

Chapter 41
**A Comprehensive Look at Hormones
and the Effects of Hormone Replacement**

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ABSTRACT

Three things define aging. They are memory, vision, and mobility. In order to maintain these functions hormone replacement is needed as one ages. Hormone replacement should not be considered without a complete understanding of how all the body's hormones interact with each other. If one is altered, or deficient it will affect the actions of all of the hormones in one's body. The hormonal response of an individual is as unique as their fingerprints. How one responds to hormone replacement is related to genetic profile, stress level, the condition of one's health, the environment, nutritional supplementation, detoxification, and what one eats.

This paper will look at the functions of estrogen, progesterone, testosterone, DHEA, and cortisol in both men and women. It will also look at types of hormonal imbalances that can occur in the body as one ages, including hypothalamic-pituitary, adrenal, gonadal, thyroid, and pancreatic. Symptoms of hormonal deficiency and excess will also be discussed along with a review of synthetic versus bioidentical hormone replacement.

INTRODUCTION

The aim of this paper is to examine the functions of estrogen, progesterone, testosterone, DHEA, and cortisol in both men and women. It will also look at types of hormonal imbalances that can occur in the body as one ages, including hypothalamic-pituitary, adrenal, gonadal, thyroid, and pancreatic. Symptoms of hormonal deficiency and excess will also be discussed along with a review of synthetic versus bioidentical hormone replacement.

MENOPAUSE

Menopause typically occurs between the age of 35 and 55, and menopause occurring between those ages is described as normal. Many women have symptoms of menopause five or even 10 years before they actually go through menopause, these are known as perimenopausal symptoms. The menopausal response is as unique to an individual as his or her own fingerprints. One size does not fit all, and therefore hormonal replacement should be unique as well. The hormones in the body can be compared to a symphony, and we don't want any of the members of the symphony playing out of tune. Why consider hormone replacement? Relief of symptoms is certainly a major reason why we would want to look at hormonal therapy. Other reasons why it is important to consider replacing hormones as we age include: prevention of memory loss, heart health, bone health, and growth and repair. Hormones that regulate growth and repair are: insulin, growth hormone (GH), testosterone, estrogens, and DHEA.

It is important to consider the symptoms of menopause because many women think their menopausal symptoms are caused by stress. This is because when women think of menopausal symptoms they think of hot flashes and night sweats, and they don't think or aren't aware of the other symptoms, such as vaginal dryness, anxiety, mood swings, irritability, insomnia, and depression. In our practice, 96% of the women who came in taking anti-anxiety or anti-depressive drugs left without them. They really didn't have true depression or anxiety. Their symptoms were coming from hormonal loss. Only 4% stayed on the medications and that was because they had an anxiety disorder or they had true depression. Other symptoms of menopause include: loss of sexual interest, hair growth on face, painful intercourse, panic attacks, weird dreams, urinary tract infections, vaginal itching, lower back pain, bloating, gas, indigestion, bone loss, pain in the ankles, knees, wrists, shoulders, and heels – arthritic symptoms can get dramatically better if a woman is hormonally sound, hair loss, frequent urination, snoring, sore breasts, palpitations, varicose veins, urinary leakage, memory loss, weight gain – the average woman gains 20 pounds at menopause, migraine headaches, skin feeling crawly, and dizzy spells. All of these are menopausal symptoms.

ESTROGEN

Estrogen has 400 functions in a woman's body, among which are that it:

- Stimulates the production of choline acetyltransferase, an enzyme that prevents Alzheimer's disease
- Increases metabolic rate
- Improves insulin sensitivity
- Regulates of body temperature
- Prevents of muscle damage
- Helps to maintain muscle
- Improves sleep
- Reduces the risk of cataracts
- Helping to maintain the elasticity of arteries
- Dilates small arteries
- Improves blood flow
- Inhibits platelet stickiness.
- Decreases accumulation of plaque on the arteries
- Enhances magnesium uptake and utilization
- Maintains the amount of collagen and the elasticity of the skin
- Decreases blood pressure.
- Decreases LDL cholesterol and prevents its oxidation.
- Helps maintain memory
- Increases reasoning and new ideas
- Helps with fine motor skills
- Increases the water content of the skin, and is responsible for its thickness and softness
- Enhances the production of nerve-growth factor
- Increases HDL by 10% to 15%
- Reduces the overall risk of heart disease by 40% to 50%
- Decreases lipoprotein(a)
- Acts as a natural calcium channel blocker to keep arteries open
- Enhances energy
- Improves mood and increases concentration
- Helps to maintain bone density
- Increases sexual interest
- Reduces homocysteine
- Decreases wrinkling
- Prevents macular degeneration
- Decreases the risk of colon cancer
- Helps prevent tooth loss
- Aids in the formation of neurotransmitters in the brain, for example serotonin, which decreases depression, irritability, anxiety, and pain sensitivity

Symptoms of Estrogen Excess

Many women have estrogen excess because they have estrogen but they lose progesterone long before the menopause, and estrogen and progesterone need to fit into a nice ratio. What are the symptoms of estrogen excess? Cervical dysplasia, depression with anxiety or agitation, weight gain, water retention, headaches, poor sleep, panic attacks, swollen breasts, heavy periods, hypothyroidism, fatigue irritability/mood swing, uterine fibroids, and bloating. Excess estrogen also leads to an increased risk of uterine cancer, breast cancer, and autoimmune disease. What causes estrogen excess? An obvious reason is taking too much supplementary estrogen, and many of my patients come to me having taken too much estrogen. They will come from another practitioner who did not measure their estrogen levels, and because these women complained that they were having hot flashes, the doctor gave them more and more estrogen. It is important to remember that other things can cause hot flashes. Impaired

elimination of estrogen can lead to an excess, as can a lack of exercise and diets that are low in grains and fiber. Environmental estrogens are an ever-increasing problem – there are environmental estrogens everywhere, for example in the meat we eat and in plastic.

Synthetic and Natural Estrogens

Synthetic estrogen or Premarin is made from estrone, sodium equillin sulfate, and concomitant components – 17 alpha-dihydroequillin, 17 alpha-estradiol, 17 beta-dihydroequillin. The human body produces three main estrogens: E1 (estrone), E2 (estradiol), and E3 (estriol). E1 is the main estrogen that the body makes postmenopausally. Many researchers believe that high levels of E1 significantly increase the risk of breast cancer. E1 estrogen, or estrone, is one-half of Premarin. E2 estrogen, or estradiol, has many functions. All the benefits of estrogen mentioned above, including increasing HDL cholesterol and decreasing LDL cholesterol, come from the E2 component. There is an increasing body of evidence to suggest that E3 estrogen, or estriol, helps to prevent breast cancer. Estriol is used in Europe, and now in the United States, as a treatment protocol for breast cancer. Estriol is now also being used to treat multiple sclerosis. Estriol estrogen by itself, however, does not have the bone, heart, or brain protection that estradiol does.

Estrogen Metabolism

Estrogen metabolism should always be considered, as the metabolism of estrogen can change after menopause, and consequently a woman may respond differently to estrogen replacement. When estrogen is metabolized, it goes through two different major pathways and one minor pathway. The minor pathway is 4-OH estrone. The two major pathways are 2-OH estrone and 16-OH estrone. The 2-OH estrone is the good estrogen. It does not stimulate cell growth and it helps and it blocks the action of stronger estrogen products that may be carcinogenic. Thus, we ideally want everything to go down the 2-OH pathway in order to decrease the patient's risk of breast cancer. The 16-OH estrone has strong estrogenic activity. 16-OH estrone is linked to an increased risk of breast cancer, as is 4-OH estrone. Studies on 4-OH estrone suggest that it may directly damage DNA and cause mutations, and therefore it is linked to an increased risk of cancer. Equine estrogens, such as Premarin, are metabolized into 4-OH estrone.

Is it possible to raise levels of 2-OH estrone? Yes it is, and it can be done quite simply by eating certain foods, taking supplements, and taking regular exercise. Foods that can push estrogen metabolism down the 2-OH pathway include: cruciferous vegetables (broccoli, kale, brussel sprouts, cauliflower) flax, soy, kudzu, and a high protein diet. Useful supplements are indole-3-carbinol (200 to 300 milligrams a day), omega-3 fatty acids, vitamin B6, B12, and folate. The literature suggests that 500 milligrams a day of indole-3-carbinol helps to prevent a reoccurrence of breast cancer. When you replace estrogen itself – any kind of estrogen, whether its birth control pills, synthetics, or biologically identical estrogen – all of those deplete the body of B-vitamins. Therefore it is prudent to give patients that are taking any kind of estrogen replacement, including birth control pills, supplementary B-vitamins.

There are two other factors that affect estrogen metabolism. One of those is obesity. The more obese a woman is, the more 16-OH estrone she makes. Therefore women who are heavier do have an increased risk of breast cancer. Environmental estrogens or xenoestrogens also affect estrogen metabolism. There are 50 chemicals that imitate estrogen and are toxic. These chemicals are found in pesticides, synthetic hormones fed to animals, plastics, and cosmetics.

Estrogen and the Brain

Estrogen does affect the brain. It increases blood flow. It increases the supply of glucose and oxygen to the neurons. Glucose itself is the major fueling source of the brain, 25% of the glucose that goes inside a woman's body goes directly to the brain to fuel it. So people who are on an Atkins-type approach and aren't eating enough carbohydrates will actually have decreased memory. Estrogen protects neurons, increases neurotransmitter levels, keeps the blood brain barrier working properly, increases the body's sensitivity to nerve growth factor, and decreases the neuronal generation of Alzheimer's-linked beta-amyloid peptides.

Estrogen Replacement

The best way to deliver estrogen replacement is transdermally, and the reason for that is that estrogen can increase blood pressure when given orally. That does include birth control pills. Oral estrogen can also increase triglycerides, increase E1 estrogen (estrone), and cause gallstones. When I did my medical training we were told to look for the 4-F's – fair, fat, forty, and fertile – when looking for gallstones, that doesn't hold true anymore because so many women in their 20's take birth control pills. Those women have gallstones. Gallstones are not uncommon now in women who are 20 or 25 years of age, and the major cause of that is due to oral estrogen. Oral estrogen can also elevate liver enzymes. It can decrease GH levels – the hormone that keeps us younger. Anti-aging specialists obviously don't want to do that, and therefore estrogen should only be given transdermally. Estrogen by mouth can increase carbohydrate cravings, increase sex hormone binding globulin (SHBG), which is a problem because it decreases testosterone levels, and interrupt tryptophan metabolism and consequently serotonin metabolism.

Thus it is best to deliver estrogen transdermally. Patients should put it on their abdomen or thigh, and rub it in for two minutes. If they don't rub it in properly they won't get the full effect of a transdermal estrogen. It is also a good idea to put it on in the morning, mainly because if they lay next to someone in the evening the estrogen can rub off on that person. That not only includes their spouse or significant other, but it can include their grandchildren and etcetera. We do not use serums in our practice except for in the treatment of breast cancer.

Tamoxifen and Evista do not have the same positive effects on the brain as natural bioidentical hormone replacement does. They maintain bone, but they do not maintain memory, and so a biologically identical approach is recommended. The treatment can be compounded by a pharmacy. This has several benefits. The main one being that each patient's treatment can be individualized because the physician can use any mix of biest (E2 and E3). E3 estrogen is not patentable as it is biologically identical, and therefore no drug company makes it. Most of our patients begin at approximately 20% E2 and 80% E3. But we do measure levels of E1, E2, and E3, usually by saliva testing. Saliva testing is a little bit more accurate than blood testing, especially for women who are perimenopausal. And the reason for that is twofold. If you use a blood test only and a woman's hormones are changing, then you are only getting a small snapshot of the situation, you are not getting the big picture. Also, saliva testing looks at the amount of free hormone, and it is important to know how much is available for the body to use. Blood levels are only showing the level of free plus bound hormones, and since we don't know how to unbind estrogen from its receptor sites yet, saliva testing is the method of choice.

PROGESTERONE

Symptoms of progesterone loss frequently bring patients into the office, these include: anxiety, depression, irritability, mood swings, insomnia, pain and inflammation, osteoporosis, decreased HDL cholesterol, and excessive menstruation. What causes progesterone loss? Progesterone production can be impaired by low levels of luteinizing hormone (LH) and increased prolactin levels. Therefore it is wise to check prolactin levels if you suspect progesterone loss. Stress can cause low progesterone. We live in a very stressful society, and it is amazing how many women have low progesterone levels because of this. Antidepressants themselves can lower progesterone. So if a patient is taking an antidepressant drug that may be a reason why their progesterone level is low even if there are just 25 years of age. Excessive arginine consumption can also lead to progesterone loss. Many of my patients that body build use arginine, and this can lead to a wrong ratio between arginine and other amino acids, and this may ultimately cause a problem with progesterone production. Sugar itself can lower progesterone in a female, as can saturated fat, and deficiencies of vitamin A, B6, vitamin C, and zinc. Therefore the very first thing a doctor suspecting progesterone loss should ask the patient about is their diet. Are they nutritionally sound? It is important to remember that hypothyroidism can decrease progesterone production, as progesterone and thyroid are directly tied to each other.

Synthetic Progesterone Versus Natural Progesterone

Synthetic progesterones are called progestins. Progestins do not reproduce the same actions of natural progesterone. What are the side effects of progestins? Progestins increase appetite, and therefore they can cause weight gain. They can also cause fluid retention, irritability, and depression. In other words, many of the symptoms of progesterone loss are exacerbated by progestin itself. It can

decrease energy and sexual interest, and cause headaches, bloating, breast tenderness, acne, hair loss, nausea, and insomnia. Progestins interfere with the body's normal production of progesterone. They do not help to balance estrogen – remember, estrogen and progesterone need to fit in a ratio, progestins do not help that relationship. Progestins stay in the body longer than natural progesterone, they can stay on the receptor site for up to six months. They inhibit the protective effects that estrogen has on the heart and they can cause spasms of coronary arteries – this is the reason that many believe that the Women's Health Initiative Trial showed an increase in heart disease. It wasn't the estrogen that was the issue. It was the synthetic progestins causing vasoconstriction, which therefore increased the risk of heart disease. Progestins also increase LDL cholesterol levels and decrease HDL cholesterol levels. In our practice we do not use birth control pills for perimenopause. We do not want LDL cholesterol levels rising and we don't want HDL cholesterol levels declining. Progestins protect only against cancer of the uterus. They don't have any protective effects on the breast tissue. Progestins counteract many of the positive effects that estrogen has on serotonin. Basically, there are a lot of effects of progestins that many people are not aware of.

Natural progesterone is very different. It helps balance estrogen. It improves sleep. It has a very wonderful, natural calming effect. It helps lower blood pressure. It helps the body use and eliminate fats. It lowers cholesterol. It offers some protection against breast cancer. It increases scalp hair. It helps balance fluid in the cells. Natural progesterone increases the beneficial effects of estrogen on blood vessels. It increases metabolic rate. It functions as a natural antidepressive and as a diuretic.

The Estrogen/Progesterone Ratio

It is extremely important that estrogen and progesterone are present in the body in the correct ratio. A lot of women have become afraid of estrogen, and this has led to a lot of patients taking progesterone on their own. What happens if you take progesterone by itself and therefore there is not the correct ration between progesterone and estrogen? This does not apply to women who are estrogen dominant. Women who still have their own estrogen can take progesterone alone, but doing this in women who are deficient in estrogen can lead to weight gain, an increase in total cholesterol, decrease in HDL cholesterol, increase in LDL, increase in triglyceride levels, depression, fatigue, a waning libido, and insulin resistance and eventual diabetes.

Progesterone Replacement

Progesterone can be given transdermally or we can give it PO. If the patient has insomnia, it is often better to give them progesterone P.O, and the reason for that is that it will then affect the GABA receptors.

Prometrium is a natural form of progesterone, however we tend not to use very much because it has a peanut oil base and many people become allergic to peanuts. Nobody eats peanut butter or peanuts everyday. But, if you are giving a patient a daily dose of progesterone that contains peanut oil, this can cause sensitivity issues. Therefore, it is often better to have progesterone compounded.

Most of the time when I replace hormones in women, I do give them daily. You can cycle your patients. Some of my patients want to cycle, so, we have them cycle if they want to. If you use higher dose hormone replacement, then it is essential to cycle your patients. If you are using low-dose hormone replacement is it best to leave it up to the patient as to whether she wants to cycle or not. Most women feel that not cycling is probably the best part of menopause, plus you don't get so many ups and downs if you don't cycle.

TESTOSTERONE IN WOMEN

In women, testosterone increases sexual interest and a sense of emotional well-being. It helps maintain muscle mass and strength. It maintains memory. It helps the skin from sagging. It decreases excess body fat. It helps maintain bone strength. And it elevates levels of norepinephrine in the brain, therefore it has a tricyclic effect.

Symptoms of testosterone loss in a woman include: muscle wasting, weight gain, fatigue, low self-esteem, decreased HDL cholesterol, dry and thin skin with poor elasticity, thinning and dry hair, droopy eyelids, sagging cheeks, thin lips, and anxiety. It is important to remember that some women have increased testosterone levels. Joseph Collins wrote a very good book on this subject called "*What's Your Menopause Type?*" that explained that many women can be put into categories of 12 different modalities

that they go through hormonally in menopause. Three of those leave a woman with a high testosterone level. High testosterone levels can cause anxiety, depression, fatigue, hypoglycemia, salt and sugar cravings, agitation and anger, facial hair and acne, insulin resistance – many of the same things we see with polycystic ovarian syndrome, weight gain, and hair loss. More importantly, at least from a physician's viewpoint, increased testosterone levels after menopause increase a woman's risk of heart disease.

Testosterone Replacement in Women

Testosterone can be used P.O. or transdermally. We do not use synthetic testosterone, which is known as methyltestosterone. Methyltestosterone itself is associated with an increase in cancer of the liver in some patients, so we use natural testosterone. If testosterone is used transdermally it is important to rotate sites. If a woman keeps putting it on the same site every day, they will grow hair there. Without estrogen, testosterone cannot attach to the brain receptors. So it is very important that estrogen and testosterone also sit in a ratio. It is also important not to replace testosterone without replacing estrogen because doing that can increase a patient's risk of heart disease. Therefore, if you want to replace testosterone, replace estrogen as well or you will increase a woman's risk factors for heart disease.

If a woman's testosterone levels are too high this can be treated with metformin and/or saw palmetto.

Causes of Low Testosterone Levels in Women

The two main causes of low testosterone levels in women are menopause and childbirth. Chemotherapy can lower testosterone. As can adrenal stress or burnout, as the adrenal glands are intimately involved with testosterone. Other things that can lower testosterone levels in women include: endometriosis, depression, psychological trauma, birth control pills, and statin drugs.

THE MALE MENOPAUSE

Men do go through menopause; except for in men it is called andropause. Testosterone replacement therapy for men is safe and can provide significant benefits. What are the symptoms of male hormonal loss? Fatigue, tiredness, and loss of energy, are one of the main complaints I get from my male patients, and 35% of our practice is male. Other symptoms of andropause are depression, low mood, negative mood, irritability, anger, bad temper, anxiety, nervousness, loss of memory and concentration, decreased libido and drive, loss of erections, decreased intensity of orgasms, backache and joint aches, loss of fitness, feeling over-stressed, decrease in job performance, decline of physical abilities, bone loss, and elevated cholesterol levels.

As we all know, testosterone is a sex hormone. There are testosterone receptors all over the male body – not just in the obvious locations. Testosterone is also involved in the making of protein and muscle formation. It helps manufacture bone, it improves oxygen uptake throughout the body, and it helps to control blood sugar – you can treat diabetes with testosterone. It helps regulate cholesterol. It helps maintain a powerful immune system. It aids in mental concentration and memory, and as we know memory is an issue as we age. It improves mood and helps prevent Alzheimer's disease.

Half of healthy men between the ages of 50 and 70 years will have a testosterone level below the lowest level seen in healthy men that are 20 to 40 years of age. The way we replace testosterone in men is that we usually look at a blood level of 600. A study of 25-year-old men revealed that the average testosterone level at that age was 601, and that is the reason why we use 600 as the number to replace testosterone to. The normal in the laboratory in Detroit that we use is 280 to 1100. So, for someone who is used to running at 1000, 600 is probably not going to be enough. However, the current thinking is to at least correct it to 600.

Estrogen in the Male

Estrogen is a problem in men. Estrogen levels rise as men age; this is mainly because of the increased production of an enzyme called aromatase. However, other factors also cause estrogen levels to become elevated, for example: alterations in liver function, zinc deficiency, obesity, overuse of alcohol, environmental estrogens, and medications. A number of medications increase estrogen in men; these include statin drugs, and some blood pressure drugs, antidepressants, and nonsteroidal anti-inflammatory drugs. Estrogen really is an issue with men – if estrogen levels go too high the risk of heart disease rises dramatically.

Testing the Menopausal Male

When thinking about laboratory tests for testosterone replacement candidates, the two obvious laboratory tests that should be carried out are total testosterone and free testosterone. We measure estradiol in our patients, and we are now starting to also measure estrone in men. The reason we are doing that is that we are finding that some of the estradiol is becoming estrone, and we are trying to decide really what that means. We don't know yet, but we now measure E2 and E1 in men. We also look at sex hormone binding globulin (SHBG), which increases with age. SHBG binds testosterone. Estrogen increases the body's production of SHBG, and high levels of testosterone suppress SHBG. Other laboratory tests that should be conducted include: dihydrotestosterone, DHEA, cortisol, progesterone, and prostate specific antigen (PSA). All male patients taking testosterone replacement should have their PSA levels and a digital rectal exam every six months.

Testosterone Replacement and Prostate Cancer

The most common question asked about testosterone replacement is: Does it increase the risk of prostate cancer? Prostate cancer itself is a contraindication for testosterone replacement. Therefore it should not be given to patients who have prostate cancer. I have one exception to that in my practice, and that is a man of 94 years of age. He understands the risks and benefits. He is probably not going to die of prostate cancer at 94. He would like to live the last few years of his life to the fullest he possibly can, and so he has signed to say that he knows the risks and benefits. The incidence of prostate cancer itself is not increased by testosterone replacement. There are several studies to show that. There is no evidence that testosterone replacement accelerates benign prostatic hyperplasia (BPH) either. Even so a digital rectal exam and PSA testing is paramount every six months.

Dihydrotestosterone

Dihydrotestosterone (DHT) is more potent than testosterone. Testosterone is converted to DHT by the enzyme 5-alpha reductase. DHT cannot be turned into estrogens. DHT has some interesting effects, and there is a lot of discussion in the literature as to whether DHT is the evil twin of testosterone or it is really a good testosterone. At present, we aim to lower DHT levels in our patients. In the future that may not happen. At the moment we give our patients 1% progesterone to lower their DHT levels. We try not to use 5-alpha reductase inhibitors.

Testosterone Replacement Therapy

For testosterone replacement in men, testosterone is given transdermally. Once again, there are many advantages of using a compounding pharmacy. If you use Androgel, it is much more expensive and there are only a few dosages available to choose from. Furthermore, if it is compounded it can be combined with other hormones or drugs.

When it comes to erectile function, testosterone is far more effective when administered transdermally. Jain *et al* found that when treating erectile dysfunction transdermal testosterone worked 81% of the time, compared with just 53% for intramuscular administration and 51% when given orally. Erectile dysfunction is an issue with older men, and the effectiveness of testosterone for treating this problem when given transdermally is one of the reasons why we choose to administer it this way.

Testosterone replacement has been shown to improve cognitive function, reduce the risk of developing Alzheimer's disease, prevent heart disease, improves exercise-induced myocardial ischemia, dilate the coronary arteries, and decrease insulin resistance. It should be noted that low testosterone levels are associated with dyslipidemias.

DHEA

Both men and woman make DHEA. DHEA is made by the adrenal glands, and a small amount is also made in the brain and in the skin. DHEA production declines with age, starting the late twenties. By the age of 70, the body may only make one quarter of the amount of DHEA that it made at its peak. DHEA is extremely important because it makes estrogen, progesterone, and testosterone in both men and women. However, it also has a number of other important functions, for example, it: decreases cholesterol levels, decreases the formation of fatty deposits, helps prevent blood clots, increases bone growth, promotes weight loss, increases brain function, increases the sense of well being, helps the body

deal with stress, supports the immune system, helps the body repair and maintain itself, and decreases allergic reactions.

A number of things lower DHEA levels, these include: aging, the menopause or andropause, stress, and smoking. If you have a patient who is a big smoker they may have a low DHEA level regardless of their age.

Do we replace DHEA? Yes we do. You can buy DHEA without a prescription. As we know, DHEA does affect the other hormones; therefore it is a good idea to encourage patients not to do that. Replacement of DHEA increases muscle strength and lean body mass, improves immune function, increases quality of life, improves sleep, increases the sense of well being, decreases joint soreness, improves insulin sensitivity, lowers triglyceride levels, and helps to lessen the damaging effects of stress. Women are more sensitive to DHEA than men, 15 mg of DHEA is enough for women unless they are being treated for rheumatoid arthritis, in which case a dose of 50 to 100 mg is appropriate. Men metabolize DHEA much faster than women, and therefore a dosage of 25 or 50 mg is recommended. For women who have a high testosterone level – remember DHEA makes testosterone – it is possible to use keto-DHEA. If you put a keto group on to the DHEA, then it will not go down the testosterone pathway.

As with most things, you can have too much of a good thing, and you can have too much DHEA. Symptoms of DHEA excess include: fatigue, anger, depression, deepening of voice, insomnia, mood changes, weight gain, facial hair, acne, sugar cravings, restless sleep, and irritability.

CORTISOL

Cortisol, which is made by the adrenal glands, is the only hormone in body in which levels increase with age. Cortisol has a number of functions. It balances blood sugar, and plays a role in weight control, the immune system response, bone turnover rate, stress reaction, sleep, protein synthesis, and mood and thoughts. It also influences the testosterone/estrogen ration, the DHEA/insulin ratio, and affects the pituitary/thyroid/adrenal system. Cortisol is necessary for life, however too much cortisol has a deleterious effect on the body. A number of things elevate cortisol levels, the main factors are stress, depression and high progesterin intake. It is important to keep cortisol at normal levels, if it is increased it will impair the immune system, increase osteoporosis risk, blood pressure, cholesterol levels, triglyceride levels, blood sugar levels, and insulin resistance.

If a patient complains that they are still gaining weight or an unable to lose weight even if they are eating properly and taking plenty of exercise, and their thyroid levels are normal, check their cortisol levels. In very stressed people with elevated cortisol levels it can take an entire year to get their adrenal system back to normal, so it is not a quick fix. Let your patients know that they will lose weight when you lower their cortisol levels, but that their body is in a state of emergency when their cortisol levels are not correct, and it could take a year before they are going to see a good weight reduction.

Abnormal cortisol levels are associated with menopause or andropause, chronic fatigue syndrome, fibromyalgia, depression, impotence, anorexia, panic disorders, PMS, infertility, sleep disorders, osteoporosis, and heart disease. With people with those diagnoses you need to make sure you evaluate their adrenal system along with the rest of their hormones, as they may be suffering from adrenal burnout. When the body is first put under stress it will increase production of DHEA and cortisol. After the body has been stressed for a long time it will no longer do that. The body is not able to keep up with itself anymore and DHEA and cortisol levels decline and they will go into adrenal burnout. Symptoms of adrenal burnout include: fatigue, low blood pressure, sensitivity to light, insomnia, digestive problems, emotional imbalances, hypoglycemia, and decreased sexual interest. Remember, hormones have complex relationships. If cortisol is increased it decreases the making of progesterone and its activity. Cortisol also competes with progesterone receptors. Therefore it is extremely important to check a woman's progesterone levels if you suspect adrenal burnout. When cortisol is elevated thyroid hormone is more bound and less active, and levels can therefore decline. Decreased estradiol (E2) in a woman is a stressor to her body and therefore decreased estradiol will elevate cortisol levels. So, if there is no other reason for estrogen replacement in women, that fact that it will help to keep cortisol levels normal is enough.

INSULIN

Insulin, estrogen, progesterone, DHEA, and thyroid hormones are all important for the regulation of glucose in the body. Estrogen lowers blood sugar in women and testosterone lowers blood sugar in men. Progesterone can raise blood sugar in women if it is not balanced with estrogen. Insulin elevation, or even insulin being too low, is not good. A number of things elevate insulin levels. A major factor is eating a high-carbohydrate diet. Even a patient who does not have diabetes in their family, can develop insulin resistance if their diet contains too much carbohydrate. The completion of the Genome Project was a turning point in medicine, and we now know that inheritance counts for 20%, but environment counts for 80%. Thus if a patient's entire family has diabetes, it does not mean that they have to become diabetic as well. They do not have to display that gene, if their environment is controlled. However, the reverse is also true. If a patient does not have a gene for diabetes, they can eat the wrong diet, live a stressful life, develop insulin resistance, and end up with diabetes. Stress also elevates insulin levels. Decreased estrogen, increased testosterone, and excessive progesterone all elevate insulin levels in women. Insomnia increases insulin. Elevated DHEA elevates insulin, as does decreased thyroid hormone levels. A lack of exercise is also a factor.

PREGNENOLONE

Pregnenolone is a precursor to DHEA, estrogen, progesterone, and testosterone, and like those hormones its levels decline with age. By the age of 75, most people's production of pregnenolone has dropped by 65% compared to when they were 35. Pregnenolone is extremely important for memory, so it is often replaced. Like DHEA, pregnenolone can be obtained without a prescription in the United States, however patients should be encouraged not to take it unless they extremely low pregnenolone levels. Pregnenolone regulates the balance between excitation and inhibition in a nervous system, it increases resistance to stress, it improves physical and mental energy, enhances nerve transmission and memory, reduces pain and inflammation, and it blocks the production of acid-forming compounds. Remember, the body should be alkaline. Most of us eat acidic foods. Having an acidic body encourages aging. So one of the very important functions of pregnenolone is to make everything more alkaline by blocking the production of acid-forming compounds. Pregnenolone is used in the treatment of arthritis, depression, memory loss, fatigue, and moodiness. You can have too much pregnenolone, just like any other hormone, and too much causes acne and drowsiness.

THYROID HORMONE

Thyroid hormone is the body regulator. There are three thyroid hormones: T2, T3, and T4. T2 is something that we may not always look at. T2 increases the metabolic rate of muscles and fat tissue. The systems of low thyroid hormone are well known and include: depression, weight gain, constipation, headaches, brittle nails, dry skin, menstrual irregularities, fluid retention, poor circulation, elbow keratoses, diffuse hair loss, slow speech, anxiety and panic attacks, decreased memory, inability to concentrate, muscle and joint pain, reduced heart rate, slow movements, morning stiffness, puffy face, swollen eyelids, decreased sexual interest, cold intolerance, cold hands and feet, swollen legs and feet, swollen hands, swollen abdomen, insomnia, fatigue, low body temperature, husky voice, low blood pressure, coarse dry hair, dull facial expression, yellowish discoloration of the skin, muscle cramps, and carpal tunnel syndrome.

Thyroid hormone affects muscle metabolism, however it does not build muscle. It can cause low pregnenolone levels. Decreased T3 production raises LDL cholesterol. 95% of people with fibromyalgia have hypothyroidism, so if a patient has fibromyalgia check their thyroid levels. We measure thyroid stimulating hormone (TSH), T3 T4, reverse T3, and thyroid antibodies. We used to only replace T4 only, because the general consensus was that the body converts T4 into T3. However, research over the past few years has shown that with most people you need to replace both T3 and T4.

Factors that cause decreased production of T4 include deficiencies of zinc, copper, vitamin A, vitamin B2, vitamin B3, vitamin B6, and vitamin C. The conversion of T4 to T3 is dependent upon the enzyme 5'diodinase. A number of factors affect the production of 5'diodinase, these include: selenium deficiency, stress, cadmium toxicity, mercury toxicity, lead toxicity, starvation, inadequate protein intake, elevated cortisol – remember there is a direction relationship between cortisol and thyroid, chronic illness, decreased kidney function, and decreased liver function. There are other reasons that affect the body's ability to convert T4 to T3; these include nutritional deficiencies (iodine, iron, selenium, vitamins A, B2,

B6, and B12), medications (beta blockers, birth control pills, estrogen, lithium, phenytoin, theophylline, and chemotherapy), and diet (too many cruciferous vegetables, low protein diet, low fat diet, low carbohydrate diet, excessive alcohol, soy, and walnuts). Other factors include: aging, excessive alpha-lipoic acid, diabetes, fluoride, lead, mercury, pesticides, radiation, stress, surgery, copper excess, calcium excess, dioxins, PCB, inadequate production of DHEA and/or cortisol, and phthalates.

You can have a low T3 or you can have an increase in reverse T3. Factors associated with low T3 or increased reversed T3 include: increased epinephrine or norepinephrine, free radicals, aging, fasting, stress, prolonged illness, diabetes, toxic metal exposure, and certain changes in the immune system.

So, how do we increase the conversion of T4 to T3? Selenium, potassium, iodine, iron, zinc, high protein diet, the herb ashwaganda, vitamin A, vitamin B2, vitamin E, growth hormone, testosterone, insulin, glucagons, melatonin, and tyrosine can all increase the conversion of T4 to T3.

When evaluating thyroid function basal body temperature should be measured. Approximately 10% of patients will have very normal laboratory results, and those people should have their basal body temperature assessed, if it is below 97.4 then the physician should think about trying to change things nutritionally or by giving thyroid. The new norm for TSH is 1.5 to 2. The natural average TSH in the United States is 1.5. If TSH is above 2 then T3 and T4 should be replaced. The same compounding pharmacist that makes up the prescriptions for male and female hormone replacement can also make T3 and T4 compounds, and thus they can be made up to the physician's exact specifications. Things like omothyroid are a particular ratio – four parts T4 to one part T3. That ratio is not right for everyone. A compounding pharmacist can make the ratio one to one, or 15 to 1.

CONCLUSION

All the hormones in the body are designed to work together. However, one size does not fit all, and it is very important as an anti-aging specialist that you look at customizing replacement for each individual patient.

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