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Bioidentical Hormone Replacement Therapy *for* Women, Part I

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In the U.S., at least 40 million women are currently experiencing menopause, and an additional 20 million women will reach menopause during the next decade. Treatment of menopause includes hormone replacement therapy (HRT), which is a topic that has gained national and international prominence in recent years. Today, Bioidentical HRT (BHRT) is rapidly becoming more widely used and has been in the press extensively.

In the past, conjugated equine hormones (Premarin) and progestins (Provera) have been used in HRT. Conjugated hormones are extracted from the urine of pregnant mares, a natural source, similar to the way insulin was extracted from pigs and cows, and thyroid supplements were originally extracted from pigs. However, with genetic modification, insulin is now prepared to be "identical" and is "human insulin," thyroid is now levothyroxine and triiodothyronine, and the conjugated equine hormones are being replaced with "bioidentical" estradiol, estrone, and estriol, as well as progesterone and testosterone being commonly used. Table 1 illustrates the progress that has been made.

TABLE 1. Progress Made in Bioidentical Drugs.

HORMONE	SOURCE	REPLACED BY BIOIDENTICAL
Insulin	Pigs, Cows	Human insulin
Thyroid	Pigs	Levothyroxine/ Triiodothyronine
Conjugated estrogens	Mare's urine	Estradiol, estrone, estriol

Bioidentical hormone dosage forms are both manufactured and compounded. They are identical to those produced by the human body and should cause fewer adverse effects than do their synthetic counterparts, if dosing is properly prescribed for each patient. Examples of manufactured BHRT include Estragel, Prometrium, and Androgel.

Over the past 15 to 20 years, practitioners have quietly prescribed natural forms of BHRT (estrogen, progesterone, testosterone). One problem is that many have been led to believe that menopausal symptoms can be alleviated only by patented pharmaceuticals (Premarin, Provera); which is not true. BHRT treatments have included the use of various compounded hormone creams, capsules, troches, and sublingual drops, as well as manufactured oral and patch-delivery hormones. The common theme is that BHRT is identical to hormones produced in the human body, and the doses are often individually tailored to the biochemical individuality of the patient. Anecdotally, BHRT has been well tolerated with good long-term compliance and efficacy. It has been suggested that women who are trying to access BHRT are motivated by three key factors: (1) adverse symp-

toms of menopause, (2) concerns with side effects of conventional synthetic hormone therapy, and (3) personal preferences.

Symptomatology

Symptoms that can occur from too much or too little of the estrogens or progesterone are listed in Table 2. As an example of the advantages of BHRT, in one study, before treatment, 52% to 70% of women complained of moderate-to-severe symptoms of hot flashes, night sweats, sleep problems, dry skin/hair, vaginal dryness, foggy thinking, mood swings, and decrease in sex drive. After BHRT initiation, these symptoms dropped to between 4% to 20%. The most commonly reported side effects with BHRT were weight gain, breast tenderness, and bloating. Symptoms or side effects can occur with both conventional and bioidentical HRT; example frequencies of their occurrence are listed in Table 3.

Safety

Bioidentical hormones are considered by many to be safer and more effective than conjugated equine estrogens (Premarin) and medroxyprogesterone acetate (Provera). Premarin does provide relief from hot flashes and urogenital symptoms, but it is a nonhuman formulation. It consists of about 11 compounds, each of which is further broken down and metabolized into several other compounds. One ends up with a large mixture of estrogens circulating through the body that, although having some benefit, they also exert other effects that are not well defined and may be harmful. In addition, one cannot monitor the level of Premarin because it is a complex mixture.

BHRT levels can be measured, as they are dosed individually and adjusted after the initiation of therapy to accurately determine the level of that hormone in the blood. This allows physicians to know if the dose is insufficient or excessive.

Given the results of the Women's Health Initiative (WHI) study, many women reconsidered their decision to continue treatment with conventional HRT; some terminated therapy abruptly, and others opted for BHRT. BHRT is "natural" because these hormones are identical to the hormones that are produced "naturally" in the body. In addition, the doses and dosage forms can be easily and conveniently tailored to the patient.

The Writing Group for the WHI concluded that: "...transdermal estradiol and progesterone, which more closely mimic endogenous hormones when used in replacement therapy, may have more favorable outcomes as compared to conjugated equine estrogens and medroxyprogesterone acetate".

There has been good evidence for many years that progesterone is a safe hormone and that it should be the preferred progestin for use in hormone replacement. Progesterone can be effectively administered orally, transdermally, intravaginally, sublingually, and parenterally. Progesterone is absorbed by the gastrointestinal tract (although it does undergo some first-pass metabolism), and it works very well when applied in a cream to the trunk or the arms.

Therapy and Prescribing

The foundation of optimal women's health begins with balance: a wholesome diet, exercise, stress management, sleep, and, as appropriate, nutritional supplements and natural or bioidentical hormones. There is no single dose or approach to natural hormone balance that fits every woman. Women should work with their healthcare professional that is knowledgeable about hormone balance to determine whether supplemental hormones are needed.

To assist in prescribing, conversion data going from conjugated estrogens and medroxyprogesterone acetate to BHRT is shown in Table 4. For menopausal patients, example starting doses are provided in Table 5; example starting doses for post-menopause are shown in Table 6.

TABLE 2. Examples of Symptoms With and Without Estrogen and Progesterone.

LACK OF ESTROGEN	LACK OF PROGESTERONE
Hot flashes	Headache
Shortness of breath	Low libido
Night sweats	Anxiety
Sleep disorders	Swollen breasts
Vaginal dryness	Moodiness
Dry skin	Fuzzy thinking
Anxiety	Depression
Mood swings	Food cravings
Headache	Irritability
Depression	Insomnia
Memory loss	Cramps
Heart palpitations	Emotional swings
Yeast infections	Painful breasts
Vaginal shrinkage	Weight gain
Painful intercourse	Bloating
Inability to reach orgasm	Inability to concentrate
Lack of menstruation	Early menstruation
	Painful joints
	Asthma
	Acne
EXCESSIVE ESTROGEN	**EXCESSIVE PROGESTERONE**
Water retention	Depression
Fatigue	Somnolence
Breast swelling	
Fibrocystic breasts	
Premenstrual-like mood swings	
Loss of sex drive	
Heavy or irregular menses	
Uterine fibroids	
Craving for sweets	
Weight gain	

TABLE 3. Reported Side Effect Incidences of Compounded BHRT and Conventional HRT.

SYMPTOM	BHRT	CONVENTIONAL
Breast tenderness	19.2%	54.5%
Breakthrough bleeding	16.6%	23.6%
Weight gain	37.2%	56.4%
Mood swings	5.1%	36.4%
Bloating	23.1%	40%
Difficulty sleeping	16.6%	30.1%
Headaches	6.4%	27.3%
Fluid retention	15.4%	30.1%
Upset stomach	3.8%	11%
Drowsiness	6.4%	5.5%
Leg pain	5.1%	11%

TABLE 4. Approximate Conversion Doses from Non-bioidentical to Bioidentical Estrogens and Progesterone.

CONJUGATED ESTROGENS	TRI-EST	BI-EST
0.3 mg	1.25 mg	1.25 mg
0.625 mg	2.5 mg	2.5 mg
1.25 mg	5 mg	5 mg
MEDROXYPROGESTERONE	**PROGESTERONE**	
2.5 to 5 mg	100 mg	
10 m	200 mg	

Note: Tri-est consists of estriol, estrone, and estradiol; Bi-est consists of estriol and estradiol.

TABLE 5. Example Starting Doses in Menopause

Tri-Est or Bi-Est	1.25 to 2.5 mg twice daily
Progesterone	50 mg to 200 mg twice daily
Testosterone	0.25 to 2 mg daily

TABLE 6. Example Starting Doses in Post-menopause.

Tri-Est or Bi-Est	0.625 to 1.25 mg twice daily
Progesterone	25 to 100 mg twice daily

Dosage Forms

There are many different formulations and dosage forms that are available from your compounding pharmacist; also, the patient can provide valuable input on what fits best with their lifestyle, which will enhance compliance. Example dosage forms are provided in Table 7 and can be individualized for specific patients.

References

Available upon request from www.ijpc.com.

TABLE 7. Example Formulations for BHRT Administration.

ORAL
Capsules/Tablets/Liquids
Oral Troches/Lozenges
TOPICAL/TRANSDERMAL
Transdermal Gels
Transdermal Creams
Transdermal Solutions
PARENTERAL
Injections
OTHER
Vaginal Suppositories/Inserts

