

# *Answers to Your Questions on Bioidentical Hormone Therapy*

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## *Question #1:*

### *What is bioidentical hormone therapy?*

There is no real scientific definition for bioidentical hormones, because this term originated as a marketing term. Bioidentical hormone therapy refers to the use of any hormone that is “identical in molecular structure to human hormones.”<sup>1</sup> These include the use of estrogens such as estradiol, estrone and estriol, micronized progesterone, testosterone and DHEA. Bioidentical hormones are available in many commercial hormone therapy (HT) products that have been approved by Health Canada, as well formulations that are compounded by pharmacies that specialize in compounding. Bioidentical hormones found in commercial HT products include 17  $\beta$ -estradiol (oral, patches, gels, vaginal products), estrone (vaginal cream) and micronized progesterone.

## *Question #2:*

### *What is compounded BHT?*

Compounded BHT (cBHT) products are hormone therapy formulations which are prepared by a pharmacy specializing in compounding. Any of the bioidentical hormones can be compounded to provide a variety of doses and administration routes such as oral, transdermal creams, or vaginal products. There is a role for compounding as it can provide delivery formulations or doses that may not be commercially available. However, the issue is the way cBHT is sometimes promoted as being better tolerated or

safer than commercial HT. Unfortunately it is difficult to support these claims without further evidence.

The most commonly promoted cBHT products include the use of bioidentical hormones, formulations or combinations that are not currently found on the Canadian market, such as the use of estriol or compounded progesterone creams. Sometimes testosterone and/or DHEA also are added to the regimen. Estriol usually is compounded as a formulation in combination with other estrogens, particularly estradiol. Bi-Est, the most popular, is available as either as an 80:20 or 50:50 ratio of estriol to estradiol. Tri-Est, another common formulation, is estriol with estradiol and estrone (in a ratio of 80:10:10).

*Estradiol* is the most biologically active of the estrogens, followed by *estrone* (one-third the activity), then *estriol* (approximately 1/80<sup>th</sup> potency). Estradiol, produced by the ovaries, is the predominant circulating estrogen during the reproductive years (before menopause). After menopause, estrone is the predominant estrogen. Estriol is a metabolite of estradiol and estrone. As it is produced by the placenta, the highest amounts are found during pregnancy. *Estriol*, the weakest and shortest acting of the estrogens, is commonly included in cBHT formulations and is often claimed (as having) to have less breast cancer risk than the other estrogens. However, there is no clear evidence that it is safer compared to other estrogen formulations (see question #4 regarding safety).<sup>2</sup> As the result of the way these products are marketed on the internet and also endorsed by celebrities, there are many misconceptions about the greater safety and benefits of cBHT over commercial HT<sup>3</sup>

### Question #3:

#### Is cBHT natural?

One common misnomer is that cBHT is “natural” as this is often the way it is promoted.<sup>3</sup> Even though the initial compounds are extracted from plant-based sources such as soy and Mexican yam, they are then chemically converted or synthesized to the same

molecular structure as human hormones. It is worth noting that the same or similar sources are used in the production of most commercial hormones. There are no bioidentical hormones that can be considered completely natural. Furthermore, the use of the word “*natural*” often gives the connotation that a product is in some way better for the human body. However, being natural does not guarantee it is safe.

#### Question #4:

##### *Is cBHT safer than CHT?*

There are many misperceptions about cBHT including that it is more efficacious and safer than commercial HT (CHT) products. With respect to safety, the lack of evidence from “direct head to head studies” (i.e. directly comparing the two products one to the other) makes the answer to this important question difficult.

Unfortunately, many women continue to believe that cBHT is safer than commercial HT.<sup>4,5</sup> There is preliminary evidence that some benefits may exist with certain bioidentical hormones found in commercial HT products. For example, micronized progesterone taken orally may have better sleep, mood and possibly breast cancer outcomes as compared to synthetic progestins.<sup>6,7</sup> Additionally, transdermal formulations containing estradiol, are directly absorbed into the blood stream bypassing the liver i.e avoiding the “first pass effect” in the liver. As a result, transdermals may have less blood clot risk at low to standard doses compared to standard doses of oral estrogens.<sup>8</sup>

Claims of less breast cancer risk by cBHT proponents are especially misleading. Breast cancer with the use of HT is one of the greatest safety concerns expressed by women. This fear can drive women to use cBTH if they feel it is safer with regard to breast cancer risk. Estriol is often used in cBHT formulations because it is promoted as being safer for breast cancer. However there are no published peer reviewed data to support these claims.<sup>2</sup> In laboratory/experimental studies estriol has been shown to stimulate breast

cancer cells just as do other estrogens.<sup>9</sup> The claim that estriol may competitively inhibit estradiol binding on breast tissue thereby protect the breast, has not been proven in controlled trials.<sup>10</sup>

Many professional organizations such as North American Menopause Society, the Endocrine Society, the International Menopause Society, Society of Obstetricians and Gynecologists of Canada and SIGMA Canadian Menopause Society caution against the use of cBHT.<sup>2, 11-14</sup> Based on the currently available information, the known risks and benefits of hormones should be applied equally to all menopausal hormone therapies.<sup>12</sup>

### Question #5:

#### Is BHT more efficacious than HT?

This is an excellent question which unfortunately is difficult to answer because of a lack of scientific data and of quality clinical evidence from head to head trials comparing commercial HT and cBHT. A 2015, NAMS survey reported on more than 1000 women using menopausal hormone therapy, of whom approximately one third were using cBHT and 2/3 were using commercial HT.<sup>4</sup> The major indication for prescribing HT was the treatment of vasomotor symptoms, and both succeeded in providing relief. However, more women who were on commercial HT indicated improvement in vasomotor symptoms and vaginal dryness as compared to cBHT. Because of the small numbers, statistical significance was not calculated. Interestingly with respect to improved mood and “better sex” (i.e. improved libido/less pain), the score for cBHT was a bit higher than commercial HT (also not a statistically significant difference). The authors suggested that this may be an “androgen-related effect” in the cBHT population group, notably in those whose cBHT may have contained added testosterone or other androgens.

Question #6:

Is individualization or custom-tailoring with hormone testing beneficial?

Custom-tailoring of menopausal HT to the specific needs of an individual is certainly appealing, but not readily achievable because 1) the optimal level for each of the hormones has not been defined, 2) these hormones can fluctuate widely throughout the day, and 3) most importantly there are also individual differences between women's responses to hormone levels, which may be genetically predetermined. So rather than pre-determining a specific level to be achieved or a customized HT dose, instead we aim for a "clinical goal" i.e. we titrate the HT dose to achieve relief of the women's menopausal symptoms that are being treated. Current guidelines advise starting treatment at a low dose and increasing as needed to achieve symptom relief.<sup>12,14</sup>

Question #7:

What about salivary testing of hormone levels?

Measurement of salivary hormone levels is sometimes recommended by cBHT prescribers to help them adjust doses in order to provide a "balanced" product individualized for the woman. Scientific evidence to support this practice is lacking, however. Salivary hormone testing is unreliable and may have little correlation with symptoms. Dose adjustments of HT should be based on clinical symptoms.

Question #8:

What about the use of topical progesterone cream?

Progestogen is an important component in HT as it protects the uterine lining from overgrowth which is caused by estrogens and thereby also reduces the risk of uterine cancer. A number of progestogen products are commercially available in Canada, including *micronized progesterone*. Topical progesterone creams are also custom

compounded or sometimes sold in health food stores. Those using “*topical progesterone creams*” should be aware of two issues:

- 1) “***Mexican YAM Cream***” is NOT a progesterone product, although it may be sold as such. While it is true that Mexican yams are used as precursors for hormones that are used in the preparation of both commercial and compounded formulations, unfortunately the human body is not able to convert the precursors in yam cream to progesterone.
- 2) Secondly, the absorption of topical progesterone creams may be variable and unpredictable. This raises the concern that the absorption of topical progesterone cream may not be adequate to achieve the serum progesterone levels required to protect the endometrium that has been treated with estrogens.

**\*\*Therefore, use of transdermal progesterone creams is not recommended for the management of menopausal symptoms nor as part of an HT regimen. \*\***

*Question #9:*

*What about the use of testosterone and DHEA as part of the BHT regimen?*

There is no Health Canada approved testosterone product in Canada that has an indication for use in women. Many health care providers do provide testosterone to women when indicated (usually using a product approved for men at approximately 1/10<sup>th</sup> the dose). Nonetheless, treatment of women with testosterone products is considered ***experimental***. Women who are on testosterone should be carefully monitored clinically and should also undergo regular testing of serum testosterone levels to ensure overdosing is not occurring. Serum testosterone levels should not exceed the upper limit of normal for women.

In Canada, DHEA is a controlled drug available only on prescription. DHEA is commonly used in cBHT formulations. Unfortunately, neither the evidence for DHEA use in the treatment of menopausal symptoms nor its safety are clearly established. Current guidelines do not recommend the routine use of DHEA in post-menopausal women.<sup>15</sup>

### Question #10:

#### Is BHT an anti-ageing approach?

cBHT is sometimes promoted as an antiageing agent with the belief that it will restore hormone balance to levels found in a younger woman and that this will prevent long term health risks.<sup>3, 16,17</sup> In the NAMS 2015 survey, reasons for some women taking BHT included “prevent or control ageing” or “help with overall appearance”.<sup>4</sup> However, cBHT is **NOT** an agent to help with anti-ageing. There is no evidence that cBHT will prevent the normal ageing process. Presenting cBHT as part of anti-ageing regimen is solely a marketing tactic as it appeals to our society’s obsession with youth.<sup>18</sup>

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