

Answers to Your Questions on Bioidentical Hormone Therapy

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.”¹ 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 β -estradiol (oral, patches, gels, vaginal products), estrone (vaginal cream) and micronized progesterone.

Question #2: What are 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 1/80th 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).² 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 HT³

Question #3: Is BHT natural?

One common misnomer is that BHT is “natural” as this is often the way it is promoted.³ 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 BHT safer than CHT?

There are many misperceptions about BHT including that it is more efficacious and safer than commercial HT 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.^{4,5} 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.^{6,7} 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.⁸

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 in regards to breast cancer risk. Estriol is often used in cBHT formulations as it is promoted as being safer for breast cancer, however there are no published peer reviewed data to support these claims.² In laboratory/experimental studies estriol has been shown to stimulate breast cancer cells similar to other estrogens.⁹ The claim that estriol may competitively inhibit estradiol binding on breast tissue thereby protecting the breast has not been proven in controlled trials.¹⁰

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.^{2, 11-14} At this time, the risks and benefits should apply equally to all the menopausal hormone therapies.¹²

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 over a 1000 women using menopausal hormone therapy, of whom approximately a third of women were using cBHT and 2/3 were using commercial HT.⁴ 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 compared to cBHT. Because of the small numbers, statistical significance was not calculated. Interestingly with respect to improved mood and “better sex (improved libido/less pain). the score for cBHT was a bit higher than commercial HT (also not a statistically significant difference). The authors noted that this may be an “androgen-related effect” in the cBHT population group of those whose cBHT may have contained added testosterone and 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 determining a specific level to be achieved or customized HT dose rather we aim for a “clinical goal” i.e. the HT doses are titrated to 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.^{12,14}

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. However, scientific evidence to support this practice is lacking. 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 also reduces the risk of uterine cancer. A number of progestogen products are commercially available in Canada, including micronized progesterone. Topical progesterone creams can also be custom compounded or sometimes sold in health food stores. The use of “topical progesterone creams” requires awareness of two issues:

- 1) The use of “**Mexican YAM Cream**” is NOT a progesterone product, although it may be sold as such. Although Mexican yams are used as precursors for hormones that are used in both commercial and compounded formulations, unfortunately the human body cannot convert the precursors in yam cream to progesterone.
- 2) The absorption of the topical progesterone cream may be variable and unpredictable. There is concern that the absorption of topical progesterone cream is not able to achieve the serum progesterone levels needed to adequately protect the endometrium when used with estrogens.

Use of transdermal progesterone creams is not recommended for 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 1/10th 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, the evidence for use of DHEA for menopausal symptoms is not clear. At this time, guidelines do not recommend the use of DHEA routinely in post-menopausal women.¹⁵

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.^{3, 16,17} In the NAMS 2015 survey, reasons for some women taking BHT included “prevent or control ageing” or “help with overall appearance”.⁴ 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 is solely a marketing tactic as it appeals to our society’s obsession with youth.¹⁸

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