

## Hormone Replacement Therapy BHRT

### Synthetic vs Bioidentical Hormone Replacement

Synthetic hormones are hormones which are not biologically identical to human hormones and thus are recognized by the body as “foreign.” For example, Premarin®, a drug commonly used in estrogen replacement therapy, is derived from pregnant mares’ urine. In fact, there are more than 50 horse estrogens in Premarin®. Because horse estrogen is foreign to the human body, women lack the enzymes and cofactors to metabolize it safely. Foreign estrogens, like those in Premarin®, are called xeno-estrogens. With potentially dangerous side effects, they are also found in insecticides and plastic bottles. Synthetic progesterone (progestins, like Provera™, which is medroxyprogesterone acetate or MPA) can have negative side effects including possible blood clots, an increased risk of heart disease, headaches, fluid retention, weight gain, mood swings, and breakthrough bleeding. In addition, other chemicals that may produce adverse side effects must be added to the synthetic hormones to facilitate absorption and utilization by the body.

Sometimes called natural hormones or human identical hormones, biologically identical hormones are derived from plants, such as the wild yam or soybean plant, and are chemically and functionally identical to human hormones. The wild yam is rich in precursor molecules that can be converted in the laboratory into estrogens and other hormones whose molecular structure is the same as those produced in the human body. Biologically identical hormones produce the same physiologic responses in the body as endogenous hormones (those made by the body). Substances that are most similar to what our body produces naturally support human functioning without increased risk of allergic reactions and sensitivities. For example, studies have shown human-identical insulin to be more effective for diabetic patients. Moreover, an often-over-looked aspect of biologically identical hormone replacement therapy (BHRT) is that it may vastly improve the quality of life for women and men suffering from a wide range of physical, mental, and emotional symptoms.

There are a wide variety of symptoms attributed to abnormal hormone levels, however it can be difficult to determine exactly what replacement is needed. The hormone survey is

essential for initial diagnosis, treatment decisions, and dosage adjustments. In addition to symptom relief, optimal hormone balance reduces other risks.

- 1) Testosterone has been shown to have a protective effect against breast cancer and may help to optimize treatment of breast cancer.
- 2) Early treatment with estrogen has a protective effect against cardiovascular disease in women.
- 3) Testosterone has been shown to help reduce all-cause mortality in men helping to prevent insulin resistance and cardiovascular disease
- 4) Good estrogen metabolites act as powerful antioxidants. These metabolites reduce the risk of certain cancers that are associated with free radical damage.
- 5) Estrogen and testosterone have both been shown to increase bone mineral density
- 6) Estrogen and testosterone have been shown to be protective against neurological disorders such as Alzheimer's Disease and epilepsy

There are many synergistic aspects to combination hormone therapy. For example, tiredness can be related to lack of sleep, which is primarily an estrogen issue, but it can also be both a testosterone as well as a thyroid issue. It is important to look at all possible interactions. One of the most important medical history questions is the regularity of the menstrual cycle. If a woman is pre- or peri-menopausal, her hormone balance (estrogen, progesterone, FSH) will be reflected by the characteristics of her cycle. Blood levels are difficult to interpret because of the normal fluctuations of hormones during the cycle. Hormone levels should still be checked to establish a baseline and to rule out other abnormalities. Testosterone does not affect the menstrual cycle, so these levels are not cyclical.

## Initiating BHRT

Bloodwork is required before we can start any hormone replacement therapy. We want to ensure you are ready and need hormone replacement therapy. The following information is collected.

- Complete medical history
- Vital signs, including height, weight and BMI
- Blood work for women;
  - FSH, TSH, Total T4, Free T3, TPO, Estradiol, Total testosterone, Vitamin D, Vitamin B12, Comprehensive Metabolic Panel, Lipid panel, direct LDL, Iron, Folate
- Blood work for men;
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- CBC, PSA, TSH, Total T4, Free T3, TPO, Testosterone-total and free, Estradiol (to check for aromatization), Vitamin D, Vitamin B12, Comprehensive Metabolic Panel, Lipid Panel, direct LDL, Iron, Folate
- Review lab results
- Direct placement of pellets
- Start on DIM (males 300mg/day, females 100mg/day)

## Follow-up

- Male
  - Follow-up blood work in 4 weeks
  - Normal testosterone levels are 900-1100 ng/dl but may be as high as 1500 ng/dl without any complications; a typical boost would be 200-400 mg based on levels and patient's symptoms.
- Female
  - Follow up blood work in 6 weeks
  - Normal estradiol levels are 150-250 pg/ml.
  - Normal testosterone levels are 150-400 ng/dl. Decision about a boost depends on the age of the patient, as well as symptom relief. Typically, a 37.5-50mg testosterone boost is needed.

## Common Patient Concerns

Many patients who experience significant improvement in symptoms after 1<sup>st</sup> pellet therapy but do not see the same degree of improvement with the 2<sup>nd</sup> pellet insertion. They become concerned that the pellets are not working.

- It is very important to understand the hormone survey because it is common to forget how significant your symptoms were before initiating therapy.
- Increased stress, either physical or mental, can affect the function of the pellets and symptoms may return sooner
- Diet high in refined foods and processed carbohydrates and low in fat may also affect the pellets' function.
- Lack of exercise may also play a role especially if there has been a significant change from what the patient was used to getting.

## Estrogen Therapy

Primary symptoms of low estrogen are hot flashes, night sweats, loss of sex drive, vaginal dryness leading to pain with intercourse, and mood swings. These are reason enough to consider hormone replacement, however the most important reason to maintain normal estrogen levels is to prevent osteoporosis. Estrogen helps prevent bone loss by reducing the activity of the cells that break down bone and by improving the body's absorption and retention of calcium.

Estrogen is available in a variety of forms (sublingual tablets, patches, injections, creams, and pellets). The goal of hormone replacement is to maintain a relatively steady level of estrogen and pellets seem to provide the least amount of variation.

## Side Effects of Estrogen Therapy

- Patients may experience fluid retention.
- Breast tenderness is not uncommon and can be treated.
- Mood changes may be from estrogen therapy or B vitamins

## Breast cancer consideration

For patients with a family history of breast cancer, there must be documentation of a mammogram and a waiver signed that they agree to continue appropriate screening.

- For patients with a history of breast cancer
  - We require a record BRCA or estrogen dominance of the tumor.
  - Testosterone therapy is indicated with increased vigilance to follow for aromatization. Patients may benefit from treatment with an aromatization blocker such as anastrozole or femara. If they choose this therapy, they must sign a waiver that there is not full agreement as to the effect of testosterone supplementation for patients with a history of breast cancer.
- Many patients have significant symptoms of low estrogen following breast cancer and request estrogen supplementation. If they are willing to take the risk they must sign a consent saying they understand the risks and benefits of estrogen therapy with a history of breast cancer.<sup>1</sup> We do not recommend that they use estrogen but we will help them if that is what they decide.

## Progesterone Therapy

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<sup>1</sup> An Obstetrical Gynecology 2001 study reviewed 45 studies between 1975 and 2000. Risk estimates were reported as 1 in 82% of the studies, reported as greater than 1 but none greater than 2 in 13% of the studies, and reported as less than 1 in 2% of the studies. None of these studies were done with bioidentical hormones. Testosterone has also been shown to have some protective effect against breast cancer.

Progesterone is essential if the patient still has their uterus, however it also may be helpful for other symptoms commonly associated with premenstrual syndrome such as headaches, bloating, and mood swings. It also acts with estrogen to decrease bleeding from fibroids and enhances the estrogen effect on bone and lipids.

Patients should start on bioidentical progesterone, either regular progesterone or micronized progesterone. They should not use synthetic progestin such as Provera. If the patient does not have a uterus and wants to try progesterone for other symptom relief, the appropriate dosage is in the form of a cream (25-50 mg/application) once daily. The dose needs to be titrated to the patient's symptoms. Measuring levels is not helpful.

## Testosterone Therapy

Primary symptoms of testosterone deficiency include loss of energy, loss of mental clarity, loss of muscle mass, weight gain, decreased exercise tolerance, irritability, anxiety, decreased libido, loss of erectile ability and increased recovery time in exercise.

Often patients taking oral contraceptives have testosterone levels that are very low and have the symptoms listed above. If the symptoms are significant, it is appropriate to treat them. The typical starting dose would be 1-2 mg of testosterone sublingually daily

Replacement therapy should be with bioidentical testosterone in the form of sublingual tablets, creams, or pellets. Injectable testosterone is also a possibility; however, the levels fluctuate significantly throughout the week and there seems to be a higher rate of aromatization with the injectable replacement therapy.

## Side Effects of Testosterone Therapy

- Acne
- Mild facial and neck hair
- Male pattern baldness or hair thinning
- Insulin resistance leading to obesity
- Suppression of sperm production
- Slight decrease in testicular size.
- Erythrocytosis

## Prostate Cancer Considerations

- Pellets are only indicated if the patients are at least 3 years post treatment and if the PSA is less than 2.5. Studies have shown the men with high levels of testosterone are not at increased risk for prostate cancer, however low testosterone levels have been associated with increased risk for prostate cancer as well as cardiovascular disease.
- PSA levels can be falsely elevated if there is a history of recent prostatitis, prostatic massage, or sexual activity. The recommendation is to repeat the blood levels 48 hours after treatment for prostatitis and to pause sexual activity and prostatic massage for 48 hours prior to blood levels being drawn.
- The association of low testosterone and low vitamin D has been shown to increase risk for non-cardiovascular mortality. Treatment with 5000 – 10,000 units/day of vitamin-D should be started for levels < 50 ng/ml. Levels should be rechecked in 3-6 months to make sure that they are on adequate vitamin D replacement.

## Supplements

### DIM (diindolylmethane)

- 300mg daily for males
- 100 mg daily for females
- DIM is a plant compound with health promoting properties. It is found in cruciferous vegetables such as cauliflower, cabbage, kale, garden cress, bok choy, broccoli, and Brussel sprouts. DIM contributes to better metabolism in the most natural way working with our own hormones and adjusting their actions to avoid hormone imbalance.
- DIM has 3 main benefits:
  - causes estrogen is be metabolized down the 2-hydroxy-estrone pathway
  - releases free testosterone which is better used by the body
  - acts a natural aromatase inhibitor preventing the conversion of testosterone to estrogen

Good metabolites are known as 2-hydroxy estrogens. Many of the benefits that are attributed to estrogen, including the ability to protect the heart and brain with its antioxidant activity, are now known to come from these metabolites. When DIM increases the 2-hydroxy estrogens, there is a simultaneous reduction of undesirable estrogen metabolites. These include the 16-hydroxy and 4-hydroxy estrogens which are not antioxidants and have been

shown to increase certain types of cancer. Greater production of these harmful estrogens is promoted by obesity and exposure to several man-made environmental chemicals. Another attribute of good estrogen metabolite is their ability to regulate cell growth by getting rid of damaged cells. These metabolites support the process of cell death whereby damaged cells are naturally eliminated from the body.

DIM increases production of good estrogen metabolites, which compete with testosterone for protein binding on sex hormone binding globulin. This increases the levels of free testosterone which is the form best utilized by the body.

Increased aromatase activity, seen mainly in fat tissue, is a natural process of aging. This causes testosterone to be converted to estrogen leading to all the symptoms of low testosterone levels. Aromatase enzyme activity is also linked to chronic inflammation and obesity. Because DIM is an aromatase inhibitor, it becomes a critical component of bioidentical hormone replacement therapy, by increased levels of free testosterone.

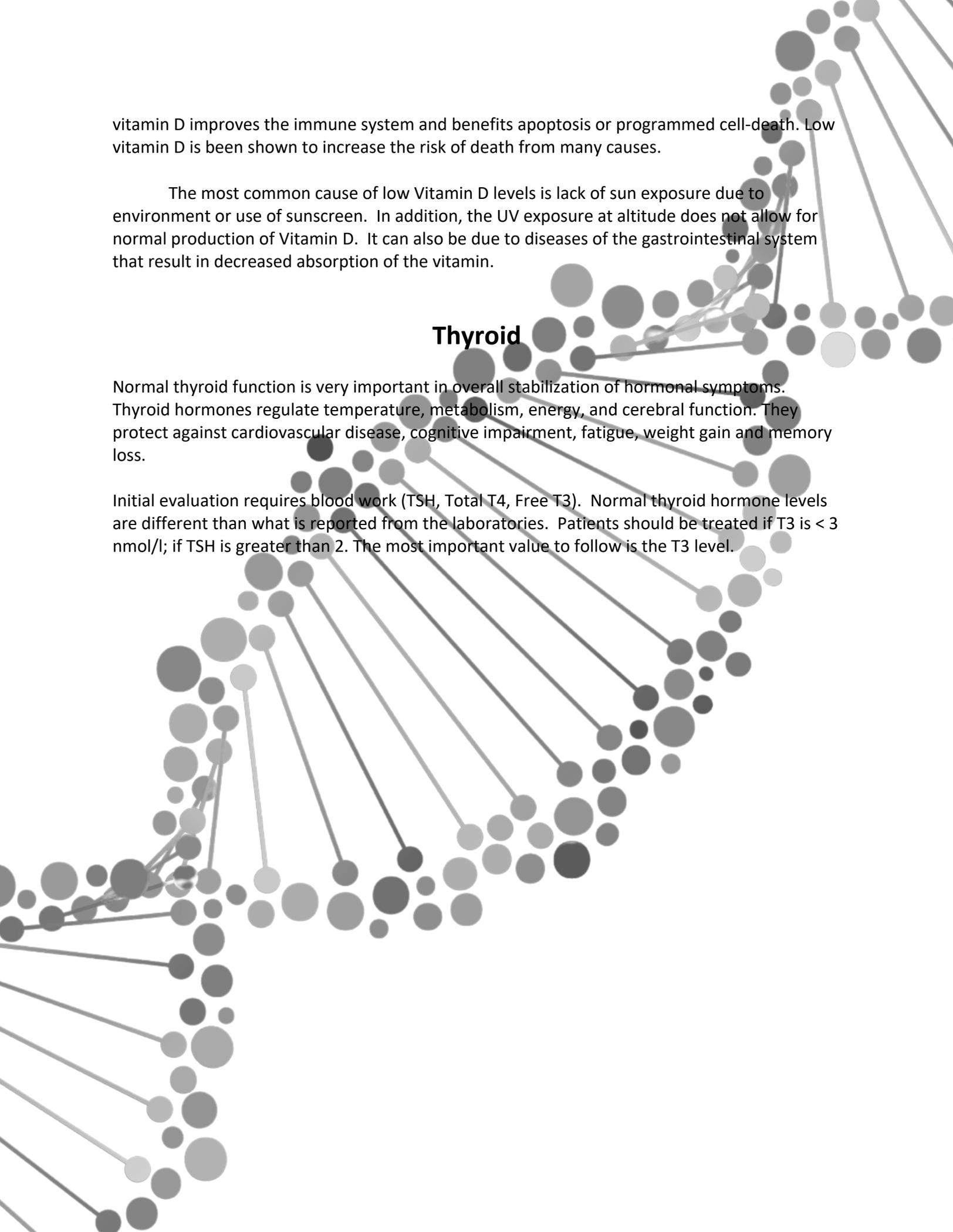
## DHEA

DHEA is the most abundant steroid hormone in your body and is produced by the adrenal glands, with the ovaries and testes producing smaller amounts. It is a major precursor to stronger androgens such as testosterone and androstenedione and the female hormone estrogen. This means that within your body it undergoes a series of chemical reactions to ultimately convert it to testosterone or estrogen as required.

DHEA levels rapidly rise from puberty, continuing to rise until early adulthood (25 to 30 years of age). After the age of 30, production begins to decline at a rate of around 2% per year, and this decline often correlated with the signs and symptoms of ageing. DHEA plays an important role in resistance to disease, with low levels being linked to increased susceptibility to ageing and disease. DHEA deficiency is very often linked with fatigue, lack of motivation, aching joints, loss of muscle tone (atrophy), weight gain and depression. Normal values for Women are 137 - 336 and for Men: 106 – 300.

## Vitamin D

Vitamin D is the building block for all hormones. Normal levels are between 50-60 ng/ml. Vitamin D is very important for bone health. There is a higher mortality rate associated with hip and spine fractures so supplementing with Vitamin D is very important, especially for women. Vitamin D improves balance and muscle performance. There is also evidence that



vitamin D improves the immune system and benefits apoptosis or programmed cell-death. Low vitamin D is been shown to increase the risk of death from many causes.

The most common cause of low Vitamin D levels is lack of sun exposure due to environment or use of sunscreen. In addition, the UV exposure at altitude does not allow for normal production of Vitamin D. It can also be due to diseases of the gastrointestinal system that result in decreased absorption of the vitamin.

## Thyroid

Normal thyroid function is very important in overall stabilization of hormonal symptoms. Thyroid hormones regulate temperature, metabolism, energy, and cerebral function. They protect against cardiovascular disease, cognitive impairment, fatigue, weight gain and memory loss.

Initial evaluation requires blood work (TSH, Total T4, Free T3). Normal thyroid hormone levels are different than what is reported from the laboratories. Patients should be treated if T3 is  $< 3$  nmol/l; if TSH is greater than 2. The most important value to follow is the T3 level.