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

What are Pellets?
Pellets are made up of hormones, most commonly either Estradiol or Testosterone; however, College Pharmacy also
compounds pellets with DHEA, Biest, Progesterone, Pregnenolone, and Testosterone/Anastrozole . The hormones
are pressed or fused into very small solid cylinders. These pellets are larger than a grain of rice and smaller than a
‘Tic Tac’. In the United States, the majority of pellets are made by compounding pharmacists and delivered in sterile
glass vials. There is an FDA approved 75 mg testosterone pellet.

Why pellets?
Pellets deliver consistent, healthy levels of hormones for 3-4 months in women and 4-5 months in men. They
avoid the fluctuations, or ups and downs, of hormone levels seen with every other method of delivery. Estrogen
delivered by subcutaneous pellets, maintains the normal ratio of estradiol to estrone. This is important for optimal
health and disease prevention. Pellets do not increase the risk of blood clots like conventional or synthetic hormone
replacement therapy.

In studies, when compared to conventional hormone replacement therapy, pellets have been shown to be superior
for relief of menopausal symptoms, maintenance of bone density, restoration of sleep patterns, and improvement in
sex drive, libido, sexual response and performance.

Testosterone delivered by a pellet implant, has been used to treat migraine and menstrual headaches. It also
helps with vaginal dryness, incontinence, urinary urgency and frequency. In both men and women, testosterone
has been shown to increase energy, relieve depression, increase sense of well being, relieve anxiety and improve
memory and concentration. Testosterone, delivered by pellet implant, increases lean body mass (muscle strength,
bone density) and decreases fat mass. Men and women need adequate levels of testosterone for optimal mental
and physical health and for the prevention of chronic illnesses like Alzheimer’s and Parkinson’s disease, which are
associated with low testosterone levels.

Even patients who have failed other types of hormone therapy have a very high success rate with pellets. There
is no other ‘method of hormone delivery’ that is as convenient for the patient as the implants. Pellets have been
used in both men and women since the late 1930’s. There is more data to support the use of pellets than any other
method of delivery of hormones. In addition, there is significant data that supports the use of testosterone implants
in both women and men (complete reference materials available by request).
How and where are pellets inserted?
The insertion of pellets is a simple, relatively painless procedure done under local anesthesia. The pellets are usually inserted in the lower abdominal wall or upper buttocks through a small incision, which is then closed with a skin tape (steri-strip). The experience of the health care professional matters a great deal, not only in placing the pellets, but also in determining the correct dosage of hormones to be used.

Are there any side effects or complications from the insertion of the pellets?
Complications from the insertion of pellets include; minor bleeding or bruising, discoloration of the skin, infection, and the possible extrusion of the pellet. Other than slight bruising, or discoloration of the skin, these complications are very rare. Testosterone may cause a slight increase in facial hair in some women. Testosterone stimulates the bone marrow and increases the production of red blood cells. A low testosterone level in older men is a cause of anemia. Testosterone, delivered by implants or other methods, can cause an elevation in the red blood cells. If the hemoglobin and hematocrit (blood count) get too high, a unit of blood may be donated.

After the insertion of the implants, vigorous physical activity is avoided for 48 hours in women and up to 5 to 7 days in men. Early physical activity is a cause of ‘extrusion’, which is a pellet working it’s way out. Antibiotics may be prescribed if a patient is diabetic or has had a joint replaced. However, this is a ‘clean procedure’ and antibiotics may not be needed.

Why haven’t I heard about Pellets?
You may wonder why you haven’t heard of pellets. Pellets are not patented and have not been marketed in the United States. They are frequently used in Europe and Australia where pharmaceutical companies produce pellets. Most of the research on pellets is out of Europe and Australia. Pellets were frequently used in the United States from about 1940 through the late 70’s when oral patented estrogens were marketed to the public. In fact, some of the most exciting data on hormone implants in breast cancer patients is out of the United States. Even in United States, there are clinics that specialize in the use of pellets for hormone therapy.

Do men need hormone therapy?
Testosterone levels begin to decline in men beginning in their early 30’s. Most men maintain adequate levels of testosterone into their mid 40’s to mid 50’s, some into their late 70’s to early 80’s. Men should be tested when they begin to show signs of testosterone deficiency. Even men in their 30’s can be testosterone deficient and show signs of bone loss, fatigue, depression, erectile dysfunction, difficulty sleeping and mental decline. Most men need to be tested around 50 years of age. It is never too late to benefit from hormone therapy.

What if my primary care physician or my gynecologist says that there is ‘no data’ to support the use of pellet implants? He or she is wrong. There is a big difference between ‘no data’ and not having read the data. It is much easier for busy practitioners to dismiss the patient, than it is to question their beliefs and do the research. It’s about a patient making an informed choice. After pellets are inserted, patients may notice that they have more energy, sleep better and feel happier. Muscle mass and bone density will increase while fatty tissue decreases. Patients may notice increased strength, co-ordination and physical performance. They may see an improvement
in skin tone and hair texture. Concentration and memory may improve as will overall physical and sexual health. There is data to support the 'long term' safety of hormones delivered by pellet implants.

**Do pellets have the same danger of breast cancer as other forms of hormone replacement therapy?**

Pellets do not carry with them the same risk of breast cancer as high doses of oral estrogens that do not maintain the correct estrogen ratio or hormone metabolites. Nor, do they increase the risk of breast cancer like the synthetic, chemical progestins used in the Women's Health Initiative Trial. Data supports that balanced, bio-identical hormones are breast protective.

Testosterone, delivered by pellet implantation, has been shown to decrease breast proliferation and lower the risk of breast cancer, even in patients on conventional hormone replacement therapy. Clinical studies show that bio-identical testosterone balances estrogen and is breast protective. This is not true of oral, synthetic methyl-testosterone found in Estratest, which gets converted to a potent synthetic estrogen, which can stimulate breast tissue. In the past, testosterone implants have been used to treat patients with advanced breast cancer. In 1940, it was theorized that treating patients with testosterone implants earlier, at the time of diagnosis, would have an even greater benefit, preventing recurrence. Androgens have also been shown to enhance the effect of Tamoxifen® therapy in breast cancer patients. References supporting these statements can be found in the data section of www.hormonebalance.org in the ‘Breast Cancer Folder’. In contrast to testosterone, Estradiol, whether delivered by pellet implant*, applied topically to the skin or taken orally has been shown to increase the risk of breast cancer. This is not surprising, as continuous Estradiol, a strong estrogen, has been shown to stimulate breast tissue. *Million Women’s Study

**Are there other hormones besides testosterone that have not been shown to increase the risk of breast cancer?**

Bio-identical progesterone (including FDA approved Prometrium®) has not been shown to increase the risk of breast cancer like the synthetic progestins. In addition, progesterone, used vaginally, does not negate the beneficial effects of estrogen on the heart like the synthetic progestins. Estriol is a bio-identical estrogen widely used in Europe that does not bind strongly to estrogen receptor and does not stimulate breast tissue. Numerous studies have shown that vaginal estriol does not increase the risk of breast cancer (RR 0.7). It has safely been used in breast cancer survivors. However, higher doses of vaginal estradiol (> 25 mcg) and vaginal Premarin® provide systemic levels of strong estrogens that may stimulate breast tissue. If you are a breast cancer survivor, it is important that your physician understands this. Balanced hormones are the key to health and disease prevention.

**Why isn't estrogen therapy or Estradiol pellet therapy recommended?** **see page 6**

We have shown that symptoms, including hot flashes, are relieved with continuous testosterone alone. Testosterone delivered by pellet implant is extremely effective therapy. In addition, it does not have the unwanted side effects of estrogen therapy. Over half of women treated with estrogen (especially the pellet implant) will experience uterine bleeding. If a menopausal patient has bleeding, she must notify her physician and have an evaluation, which may include a vaginal ultrasound and endometrial biopsy. Estrogen also stimulates the breast tissue and can cause breast pain and cysts. It also increases the risk of breast cancer. Higher levels of estrogen (in the second half of the menstrual cycle) are needed for pregnancy. Most women feel better with lower levels of estrogen.
Why isn’t estrogen therapy or Estradiol pellet therapy recommended? (continued)
Almost all symptoms, including hot flashes, are relieved with testosterone pellets alone. A study by Sherwin in 1985 looked at testosterone, testosterone with estradiol, estradiol alone and placebo. The group of women who responded best (somatic, psychological and total score)…testosterone alone! The groups that did the worst…estrogen alone and placebo. Higher levels of testosterone were associated with a better response. These results are expected. Testosterone is the major ‘substrate’ for estrogen production in the brain, bones, vascular system, breast and adipose tissue. Some physicians do not understand this and may insist that estrogen therapy is needed.

Excess estrogen can cause anxiety, weight gain, belly fat, tender breasts, emotional lability, symptoms of PMS, and mood swings. Long-term exposure to stronger estrogens like estradiol and Premarin can increase the risk of breast cancer. In addition, there is exposure to many estrogen-like chemicals. Some women (and men) ‘aromatize’ or convert too much testosterone to estradiol, which can interfere with the beneficial effects of testosterone. An ‘aromatase inhibitor’ (i.e. anastrozole) may be prescribed to prevent this. Patients, including breast cancer survivors, may be treated with the combination testosterone-anastrozole implants.

Are there side effects to estrogen delivered by pellet implantation?
When a patient first starts on hormone therapy there may be mild, temporary breast tenderness, which resolves on its own. Hormone receptors may be very sensitive and take time to adjust. There may be a temporary water weight gain, which will also resolve on its own. Women, especially those who have not had a hysterectomy, may choose a different method of delivery of estrogen, as the risk of bleeding is significant.

Will hormone therapy with estradiol and testosterone pellets help with hair loss?
Hormone deficiency is a common cause of hair loss and treatment with estradiol and testosterone implants can help to re-grow hair. Hair becomes thicker and less dry with pellet therapy.

How long until a patient feels better after pellets are inserted?
Some patients begin to ‘feel better’ within 24-48 hours while others may take a week or two to notice a difference. Diet and lifestyle, along with hormone balance are critical for optimal health. Stress is a major contributor to hormone imbalance and illness. Side effects and adverse drug events from prescription medications can interfere with the beneficial effects of testosterone implants.

How long do pellets last?
The pellets usually last between 3 and 4 months in women and 4-5 months in men. The pellets do not need to be removed. They completely dissolve on their own.

Do patients need progesterone when they use the pellets?
Women who are treated with testosterone implants alone (no estrogen therapy) do not require progestin therapy. However, if estradiol, or other estrogen therapy is prescribed, progestins are also needed. The main indication for the use of synthetic progestins, like Provera® or progesterone, is to prevent the proliferation (stimulation) of the uterine lining caused by estrogen. Progestin therapy is NOT required if estrogen therapy is not prescribed. However, there may be health benefits to the hormone, progesterone.
There are progesterone (not progestin) receptors in the bone, brain, heart, bladder, breast and uterus where progesterone has been shown to have beneficial effects. Most of the time, when estradiol is prescribed, progesterone is also prescribed even if the patient has had a hysterectomy.

Progesterone can be used as a topical cream, a vaginal cream, an oral capsule (Prometrium®), or sublingual drops. Only oral progesterone (100-200 mg) and vaginal progesterone (45-90 mg) have been studied and shown to protect the uterine lining from estrogen stimulation.

If a patient is pre-menopausal, she uses the progesterone the last two weeks of the menstrual cycle (day 1, the first day of bleeding). Hormone therapy with pellets is not just used for menopause. Women at any age may experience hormone imbalance. Levels decline or fluctuate contributing to debilitating symptoms. Pellets are useful in severe PMS, post partum depression, menstrual or migraine headaches, and sleeping disorders. Pellets may also be used to treat hormone deficiencies (testosterone) caused by the birth control pill.

Is there a role for testosterone implants (pellets) in a pre-menopausal female?
Testosterone pellets may be used in pre-menopausal females (women who have not stopped menstruating). Testosterone has been shown to relieve migraine or menstrual headaches, help with symptoms of PMS (pre menstrual syndrome), relieve anxiety and depression, increase energy, help with sleep and improve sex drive and libido. If a pre-menopausal female has a testosterone pellet inserted, she must use birth control. There is a theoretical risk of ‘masculinizing’ a female fetus (giving male traits to a female fetus).

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. Pellets are made of up testosterone, stearic acid and PVP (povidone). Patients may react to the PVP. Implants can be compounded or made without 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, 25-50 mg of Benadryl works well for the itching (but drowsiness can be a side effect).

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 physician.

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. There is more good, ‘unbiased’ data on pellets and bone density than any pharmaceutical drug on the market. It is beyond the scope of this handout to examine the cost of drugs used for insomnia, depression, sexual dysfunction, obesity, diabetes, hypertension and more.

**Will insurance cover the procedure?**

Some insurance companies cover the cost of pellets, especially in men. 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.

In conclusion, estrogen and testosterone therapy by implantation of pellets is a safe and effective method of hormone therapy for both men and women. Long, continuous administration of hormones by pellets is convenient and economical for the patient. Pellet implantation has consistently proven more effective than oral, intramuscular, and topical hormone therapy with regard to bone density, sexual function, mood and cognitive function, urinary and vaginal complaints, breast health, lipid profiles, hormone ratios and metabolites.

**(from page 3): The physicians at Pasadena Pellet Therapy disagree strongly with this comment. Estradiol supplementation can provide many benefits and can be administered safely. Estradiol can provide relief of hot flashes and night sweats, better sleep, improved memory and concentration, and an overall increased sense of well-being. Your physician will discuss with you the pros and cons of estradiol supplementation as part of your overall Bio-identical hormonal treatment plan.