, i.e. progesterone, testosterone, and estradiol.

But it isn't enough to just use bio-identical molecules: ignoring the next principle is a deal breaker.

### **2. Choose a dosage form that most closely mimics our body's distribution system.**

Clinically, this means utilizing a dosage form that avoids first pass through the liver, which is crucial when it comes to side effects, safety profile, and desired outcome. It also means avoiding dosage forms that deliver sub-therapeutic amounts to the bloodstream or make the hormones undergo fatty deposition and unwanted transformation prior to entering the bloodstream, i.e. topical skin applications.

Normally, glands like the ovaries, testicles, and adrenals

secrete hormones directly into the bloodstream where they circulate through the body and attach to receptor sites on every single cell of every tissue. Once the cells are finished with the hormones, the hormones leave the receptor sites and are carried in the bloodstream to the liver, where they are processed and prepared for elimination.

So to reiterate, the route is gland, bloodstream, cells, bloodstream, liver, elimination. Never do our glands secrete hormones directly into the stomach or intestinal tract and then shunt them to the liver as is the case with every oral dosage form, even if they are bio-identical. Oral hormones go into the liver via the portal circulation. Invariably, 90% undergo metabolic changes, most of which are not only harmful but are responsible for the “bad rap” that HRT endures, and only 10% of the original hormone makes it into the bloodstream.

Our hormones are also not introduced through the skin where a large portion becomes enzymatically transformed into other molecules and then trapped in the subcutaneous layer of fat cells, which is what happens with topical creams, ointments, and gels. However, when these are applied to mucous membranes, such as those of the vagina, they are well absorbed.

Injections and implanted pellets are typically deposited in muscles and the fat just under the skin, where they are metabolized into other unwanted hormonal molecules. For instance, with the testosterone injections used in men, laboratory testing confirms that much of the testosterone is converted to estrogen, unmasking estrogen levels that are through the roof (often, this goes undetected by practitioners because they are only ordering testosterone levels and not complete hormone panels). When pellets are deposited into skin, they are subject to the same enzymatic transformation and deposition that happens with topical applications. Pharmacokinetic studies show us that these dosage forms produce a big initial hit of the hormone which slowly slips downhill as it peaks and wanes, resulting in noticeable rollercoaster levels in the brain, heart, and other tissues. Injections and implants take days, sometimes weeks, to leave the system, causing a delay in resolution of side effects. Plus, one cannot get a full complement of hormones with these dosage forms, i.e. estradiol and testosterone are the only hormones

offered in pellets and injections are single hormone dosages, requiring more prescriptions for broader hormone coverage. We are not cattle and are capable of managing the administration of our hormones on a daily basis and without being tied to a doctor’s office visit for our next implantation.

If one doesn’t mind a bit of messiness, pessaries (vaginal suppositories), creams, and ointments have better pharmacodynamics, multiple hormone delivery, and are well absorbed. However, women often find them to be inconvenient as they make dose cycling and travel difficult due to dose timing and temperature regulations, i.e. one must remain supine for 20-30 minutes to absorb the hormones from a pessary, as it will discharge due to gravity before it can be taken up. They can also disrupt the vaginal flora, causing yeast infections. Rectal suppositories are also well absorbed, however, some women experience uncomfortable flatulence and rectal/anal yeast infections.

In order to address the problems associated with other dosage forms, French troches were adapted for systemic bio-identical hormone replacement. Due to their superior absorption, bioavailability, multiple hormone delivery, and metabolism, troches allow a higher percentage of the desired hormones to reach the bloodstream, enabling lower doses to be employed. For instance, with regard to progesterone, a 200mg troche equals a 400mg vaginal/rectal dosage form in terms of blood/tissue levels. Troches dissolve between the upper cheek and gum over a period of about 20 minutes, gradually releasing the hormones into the capillary bed of the gum tissue and the cheek cells, resulting in the most consistent natural blood levels. The troche emulates our body’s mechanism by delivering hormones into the general circulation without first passing through the liver, or being converted, or depositing into fat cells. This allows for hormone replacement without the liver induced side effects of blood clot formation, hypertension, and gallbladder/liver disease that happen with oral dosage forms.

Unlike many commercial hormones and dosage forms, bio-identical troches are efficiently recognized, utilized, metabolized, and excreted. They only have a half-life of 6-8 hours and clear the bloodstream in 8-15 hours, making it necessary to dose every 12 hours. This allows



for rapid dosage adjustments with quick resolution of sensitivities, etc. They are also convenient, easy to take, and multiple hormones can be combined into one troche, making it possible to receive a full compliment of BHRT with one prescription. Troches are the most effective dosage form with the fewest side effects (other than intravenous administration) to date. The compounding pharmacist can work with the patient and the practitioner to create a troche that is customized and addresses pharmacogenetic and hormonal individuality.

### **3. Preserve the delicate balance.**

Conventionally, clinicians have been taught that menopause is all about estrogen and andropause is all about testosterone, but estradiol and testosterone are just part of the story. Our bodies produce and use many hormones that work synergistically. Every cell has receptor sites for every single hormone produced by the body. As we age, hormone levels fall together, with the exception of cortisol. To preserve the balance as we embark upon BHRT, it is important to replace all hormones that are low, not just one or two. By the same token, it should not be assumed that every hormone needs to be replaced or augmented or that giving a precursor hormone will yield down stream molecules when certain glands and organs are no longer able to respond. Additionally, precursor hormones cannot be converted to other molecules in the presence of nutritional deficiencies coupled with the common toxic levels of hormonal disruptors, such as plastics, herbicides, and pesticides due to the consumption of meat, dairy, and eggs.

The symptoms of aging are due, in part, to the oxidative damage and the reduction in mitochondrial performance that are secondary to the drop in sex and adrenal hormone levels. Estrogens, progesterone, testosterone, DHEA, and others normally exist together in a delicate balance to promote normal functioning. They work in tandem, in a dictated order, and in opposition to signal physiological homeostasis.

If only one or two hormones are offered for HRT and others are deficient, cellular and mitochondrial receptor sites for other hormones will pick them up due to their similar molecular structures and because they are the only

ones present. This has helped to induce the untoward outcomes of HRT over the years along with the lack of adherence to the physiologic laws of pharmacokinetics (inappropriate dosage forms, molecules, timing, etc). Without balancing hormones, tissues become over-stimulated and produce too many cells, leading to cellular changes and even tumor growth, lack of receptor site accessibility to the molecule because they are not primed, diminished response, etc. It is most advantageous when all the hormones that are low are supplemented, especially the non-hormone, melatonin, which also falls with age and the oxidative stress induced by chemical exposures.

### **4. Customize the dosage to the individual!**

In my opinion, HRT was the worst place to apply “one size fits all” medicine. Our endocrine glands are how we are anchored into our bodies via the energy centers known in Sanskrit as the chakras. They translate our unique expression of Life Force into the physical being. Our hormonal signature is like our thumbprint. So, the type, amount, and ratio of each hormone administered must be based on the personality, severity, and type of symptoms, lifestyle, stress, body type (i.e. apple or pear shaped), genetic polymorphisms, health goals, and familial and personal history (medical and social) of YOU, and in the context of laboratory data. Additionally, each person is different in his or her need, production, and metabolism of hormones. With broad spectrum monitoring, practitioners can effectively make dosage adjustments accordingly.

### **5. Eat a plant based diet with as few xenobiotics and endocrine disruptors as possible and rich in organic fruits and vegetables.**

Eating 4-6 servings each of organic fruits and vegetables a day is a good start in providing the nutrients required for the safe and effective utilization of all hormones. But most notably for our hormonal and over-all health, organic plant foods have lower concentrations of the endocrine disruptors that compete with our own molecules for hormone receptor sites on every cell, especially those of the breasts, prostate, uterus, and ovaries. Animal products, be they organically, grass finished, or conven-

tionally produced, are high in endocrine disruptors in the form of pesticides, herbicides, artificial hormones, xenobiotics, as well as their own powerful endogenous hormones which negatively affect our hormone balance and jeopardize our hormone safety and over-all health. These disruptors are not only carcinogenic and trigger inflammatory conditions and weight gain, but as hormones, they are many times more potent than our bio-identical ones and they protect toxins. So to get the most out of your bio-identical HRT, quit getting your most potent HRT out of MEAT, DAIRY, AND EGGS!

## **6. Take therapeutic multi-vitamins and minerals.**

The proper absorption, cellular uptake, metabolism, and utilization of hormones depend on adequate levels of vitamins, minerals, fatty acids, and antioxidants that are not sufficiently present in the American diet. Inadequate nutritional status can lead to an incomplete breakdown of hormones and the accumulation of undesired metabolites. Hormone receptor sites need nutritional cofactors to transport hormones into the cells and mitochondria where they do their work. Supplementing with these nutrients creates the fertile environment we must have for BHRT to work more effectively and safely. The standard one-a-day is quite inadequate in meeting the therapeutic doses of vitamins and minerals.

Plus 1: Use valid & appropriately timed monitoring.

Once proper BHRT is established, it is of utmost importance to monitor the patient's change in symptoms and blood levels. Years of obtaining wisdom and clinical experience certainly lend themselves to developing the correct hormone formula fit for an individual, but sometimes it's still just not quite "right." Plus, as people age, go through stressful situations, develop health conditions, initiate drug therapies, etc. their hormone needs change. Patients are making the most of their therapy when they stay in touch with their practitioner with any developments and have hormone labs run when needed.

There are some rules to laboratory monitoring of sex hormones. First and foremost, only serum labs will do. Saliva and urine labs do not cut it. I could write an entire article on this subject alone, so for this one, I'll refer you to my book for the MANY reasons I say this and for

more pertinent history and valuable details. The second rule is the blood must be drawn 1/2 way between the first dose and the next, like for any other medication. So if you dose the hormone only once over 24 hours, then the laboratory sample needs to be taken at approximately 12 hours after the dose. If the dose is taken every 12 hours, then the sample needs to be taken 6 hours post the regular morning dose. This provides an average of the peak and trough levels in the blood over the dosing period. In my experience, many doctors pay little attention to this law of pharmacodynamics, which results in false outcomes. If blood is drawn too far away from the half-way point, the numbers will look abnormally low (time for the next dose) or abnormally high (the bulk of the dose just hit the bloodstream). If a woman is cycling, there is yet another rule: have the labs drawn on day 21 of her cycle. When a woman cycles, her hormones naturally fluctuate, and we want to capture "high tide" numbers, which typically occur around day 21 to indicate the "best case scenario" for what is happening during the cycle. If these are low, then the likelihood is that the rest of the month the levels are even lower, causing discomfort.

There is a fourth rule, but this one pertains to understanding today's reference ranges offered on lab work. It is important for a practitioner to recognize that the reference ranges of today's laboratories are based on averaging levels of people who are sick, nutrient deficient, taking oral contraceptives and drugs, and bursting with xenoestrogens. The goal is to restore hormones to optimal levels, not today's sub-optimal reference ranges, so we need to use the healthy reference values from before World War II, when our food, water, and air weren't so terribly polluted with endocrine disrupting chemicals.

Rule five is test for all of the primary sex hormones: DHEA unconjugated, total testosterone, progesterone, estradiol LC/MS/MS, estrone LC/MS/MS, DHT, and pregnenolone, etc. (In my book, I discuss why free testosterone is not useful for initial screening.) If only one or two hormones are tested, we cannot evaluate if the proper conversions of multiple hormones are happening. Again, due to the invasion of pesticides, herbicides, and other toxins, it has also become irrelevant to run some hormone tests, such as total estrogens, as they not only count the



endogenous estrogens but also the exogenous environmental chemicals that mimic estrogens.

Without an understanding of the principles, many patients and their prescribers who have struggled with hormone replacement have not been able to ascertain where they “went wrong,” even if they chose bio-identical molecules. They often believed the therapy didn’t work or was to blame for continued or exacerbated symptoms. These principles are key to accomplishing successful hormone replacement. By following the 6 + 1 Principles of healthy hormone replacement, we can minimize health risks and enjoy the physical and emotional well-being that a balanced endocrine system can offer.

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