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Pellet Implant FAQ

Introduction
Data supports* that hormone replacement therapy with pellet implants is an effective bio-identical method to deliver hormones in both men and women. Implants, placed under the skin, consistently release small, physiologic doses of hormones.

BHRT Fused Pellet Implant History
Hormone replacement using pellet implants has been used with great success in the U.S., Europe, and Australia since 1938. In fact, pellet implants were a very popular mode of hormone administration in the U.S. until the 1970s, when many oral and topical commercial products were developed. While the demand for pellets diminished in the U.S., pellet implants continued to be a very popular mode of hormone administration throughout Europe and Australia. In the last 10 years, due to advances made in processes and a better understanding of the benefits of fused pellet implants for hormone replacement, this mode of hormone administration has grown in popularity in the U.S.

Over 70 years of research has illustrated the benefits of pellet implants in administering hormones in both women and men.*

- Pellet implants deliver consistent, physiologic levels of hormones.
- The consistent and physiologic dosing has been shown to maintain and improve bone density.
- Pellet implants bypass the liver and don't negatively impact clotting factors, blood pressure, lipid levels, glucose, or liver function.

Pellet implants have consistently been shown to improve:*

- Cardiovascular Health
- Sex Drive and Libido
- Headaches and Migraines
- Insomnia
- Hot Flashes
- Mood and Depression
- Joint Aches and Pains

What Is BHRT?
An individualized approach to hormone replacement therapy, using biologically identical hormones (BHRT), pinpoints a person's exact hormone levels, and what hormones are needed to balance their hormone deficiency. The differences between synthetic and biologically identical hormones are in their chemical structures and functionality. Biologically identical hormones have the same chemical structure as the hormones created naturally in the human body.

What Are BHRT Fused Pellets Implants?
Fused pellet implants are compounded using biologically identical hormones (most often Estradiol or Testosterone). The hormones are pressed / fused into very small cylinders. College Pharmacy also compounds DHEA, Pregnenolone, Progesterone, Biest, and Testosterone with Anastrozole fused pellet implants.

***Please see "Data & References" section at the end of the document. Full-text articles are available by request.**

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Where Are BHRT Fused Pellet Implants Inserted?
Pellet insertion is a relatively simple in-office procedure done under local anesthesia. The pellets are inserted subcutaneously (under the fatty lining of skin), either in the lower abdomen or the upper buttocks through a very small incision. The incision is then closed with surgical glue or sterile-tape strips. If inserted correctly, patients cannot feel the implants under their skin. Implants placed under the skin consistently release small, physiologic doses of hormones, which have been shown to have many benefits.

How Long Do BHRT Fused Pellet Implants Last?
Fused Pellet Implants typically last between 3-5 months, depending on how rapidly the hormones are metabolized. After insertion of the pellets, vigorous physical activity should be avoided for 2-3 days, or as suggested by the healthcare practitioner. Some patients begin to feel symptom relief within 48 hours, while others may take up to two weeks to notice a marked difference. The pellets do not need to be removed. They are completely dissolved by the body.

Are There Any Side-Effects?
Generally, there are minimal side-effects associated with the pellet implant procedure. Complications include: minor bleeding, bruising, infection, and pellet extrusion. Other than slight bruising, the other complications are very rare. Hormone side-effects vary and should be discussed by your healthcare practitioner.

How Do I Know What Hormones I Need?
Before starting any hormone replacement therapy, patients should work directly with a knowledgeable healthcare practitioner to have hormone testing done to evaluate their personal hormone profile. Based on existing hormone levels and health history, the practitioner will make a hormone replacement recommendation. Once pellets have been inserted, hormone levels will be reevaluated prior to the insertion of the next round of pellets. After the first year of therapy, the practitioner may suggest testing less frequently based upon patient feedback and prior hormone levels.

How are hormones monitored during therapy?
Hormone levels will be drawn and evaluated before therapy is started. This may include a FSH, estradiol, testosterone and free testosterone for women. Men need a PSA, sensitive estradiol, testosterone, liver profile and blood count prior to starting therapy. Thyroid hormone levels may also be evaluated. Levels will be reevaluated during hormone therapy, usually prior to insertion of the next set of pellets, 4-5 months. After the first year of therapy, hormones levels may be followed less frequently. Men must notify their primary care physician and obtain a digital rectal exam each year. Women are advised to continue their monthly self-breast exam and obtain a mammogram and/or pap smear as advised by their gynecologist or primary care practitioner.

Can a patient be allergic to the implants?
Very rarely, a patient will develop local zone of redness (3-8 cm) and itching at the site of the testosterone implant. There is minimal or no tenderness and no other sign of infection. Many pellet formulations include stearic acid and PVP (povidone). Patients may react to the PVP. Many patients who develop a local reaction to the implant have low cortisol levels and upon further questioning, have symptoms of adrenal insufficiency. Cortisol testing may be recommended. If needed, 25-50mg of benedryl works well for the itching.

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How much does this cost?
The cost for the insertion of pellets will vary depending on the dose of the hormone and the number of pellets needed. Men need a much larger dose of testosterone than women and the cost is higher. Pellets need to be inserted 2 to 4 times a year depending on how rapidly a patient metabolizes hormones. When compared to the cost of drugs to treat the individual symptoms of hormone decline, pellets are very cost effective.

Will insurance cover the procedure?
Some insurance companies cover the cost of pellets. Others do not. Most physicians require payment for their services. Patients may want to contact their insurance companies to see if their costs will be reimbursed. Prevention is much more cost effective than disease. Patients are able to 'appeal' a denied claim.

How Can I Get BHRT Fused Pellet Implants?
BHRT Fused Pellet Implants require a prescription from a healthcare practitioner. It is very important to work with a practitioner that is well versed in BHRT as well as the actual pellet implant procedure. The placement of the pellet and the hormone dosing are extremely important in determining safety and efficacy. BHRT Fused Pellet Implants are most often made by special compounding pharmacies, such as College Pharmacy, using strict United States Pharmacopeia (USP) guidelines.

Local Allergic Reaction to the Implant
Very rarely, a patient will develop local zone of redness (3-8 cm) and itching at the site of the testosterone implant. There is minimal or no tenderness and no other sign of infection.

Many patients who develop a local reaction to the implant have low cortisol levels and on further questioning, often have symptoms of adrenal insufficiency.

Recommendations:
- Benedryl 25-50 mg every 6 hours as needed
- Check am and pm salivary cortisol levels PRIOR to beginning hydrocortisone therapy.
- Check for other symptoms of cortisol deficiency
- Begin therapy with hydrocortisone (10 mg BID) with or without benedryl.
- If the itching and redness do not respond to hydrocortisone, prescribe a medrol dose pack.
- Implants are not removed.
- If there is any question of infection, begin Keflex.

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Data & References: Hormone Therapy with Pellet Implants (All articles quoted are available by request.)

Hormone replacement therapy by pellet implantation has been used with great success in the United States, Europe and Australia since 1938 and found to be superior to other methods of hormone delivery (Greenblatt 49, Mishnell 41, Cantrill 84, Stanczyk 88). It is not experimental. Pellets deliver consistent, physiologic levels of hormones and avoid the fluctuations of hormone levels seen with other methods of delivery (Greenblatt 49, Thom 81, Cantrill 84 Stanczyk 88).

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

Testosterone and estradiol delivered by pellet implantation, 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, Handelsman 96, Sands 97, Seed 00, Cravioto 01).

Pellets are superior to oral and topical hormone therapy with respect to relief of menopausal symptoms (Staland 78, Cardoza 84). Estradiol and testosterone implants have consistently been shown to improve insomnia, sex drive, libido, hot flashes, palpitations, headaches, irritability, depression, aches, pains, and vaginal dryness (Staland 78, Thom 81, Brincat 84, Davis 95, 00, Cravioto 01).

Hormone replacement therapy with estradiol and testosterone implants is superior to oral and topical (both the patch and gel) hormone replacement therapy for bone density (Savvas 88, 92, Davis 95, Anderson 97). The consistent, adequate levels of testosterone delivered by pellet implant are important in maintaining bone mineral density (Aminoroaya 05) while also being available as a substrate for the production of estradiol (Simpson 02, 03). The pellets not only prevent bone loss but also actually 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).

Testosterone implants in women have been shown to improve lethargy, depression, loss of libido, and hot flashes without attenuating the beneficial affects of estradiol on cardiac and lipid profiles (Farish 84, Fletcher 86, Sands 97, Seed 00). Testosterone delivered by subcutaneous implants does not increase the risk of breast cancer (Dimitrakakis 04, Natrajan 02) as does oral, synthetic methyl-testosterone (Tamimi 06). Testosterone, delivered by pellet implant does not affect the menstrual cycle (Dewis 86) and has been used to treat endometriosis and uterine fibroids (Greenblatt 49). Testosterone pellet implants have also been used to successfully treat severe pre-menstrual syndrome unresponsive to other forms of therapy, without adverse effects (Dewis 84).

Testosterone, delivered by subcutaneous pellet implant has been shown to improve hot flashes, heart discomfort, sleep problems, depressive mood, irritability, anxiety, physical fatigue, memory loss, sexual problems, bladder problems (incontinence), vaginal dryness, joint and muscular discomfort in both premenopausal and post-menopausal patients without adverse drug events (Glaser 09).

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Pellets do not have the same risk of breast cancer as the synthetic progestins or synthetic Methytestosterone. In fact, studies show a reduction in the incidence of breast cancer with the implantation of testosterone pellets, with or without estradiol pellets (Dimitrakakis 04, Tutera 09).

Even after over 20 years of therapy with hormone implants, the risk of breast cancer is not increased (Gambrel 06). In breast cancer survivors, hormone replacement therapy with pellet implantation does not increase the risk of cancer recurrence or death (Natrajan 02) as does estrogen in combination with the synthetic progestins (Habits Trial 04).

Hormone replacement therapy with pellet implantation has an extremely low incidence of side effects (Cardoza 84, Barlow 86, Ganger 89, Pirwany 02) and high compliance rate (Gambrell 06). It has been shown to be extremely effective in the treatment of migraine headaches (Magos 83).

Testosterone replacement therapy in men with subcutaneous implants (pellets) has been show to be extremely effective, convenient and safe (Handelsman 90, 92, 97, Kelleher 01, 04, Conway 88, Jockenhoval 96, Zacharin 03, Schubert 03, Dunning 04).

The testosterone implant is licensed in England for women. The 75 mg testosterone implant is FDA approved in the US (July 13,1972, male patients). Other doses need to be compounded by trained pharmacists. *The 75 mg pellet is a sterile product is cylindrically shaped and weighs approximately 77mg (75mg testosterone). The inactive ingredients include 0.2mg stearic acid USP and 2mg polyvinylpyrroidone USP.*
The routine doses of testosterone delivered by pellet implantation in recent studies are between 800 and 1200 mg in men. The pharmacokinetics and pharmacodynamics are well established showing that these doses deliver reproducible physiologic levels of testosterone for 4-6 months. The studies show that pellets have a zero order release rate. Although individuals vary, the 75mg testosterone pellet has a consistent release rate approximately 0.5 mg of testosterone per day for a total of approximately 6 mg per day for 12 pellets. A 6-9 mg daily production of testosterone is a ‘physiologic’ level produced by the testicles.

Testosterone implants have a near linear release rate. Peak serum testosterone levels with the implants are usually seen at month one. Therapeutic testosterone levels at month one, are expected at the upper limits of normal for healthy young males (800-1100 ng/dL). By month 4 to 5 testosterone levels drop to below 500-600 ng/dL at which time symptoms return and the pellets are reinserted. Each individual has their own reproducible levels where symptoms return.

Testosterone implants have been used in women. Doses used in studies are as low as 50 mg and up to 225 mg. In the United States, common doses are 75, 100, 110 mg, 125 and 150 mg. There are minimal side effects at these doses (slight increase in facial hair 20% and mild acne 5%), which may be reduced by lowering the dose, if the patient chooses. If measured, serum treatment levels are elevated above non-treatment levels at month one (Burger 84, Dewis 84, Gambrel 06l, Thom 81, Glaser 09). Urine and saliva levels remain normal. There are no signs of androgen excess at these treatment levels. Symptoms return when testosterone levels reach the upper end of endogenous ranges (Burger 84, Glaser unpublished). End organ response to testosterone remains optimal (i.e., relief of depression, increase in bone density, relief from insomnia, relief from aches and pains, lessened anxiety, improved memory and concentration, increased energy, etc.). Testosterone implants last between 2.5 and 5 months

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in female patients. Individual treatment doses and treatment ranges are established and are reproducible.

In a paper published in the journal 'Menopause' in 2004, *'Breast cancer incidence in postmenopausal women using testosterone in addition to usual hormone therapy'* women were referred for testosterone supplementation for the following indications:

- Complaints of emotional lability
- Fatigue and loss of stamina
- Impaired concentration and memory
- Breast tenderness
- Loss of libido
- Sleep disturbance
- Muscle weakness

Patients received testosterone implant containing 50-150mg of testosterone every 5 months in addition to conventional estrogen or estrogen/progestin therapy. The testosterone dose was titrated to alleviate symptoms (listed above), improve bone mineral density and minimize adverse affects (slight increase in facial hair and acne). The most common dose was 100 mg.

Testosterone therapy alone, delivered by pellet implant is effective for the relief of both physical and psychological symptoms in pre-menopausal and post-menopausal patients. Symptoms of testosterone deficiency/hormone imbalance are often seen prior to menopause. Many women begin to experience symptoms by age 35-40, when testosterone production has declined by half (Zumoff 95).

Testosterone alone has previously been reported to be more effective than estrogen/testosterone or estrogen therapy for relief of somatic and psychological symptoms (Sherwin 85). Uninterrupted sufficiency of circulating testosterone supports the production of estradiol by aromatase in estrogen dependent tissues (brain, bone, cardiac, vascular tissue, fat and breast tissue) and affords protection against estrogen deficiency. Also, low circulating levels of estrogen have no bearing on estrogen produced locally. This may explain why continuous delivery of testosterone by pellet implant is so effective in post-menopausal patients.

All articles quoted are available in full-text by request.