

# BIOIDENTICAL HORMONE PELLETT THERAPY FOR WOMEN

AW Aesthetics and Wellness is committed to helping women restore and maintain vitality and well being through natural and safe hormonal solutions. We chose to partner with Biote to give a high quality treatment. Being proactive by supplementing hormones in the early stages of hormonal decline is key to maintaining health and vigor as we age [1,17]. We choose to prescribe bioidentical hormones, meaning they are the same molecular structure as the body's natural hormones. Bioidentical hormones are available in variety of formulations, although we chose to use subcutaneous hormone pellets, due to it being the superior choice.

## What is Bioidentical Hormone Pellet Therapy?

For women, hormone pellet therapy is considered a superior method of hormone delivery. With this unique system, 2-3 small pellets consisting of testosterone or estradiol, each about the size of a grain of rice, are inserted beneath the skin, into the fatty tissue of the hip, and the pure hormone is delivered gradually, directly into the bloodstream. The simple in-office procedure takes only a few minutes, first with numbing of the skin, and one tiny incision that only requires a small steri strip, no stitches.

The subcutaneous pellets act as a reservoir of hormones, allowing the body to receive a consistent dose throughout the day and night. The pellets gradually absorb until they are completely dissolved, leaving no residue. Typically, a woman will find that pellets will control symptoms for 3-4 months. Because of the efficient and gradual delivery system of the hormone pellets, side effects are less likely than with oral or injectable hormones, and there is less incidence of issues related to poor absorption, sometimes problematic with hormone creams, gels, or patches.

Bioidentical hormone pellets are FDA monitored, but not approved in the United States. Hormone pellet therapy has been used in both men and women for decades in Europe and Australia, and this has allowed for the generation of ample scientific data regarding the benefits and safety of this method. Hormone pellet therapy is being used more and more in the US, as women seek a more convenient and natural way to receive their hormone therapy.

## What Hormones Can Be Administered with Female Hormone Pellet Technology?

### Testosterone Pellet Therapy

Testosterone is a vital hormone in women, eliciting physiologic effects through androgen receptors in almost all female body tissues, including breast, heart, blood vessels, intestines, lungs, brain, spinal cord, nerves, bladder, uterus, ovaries, endocrine glands, vaginal tissue, skin, bone, joints, and fatty tissue. Men produce higher circulating levels of testosterone than women; however, testosterone is the most abundant active sex hormone in a woman throughout her lifespan [2]. Testosterone has been considered a “male hormone”, thus largely ignored as an essential hormone in female physiology. This has been unfortunate, since attention has not been given to diminished quality of life and potential health consequences when women begin to experience symptoms related to testosterone decline in mid life. In a woman’s body, production of testosterone peaks in her mid 20’s and begins to steadily decline, down to about 50% by age 40. This is when a woman will often present with complaints such as increased abdominal fat, hair loss, fatigue, brain fog, loss of sex drive, reduced orgasm, anxiety, irritability, depression, headaches, and general lack of well-being. Most women attribute these symptoms to a natural diminishment of vitality with aging. But, recognizing these symptoms are signaling something about our bodies, and giving attention to hormone health can improve our health and quality of life as we age.

Testosterone replacement therapy for symptomatic women has the potential to improve mood, libido, orgasm, energy level, and feeling of well-being. In addition, documented health benefits include reduced cardiac risk, reduced breast cancer risk, and improved bone density. Testosterone therapy can be beneficial for symptomatic individuals as early as a decade or more before onset of the menopause transition [5,6,7,8,9,14].

It is important to note that in both men and women, testosterone can be converted within the body’s tissues to estradiol, some of which is not measurable, as conversion takes place within cells where it immediately binds with its receptor. Interestingly, it has been demonstrated that breast cancer survivors using testosterone pellet therapy, combined with medication that blocks conversion of testosterone to estradiol, reported relief of menopausal symptoms with testosterone therapy alone [14]. Thus, for some women, testosterone pellet therapy will be all that is required to control symptoms. For others, the addition of estradiol and progesterone will be of benefit. Each woman will be individually evaluated, and appropriate options considered.

## **Estradiol Pellet Therapy**

Estradiol is the estrogen hormone that makes a woman look female and governs much of reproductive function. This hormone also plays a role in countless bodily functions, as evidenced by estradiol receptors found in the heart, brain, bones, joints, skin, eyes, teeth, gums, nerves, blood vessels, urinary tract, reproductive organs, and more. So, with estradiol depletion, a woman suffers the loss in countless ways, with deterioration of physical, mental, and emotional health that accompanies hormonal decline. Typically, a

woman's estradiol level starts to decline in her 40's, and is almost undetectable by her early 50's.

Estradiol replacement therapy relieves symptoms such as hot flashes, night sweats, insomnia, brain fog, moodiness, depression, vaginal dryness, painful intercourse, low libido, dry skin, and headaches. Health benefits from non-oral estradiol supplementation include reduced risk of cardiac disease and stroke, dementia, diabetes, and loss of bone density leading to osteoporosis [4,5,6,9,10,11,12].

## What are Risks and Side Effects of Hormone Pellet Therapy for Women?

Hormone pellet insertion is a low risk procedure. A small percentage of women may experience a procedure related issue, such as infection, bleeding under the skin, or transient discomfort. Below is a discussion of potential risks and side effects related to the hormones of which pellets are composed.

Testosterone. Significant health risks of bioidentical testosterone therapy in women have not been identified. Any adverse health risk data you may have heard about would more likely be related to a synthetic oral drug called methyltestosterone, the only FDA approved testosterone available for females in the US, and a very different compound than bioidentical testosterone. Unfortunately, when disease risk related to hormone therapy is reported, authors commonly lump all "hormones" into one big pile, seemingly not recognizing that synthetic formulations are often much more potent, are not biochemically identical to each other or to our own natural hormones, and have different effects on the body than our natural hormones. Current data specifically regarding bioidentical testosterone formulations in women have not shown increased risk in cancer, cardiovascular disease, or other serious condition. In fact, numerous scientific studies suggest non-oral bioidentical testosterone may be breast protective, as well as protective of the heart, bones, and brain. [3,4,5,6,7,8,9]

Testosterone pellet therapy is well tolerated; the majority of women report no side effects. A small number experience facial hair or acne, both of which can be managed by reducing the dose, or another specific solution. Often, the women who experience these side effects prefer to manage the issue rather than reduce their dose, a fact that reveals their satisfaction with therapeutic benefits received with testosterone therapy. [13]

Estradiol. There has been much controversy and fear surrounding estrogen replacement therapy. Concerns about risk were largely generated from a 2002 study, the Women's Health Initiative (WHI), which reported a small increase in breast cancer and cardiac risk. However, this study examined only one form of hormone, a 100% synthetic brand

(Premarin+Provera), *not* a bioidentical hormone formulation. In addition, close analysis of the WHI, plus subsequent studies, have revealed the increase in cardiac risk was related to the fact that subjects had initiated hormone therapy in their mid 60's, well past the menopausal transition, and they likely had pre-existing coronary artery plaques. It is now agreed among experts that if estrogen therapy is initiated early, within a few years of the menopausal transition, it is protective of the cardiovascular system, reducing development of coronary plaques, reducing inflammation, and lowering mortality. As for breast cancer, the WHI subjects who had increased incidence were taking a combination pill of synthetic estrogen (Premarin) + synthetic progestin (Provera). However, the subjects given estrogen with no progestin had *reduced* incidence of breast cancer. This and other studies demonstrates that the *synthetic progestin* component (not the estrogen component) of this particular hormone treatment seemed to be the responsible agent for breast cancer risk observed [15,16,17]. In contrast, bioidentical progesterone is not associated with any health risk, and is safe to use alone or in conjunction with bioidentical estrogen.

Estradiol pellet therapy is well tolerated and convenient. Upon initiation, some women report transient breast swelling and tenderness, which if persistent can be managed with reduction of dose. Uterine bleeding is sometimes a transient issue, and there are often simple, nonsurgical solutions to manage this. A few women will have fluid retention with estradiol therapy, which can be managed by lowering the dose, or using a mild diuretic.

## Consultation and Evaluation for Hormone Pellet Therapy

Completion of the Female Hormone Pellet Therapy Consultation will involve full symptom discussion and evaluation and a panel of laboratories for baseline hormone levels plus other indicated labs. Hormone Pellets may be inserted during the second visit after a discussion of lab and ultrasound results.

## Fee for Hormone Pellet Therapy for Women

Generally, health insurance will cover the cost of office visits and laboratory tests for evaluation of hormone related symptoms. However, insurance will not cover compounded bioidentical hormone pellets or the pellet insertion procedure.

The fee for female hormone pellet therapy (including the procedure and the pellets themselves) is \$375.00. The cost works out to approximately \$3.00 per day, depending on how often new pellets are needed (typically every 3 to 4 months). When one considers the amount that may be saved on medications for sleep, depression, anxiety, elevated cholesterol, diabetes, and osteoporosis, plus benefits to quality of life, relationships, and job performance, the cost of pellet therapy is well worth it.

## References Related to Testosterone, Estrogen, and Pellet Implant Therapy

1. Turner R, Kerber IJ. A theory of eu-estrogenemia: a unifying concept. *Menopause*, Vol. 24, No. 9, pp. 1086-1097. ***“Estrogen action through Estrogen Receptors is critical for homeostasis in women and men. Considering there are more than 3,600 ubiquitously distributed Estrogen Receptors and signaling pathways, it is biologically naive to conclude that estrogen, with its complex genomic and nongenomic actions, should be deficient from a menopausal woman’s body.”***
2. Glaser R, Dimitrakakis C. Testosterone Therapy in Women: Myths and Misconceptions. *Maturitas*, 2013 Mar;74(3):230-4. ***Abstract: “Although testosterone therapy is being increasingly prescribed for men, there remain many questions and concerns about testosterone (T) and in particular, T therapy in women. A literature search was performed to elucidate the origin of, and scientific basis behind many of the concerns and assumptions about T and T therapy in women. This paper refutes 10 common myths and misconceptions, and provides evidence to support what is physiologically plausible and scientifically evident: T is the most abundant biologically active female hormone, T is essential for physical and mental health in women, T is not masculinizing, T does not cause hoarseness, T increases scalp hair growth, T is cardiac protective, parenteral [non oral] T does not adversely affect the liver or increase clotting factors, T is mood stabilizing and does not increase aggression, T is breast protective, and the safety of T therapy in women is under research and being established. Abandoning myths, misconceptions and unfounded concerns about T and T therapy in women will enable physicians to provide evidenced based recommendations and appropriate therapy.”***
3. Bianchi VE. The Anti-Inflammatory Effects of Testosterone. *The Journal of the Endocrine Society*, 2018 Oct 22;3(1):91-107. ***“Low Testosterone level has implications for metabolic health in both males and females and should be considered a risk factor because of its correlation with metabolic syndrome and all-cause mortality.”***
4. Samantha Worboys, et al. Evidence That Parenteral [pellet implant] Testosterone Therapy May Improve Vasodilation in Postmenopausal Women Already Receiving Estrogen, *The Journal of Clinical Endocrinology & Metabolism*, Volume 86, Issue 1, Jan 2001, 158–161. ***“This study provides evidence that testosterone implant therapy may improve [mechanisms of] arterial vasodilation in postmenopausal women already using HRT. This supports the concept that androgens have important physiological actions in women as well as in men, and provides additional safety data pertaining to postmenopausal testosterone use.”***
5. Britto R, Araújo L, Barbosa I, Silva L. Improvement of the lipid profile in postmenopausal women who use estradiol and testosterone implants. *Gynecological Endocrinology*, 2012; 28(10):767-769. ***“The use of E and T***

*implants showed statistically significant decrease in Total Cholesterol at the beginning of the Hormone Therapy and some decrease in LDL in the group using Hormone Therapy. In the group without HT there was no difference in lipid profile."*

6. Iellamo F, et al. Testosterone Therapy in Women With Chronic Heart Failure: A Pilot Double-Blind, Randomized, Placebo-Controlled Study. *Journal of the American College of Cardiology*, Volume 56, Issue 16, Oct 2010, 1310-1316. **"Testosterone supplementation improves functional capacity, insulin resistance, and muscle strength in women with advanced Chronic Heart Failure. Testosterone seems to be an effective and safe therapy for elderly women with Chronic Heart Failure."**
7. Glaser RL, Dimitrakakis C. Reduced breast cancer incidence in women treated with subcutaneous testosterone, or testosterone with anastrozole; a prospective, observational study. *Maturitas*, 2013; 76(4):342-9. **"Testosterone and/or Testosterone+Anastrozole, delivered subcutaneously as a pellet implant, reduced the incidence of breast cancer in pre and postmenopausal women"**
8. Glaser R, Dimitrakakis C, Trimble N, Martin V. Testosterone pellet implants and migraine headaches: a pilot study. *Maturitas*, 71 (2012) 385–388. **"Continuous testosterone was effective therapy in reducing the severity of migraine headaches in both pre- and post-menopausal women."**
9. Savvas M, Studd JW, et al. Increase in bone mass after one year of percutaneous estradiol and testosterone implants in postmenopausal women who have previously received oral estrogens. *Br J Obstet Gynaecol.* 1992 Sep;99(9):757-60. **"Subcutaneous estradiol and testosterone implants will result in an increase in bone mass even after many years of oral estrogen replacement therapy."**
10. Mikkola T, Tuomikoski P, et al. Estradiol-based postmenopausal hormone therapy and risk of cardiovascular and all-cause mortality. *Menopause*, Sept 2015, Vol 22, Issue 9, 976-83. **"In absolute terms, the risk reductions mean 19 fewer coronary heart disease deaths and 7 fewer stroke deaths per 1,000 women using any Hormone Therapy for at least 10 years."**
11. Petrone AB, et al. 17 $\beta$ -Estradiol and Inflammation: Implications for Ischemic Stroke. *Aging and Disease*, Volume 5, Number 5, October 2014; 340-345. **"Estradiol has been shown to be a powerful immunomodulator and neuroprotective molecule in ischemic stroke."**
12. Matyi J, et al. Lifetime estrogen exposure and cognition in late life: the Cache County Study. *Menopause*, December 2019, Volume 26, Issue 12, p 1366-1374. **"Our results suggest that longer endogenous estrogen exposure and Hormone Therapy use, especially in older women, are associated with higher cognitive status in late life."**
13. Glaser R, Kalantaridou S, Dimitrakakis C. Testosterone implants in women: Pharmacological dosing for a physiologic effect. *Maturitas* 74 (2013) 179–184. **"Pharmacologic dosing of subcutaneous T, as evidenced by serum levels on therapy, is needed to produce a physiologic effect in female patients. Safety, tolerability**

*and clinical response should guide therapy rather than a single T measurement, which is extremely variable and inherently unreliable.” This means that it is important to treat the patient for symptoms, rather than rely solely on lab reports as a guide for hormone dose adjustments.*

14. Glaser R, York AE, Dimitrakakis C. Beneficial effects of testosterone therapy in women measured by the validated Menopause Rating Scale (MRS). *Maturitas*, 2011 Apr;68(4):355-61. **“Continuous testosterone alone, delivered by subcutaneous implant, was effective for the relief of hormone deficiency symptoms in both pre- and post-menopausal patients.”**
15. Shapiro S, Farmer RD, Mueck AO, et al. Does hormone replacement therapy cause breast cancer? An application of causal principles to three studies: Part 2. The Women’s Health Initiative: estrogen plus progestogen. *J Fam Plann Reprod Health Care* 2011;37:165–172. See also a *British Medical Journal* Editorial Commentary: Does hormone replacement therapy cause breast cancer? Commentary on Shapiro et al papers Parts 1-5. **The editorial author states “Breast cancer risks from the WHI study have been adjusted by investigators over the last decade, such that statistical significance has become borderline, with doubt cast over the association being causal.” Shapiro et al concluded that once the statistics of the WHI study were more carefully examined, estrogen therapy had not been conclusively shown to be the cause of breast cancers.**
16. Fournier A, Berrino F, Clavel-Chapelon, F. Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort study. *Breast Cancer Res Treat*, 2008 Jan: 107(1): 103-111. **Investigators found that, in comparison to synthetic estrogens and synthetic progestins, micronized [bioidentical] progesterone + bioidentical estradiol were associated with the least risk in breast cancer (no increase over baseline risk).**
17. Lobo RA, et al. Back to the future: Hormone replacement therapy as part of a prevention strategy for women at the onset of menopause, *Atherosclerosis*, 2016 Nov;254:282-290. **“We propose that HRT should be considered as part of a general prevention strategy for women at the onset of menopause.”**