

Summary of Supportive Published BHRT Medical Literature (1938-2016): Bioidentical Pellet Hormonal Therapy Implants for Women and Men

Adapted/ updated/ modified from an article by Rebecca Glaser, M.D.

Introduction

Bioidentical hormonal pellets are hormones such as estrogen (estradiol or E₂) and testosterone individually compressed into small cylinders as tiny as a grain of rice. They are derived from natural sources such as yams and soy, and are chemically identical to hormones made by the human ovary and testicle. High grade quality pellets are manufactured in FDA-regulated 503(b) pharmacies. Currently, there are many compounding pharmacies in the U.S., but there are few 503(b) compounding pharmacies. These high grade pellets differ from each other by as little as 3% in potency strength which is lower than and exceeds the quality the FDA expects from brand name FDA-approved medications (10% variance).

Many physicians are unaware there are already about 14 FDA-approved bioidentical products available, but none of them are estrogen pellets so far. Only one type of testosterone pellet is FDA-approved for usage in men with low testosterone syndrome. Why is there only one testosterone FDA-approved pellet? It costs in excess of \$1.5 Billion in 2016 to get a single drug through FDA approval, which is a definitive hurdle for many drug companies. Another problem is once a patent is actually achieved, what is the true defensible value of patent protection for a naturally occurring substance?

Testosterone is a DEA Schedule III controlled substance. Unlike other hormonal delivery systems such as pills, creams, gels, patches, or injections, **pellets are ideal in orchestrating amazingly consistent hormonal levels 24/7 over 3-5 month time intervals.** A huge advantage of multiple available pellets strengths allow the practitioner **to individualize the dose for the patient, unlike available prescription medications, which are made only in certain strengths.**

Long History of Pellet Usage

Hormone replacement therapy by pellet administration has been used with great success in the United States, Europe, and Australia since 1938, and found to **be superior to other methods of hormonal delivery** (Greenblatt 49, Mishell 41, Cantrill 84, and Stanczyk 88). **It is NOT experimental. Pellets deliver consistent physiologic hormonal levels, and avoid fluctuations seen with other delivery methods** (Greenblatt 49, Thom 81, Cantrill 84, and Stanczyk 88). Estrogen delivered by subcutaneous implants maintains the normal ratio of estradiol to estrone (Thom 81, Stanczyk 88, Owen 92, and Cravioto 01).

Liver Bypass Advantage of Pellets

Hormones delivered by subcutaneous implants **bypass the liver, do not affect clotting factors, and do not increase the risk of thrombosis** (Notelovitz 87, Seed 00), unlike oral or injectable hormones. Bioidentical testosterone is cardiac protective, unlike synthetic oral methyl testosterone (Sands 97, Worboys 00).

Positive Metabolic Effects

Testosterone delivered by pellets **does not adversely affect blood pressure, lipid levels, glucose, or liver functions** (Burger 84, Farish 84, Fletcher 86, Barlow 86, Notelovitz 84, Stanczyk 88, Davis 95, 00, Sands 97, Seed 00, Cravioto 01).

Superiority in Symptom Treatment

Pellets are superior to oral and topical hormones with respect to relief of menopausal symptoms (Staland 78, Cardoza 84). Testosterone implants also have been consistently shown to improve memory and concentration, energy levels, insomnia, sex drive, libido, hot flashes, palpitations, lethargy, headaches, irritability, depression, muscle ache, and vaginal dryness (Staland 78, Thom 81, Brincat 84, Davis 95, 00, and Cravioto 01). Usage of testosterone pellets does not affect the menstrual cycle (Dewis 86) and has used to treat endometriosis and uterine fibroids (Greenblatt 49). Severe PMS (premenstrual syndrome) unresponsive to other forms of therapy can respond

to pellet testosterone in women without adverse side effects (Dewis 84). Pellet implantation has been shown to be extremely effective in treatment of migraine headaches (Magos 83).

Significant Positive Bone Density Effect

Hormone replacement therapy with testosterone implants is **superior to oral and topical therapies (both gel and patch) for improvement in bone density** (Savvas 88, 92, Davis 95, Anderson 97). The consistent levels of testosterone delivered by pellet implant are important in maintenance of BMD (bone mineral density) (Aminoroaya 05), while being available as a substrate for production of estradiol (Simpson 02, 03). The pellets not only prevent bone loss, but also increase bone density (Savvas 88, Studd 90, Garnett 91, Savvas 92, Naessen 93, Holland 94, Studd 94, Davis 95, Anderson 97, Seed 00, Panay 00). Pellet testosterone therapy has been demonstrated to increase bone mineral density by 8.3% per year (Studd 90). Testosterone pellets produce a 4x fold increase in BMD over oral estrogen products and a 2.5x fold increase over estrogen patches. Testosterone builds trabecular (interior) bone, not the cortical (exterior) bone as bisphosphonate therapy does.

No Increase In Breast Cancer Risk (Bioidenticals Reduce Risk)

The use of pellet estradiol therapy with added oral bioidentical progesterone therapy has been shown to **reduce the risk of breast cancer** below baseline risk (0.9 Relative Risk), Int J Cancer 2005, 114: 448-456. **Indeed, the risk was lower than “no hormone therapy”.** This is in marked contrast to the increased risk (1.4 Relative Risk) of breast cancer generated by synthetic FDA-approved progestins, such as medroxyprogesterone acetate (well documented in the Women’s Health Initiative Study, JAMA 2002). **Testosterone pellets also reduce the risk of breast cancer, with or without estradiol pellets** (Dimitrakakis 04, Tuter 09). Even after 20 years of therapy with hormonal pellets, the risk of breast cancer is not increased (Gambrel 06). In breast cancer survivors, pellet replacement therapy does not increase the risk of breast cancer recurrence or death (Natrajan 02).

Reduction in Alzheimer’s disease

Testosterone has been shown **to reduce the incidence of Alzheimer’s disease** by 30% if hormonal therapy is begun within 5 years of menopause, and used for greater than 10 years (Neurology, October 2012, 30: 79: 1846-52). Similarly, females on estrogen were 50% less likely to develop Alzheimer’s disease.

Reduction in Cardiovascular Disease, Heart Attack, and Stroke

If women are begun on estrogen therapy prior to age 60, there is a reduction in carotid arterial intimal thickening, indicating a slowing of atherosclerosis (ELITE study, Hodis, 2016). No cardiovascular benefit is found after age 60.

Men over age 50 on testosterone therapy have been shown to have **a 30% reduction in heart attacks, a 43% reduction in stroke, and a 60% reduction in all-cause mortality** in the largest longitudinal study of over 43,000 veterans followed over 15 years, compared with age matched controls (Sharma, August, 2015 European Veterans’ Study, European Heart Journal).

Pellet Side Effects

Pellet implantation hormonal therapy has **an extremely low incidence of side effects** (Cardoza 84, Barlow 86, Ganger 89, Pirwany 02) and **high compliance rate** (Gambrel 06).

Female Pellet Therapy

Testosterone pellets, in addition to estradiol pellets, are used in women in doses ranging from 50-225 mg. There are minimal testosterone side effects at these doses, namely 10% facial hair, 5% hair loss, 5% acne. Vaginal spotting can also occur in 10% of patients if there is an imbalance of estrogen to progesterone. Testosterone side effects are reduced by lowering the dose of testosterone. Serum levels are above baseline at 4 weeks after insertion (Burger 84, Dewis 84, Gambrel 06, Thom81, Glaser 09). Peak levels of testosterone are in the 250-375 ng/dl range. Symptoms return when testosterone

levels return to baseline. Implant effects last from 2.5-3.5 months at which time most patients begin to feel their original symptoms start to reappear. Each individual female has her own reproducible levels where symptoms return.

Male Pellet Therapy

Testosterone pellet therapy in men with low testosterone syndrome has been shown to be extremely effective, convenient, and safe (Handelsman 90, 92, 97, Kelleher 01, 04, Conway 88, Jockenhoval 96, Zacharin 03, Schubert 03, Dunning 04). Routine doses in men can range from 1200-2600 mg. and last 4-5 months, with a near linear release rate, which is ideal, eliminating mood swings seen with injection therapies. Testosterone levels peak at month one in the 1000-1500 ng/dl range. Side effects may include acne (5%), hair loss (5%), testicular shrinkage (50%), reduction in sperm count while on therapy (50+%), and possible prostatic enlargement in some men. Each individual male has his own reproducible levels where symptoms return.