Female Hormone Restoration

Until 2002, mainstream physicians routinely prescribed conventional hormone replacement therapy (HRT) in order to alleviate menopausal symptoms such as hot flashes, mood swings, decreased sexual desire, vaginal dryness, and difficulty sleeping, as well as to prevent heart disease and osteoporosis. In 2002, however, the results of a landmark study, the Women's Health Initiative (WHI), identified dangers associated with conventional hormone replacement therapy in women. More than 160,000 women participated in this observational study. Conventional HRT side effects included a 26% increased risk of breast cancer, 29% increased risk of heart attack, 41% increase in risk for strokes, and a doubling in risk for blood clots relative to the untreated group. Moreover, women receiving conjugated equine (horse-derived) estrogen experienced a six-fold increased risk for uterine cancer. Only those women under 60 years of age who had undergone a hysterectomy (surgical removal of the uterus) experienced a reduction in breast cancer risk when using estrogen *without* medroxyprogesterone acetate (MPA), a synthetic progestogen (Rossouw 2002; Grady 2002; Hulley 2002; Azoulay 2004; Moskowitz 2006; Ragaz 2010).

Given the substantial risks associated with conventional HRT, many women began to seek alternatives. Up to 70% of women taking HRT stopped and overall, women's trust in the mainstream medical establishment declined significantly (Roumie 2004; Schonberg 2005). Data from the study also resulted in many physicians discouraging the use of conventional HRT for the prevention of osteoporosis and cardiovascular disease in aging women (Sharma 2003; Azoulay 2004).

Life Extension was not surprised by the results of the WHI study. The hormones being utilized consisted of oral *equine* (horse) estrogen and a *synthetic progestogen*, both of which differ in chemical structure from the natural hormones produced in a woman's body. Life Extension has discouraged the use of conventional HRT for many years and instead has recognized the value of *bioidentical HRT*, which uses hormones that are identical as those naturally produced in women. Conventional HRT makes use of *non-bioidentical* hormones that differ chemically from those naturally produced by a woman's body. Furthermore, the relative levels of the female hormones administered in conventional HRT are different (Turgeon 2006; Chlebowski 2010).

Bioidentical HRT is associated with far fewer side effects than conventional HRT and there is intriguing evidence that it may reduce the risk of certain cancers (Holtorf 2009).

Moreover, supplementation with scientifically studied vitamins and natural plant extracts can help promote healthy metabolism of female hormones and complement the actions of bioidentical HRT.

Understanding Conventional HRT

The rationale for conventional HRT is that women's hormone levels decline with age. Replacement, therefore, should reverse troubling menopausal consequences, which include increased risk of heart attack and cancer (Wren 2009; Lenfant 2010; Lee 2010). While the original understanding of menopause and logic behind HRT were theoretically correct, modern science is showing that the true story of HRT is much more complex (Sitruk-Ware 2007).

It is impossible to isolate estrogen and progesterone from other hormones. All steroid hormones are created from cholesterol in a hormonal cascade. The first in the cascade is *pregnenolone*, which is subsequently converted into other hormones including *dehydroepiandrosterone (DHEA)*, progesterone, testosterone, and various forms of estrogen. These hormones are interrelated, yet each performs unique physiological functions. Biologically sound hormone replacement should focus on a woman's total hormone balance, not only on estrogen and progesterone.

Mainstream physicians are just now beginning to recognize *estrogen dominance* (Turgeon 2006), a term used to characterize the relative imbalance between excess estrogen and insufficient progesterone. Estrogen dominance helps explain many of the conditions that confront modern women in Western civilization, such as fibrocystic breast disease (Kubista 1990) and cancer (Bentrem 2003; Bradlow 1995; Papaconstantinou 2000). Estrogen dominance can occur in any woman. However, perimenopausal women, who typically experience a more rapid decline in progesterone relative to estrogen, are especially at risk (Fauser 1997).

Conjugated equine estrogen (CEE) is obtained from the urine of pregnant mares (horses) (Bhavnani 2003). CEE is usually given in combination with progestin, a chemical compound modified for the purpose of appearing structurally *similar* to natural, bioidentical progesterone. However, it is not the same. The structural differences between conjugated equine estrogen and chemical progestin as well as natural hormones are responsible for many of the adverse effects resulting from conventional HRT.

Another major problem with conventional HRT is the estrogen ratio. For example, the ratio in medications such as Premarin® is considerably different than the ratio observed naturally in a woman's body (Wright 1999).

Causes of Estrogen Dominance

Beginning in perimenopause and continuing throughout menopause, the production of progesterone tends to decline more rapidly than that of estrogen. If the progesterone to estrogen ratio is unbalanced, favoring excess estrogen, a woman may become susceptible to an increased risk of fibrocystic breast disease and other health problems (Kubista 1990; Lee 1996).

Factors contributing to estrogen dominance include:

- Exposure to estrogen-mimicking chemicals found in herbicides, pesticides, petrochemicals (e.g., BPA, bisphenol A) and PCB's (polychlorinated biphenyl's) used in some cosmetics, glue, plastic, and other modern materials (Tapiero 2002)
- Obesity as well as increased intake of excess calories from simple sugars, fiber-deficient refined grains, and *trans*¬-fat from partially hydrogenated vegetable oil

Many practitioners report that estrogen dominance is often associated with symptoms such as food cravings, bloating, weight gain, fatigue, mood swings, depression, cyclical migraine headaches, decreased sexual desire, menstrual cramps, short cycles, heavy menstrual bleeding, hair loss, fibroids, and endometriosis.

IS CANCER RISK A REASON TO DEPRIVE AGING WOMEN OF NATURAL HORMONES?

Concern about cancer is an important reason why more aging women do not restore their hormones to youthful levels. Hormones like estrogen and testosterone affect cell growth and proliferation. Does that mean aging women should simply accept hormone deficiency as a part of "normal" aging?

If estrogen caused breast cancer, then we would expect to see very high rates in young women of childbearing age, with a dramatic decline after menopause. This has not been observed. To demonstrate the risk of developing breast cancer as women age, we have reprinted the following statistics (Simone 2005):

By age 25: 1 in 19,608	By age 45: 1 in 93	By age 60: 1 in 24	By age 75: 1 in 11
By age 30: 1 in 2,525	By age 50: 1 in 50	By age 65: 1 in 17	By age 80: 1 in 10
By age 40: 1 in 217	By age 55: 1 in 33	By age 70: 1 in 14	By age 85: 1 in 9

The genes that help regulate healthy cell growth can *mutate*. In fact, mutations in cells' regulatory genes are an underlying cause of cancer (Haber 2000). Breast cells with mutated genes may be more vulnerable to estrogen's growth stimulating effects.

Estrogen Explained

To fully appreciate the complexity of HRT, it is important to understand the various forms of estrogen and their physiological effects. More than 15 forms of natural estrogen have been identified (Taioli, 2010) including estrone, estradiol, and estriol.

Each of these estrogens has particular functions. Estradiol (E2) (the predominant form in non-pregnant, reproductive females) primarily aids in the cyclic release of eggs from the ovaries (i.e., ovulation). E2 has beneficial effects on the heart, bone, brain and colon. Reduction in the level of E2 causes common menopausal symptoms such as hot flashes and night sweats. Estrone (E1), produced in the ovaries and fat cells, is the dominant estrogen in postmenopausal women. Estriol (E3) is secreted in large quantities by the placenta during pregnancy. However, it is a comparatively weak estrogen, and the form of estrogen least associated with hormone-related cancers. In Europe and Japan, E3 is frequently used for HRT (Head 1998; Kano 2002; Moskowitz 2006; Holtor 2009).

The three types of estrogen convert into many metabolites. E1, for example, may convert into three different forms:

- 2-hydroxyestrone
- 4-hydroxyestrone
- 16-alpha-hydroxyestrone

Scientists have identified 2-hydroxyestrone as a “good” or chemoprotective estrogen, while 16-alpha-hydroxyestrone and 4-hydroxyestrone have been associated with the development of cancer (Bradlow 1996; Muti 2000). The relationship between 2-hydroxyestrone and 16-alpha-hydroxyestrone is sometimes expressed as the 2:16 ratio (Taioli 2010).

By increasing the ratio of 2-hydroxyestrone to 16-alpha-hydroxyestrone, it may be possible to reduce the risk of estrogen-related cancers (Bradlow 1986; Taioli 2010).

3,3’-Diindolylmethane (DIM) and indole-3-carbinole (I3C) (found in cruciferous vegetables) favorably affect estrogen metabolism and help to optimize the 2:16 ratio. A placebo-controlled, double-blind study of women at increased risk for breast cancer found that four weeks of supplementation with I3C promoted favorable changes in the urinary estrogen 2:16 ratio (Wong 1997; Dalessandri 2004).

ESTROGEN RECEPTORS AND A CLOSER LOOK AT ESTRIOL

As mentioned previously, estriol (E3) is the form of estrogen least associated with cancer. E3’s protective effects become apparent when examining the differing actions that each of the three primary estrogens exerts upon the estrogen receptors. In breast cells there are two distinct *classical* estrogen receptors that bind estrogens, estrogen receptor *alpha* (ER-a) and estrogen receptor *beta* (ER-ß). In addition, there is one *non-classical* estrogen receptor, *GPR30* (Paruthiyll 2004; Paech 1997; Katzenellenbogen 2000; Nilsson 200; Wang 2010). The binding of estrogen hormones to ER-a promotes breast cell proliferation, which can exacerbate the spread of existing breast cancer. Conversely, the binding and activation of ER-ß attenuates breast cell proliferation and thus may slow the development of a cancerous tumor (Helguero 2005; Bardin 2004; Isaksson 2002; Weatherman 2001).

Estrone (E1) and estradiol (E2) preferentially bind to and activate ER-a, thereby explaining the proliferative effects of these two hormones (Zhu 2006; Rich 2002). E3, on the other hand, binds to and activates ER-ß (Zhu 2006; Rich 2002). This helps to explain E3’s “anti-estrogenic” activity and led a noted researcher in HRT to state the following: *“This unique property of estriol, in contrast to the selective ER [estrogen receptor] alpha binding by other estrogens, imparts to estriol a potential for breast cancer prevention, while other estrogens [estrone and estradiol], would be expected to promote breast cancer… Because of its differing effects on ER alpha and ER beta, we would expect that estriol would be less likely to induce proliferative [potential cancerous growth] changes in breast tissue and to be associated with a reduced risk of breast cancer”* (Holtorf 2009).

Moreover, groundbreaking research has revealed that GPR30 mediates proliferation of breast cancer cells independently of ER-a and ER-ß. E2 strongly binds to and activates GPR30, driving proliferation. E3, on the other hand, acts as an antagonist of GPR30, though it has a much lower affinity for GPR30 than E2 (Wang 2010; Lappano 2010). Many carcinogenic toxins, including bisphenol A (BPA) and polychlorinated biphenyl’s (PCB’s), promote the growth of breast cancer cells by functioning as agonists of GPR30 (Wang 2010).

The traditional breast cancer drug tamoxifen, which blocks the activity of ER-a and ER-ß, fails to suppress the cancer-promoting effects of GPR30. It is by this mechanism that some estrogen-receptor-positive (ER-positive) breast cancers become drug-resistant. In fact, tamoxifen has been shown to *stimulate* the growth of drug-resistant breast cancer cells via activation of GPR30 (Ignatov 2010).

E3, through its estrogen receptor modulatory capacity, combats the proliferative effects of E1 and E2 (Melamen 1997; Wang 2010). These scientific findings highlight the importance of emphasizing E3 in any bioidentical hormone replacement regimen intended to restore youthful hormone balance and guard against breast cancer development.

The Dangers of Age-Related Hormone Decline

By the time a woman enters menopause, she may have already experienced two decades of hormonal imbalance. During the postmenopausal period, when sex hormone levels decrease significantly, aging women are at increased risk of the following diseases: heart disease, osteoporosis, Alzheimer’s, dementia, among others.

Heart disease. According to the Centers for Disease Control and Prevention (CDC), heart disease is the leading killer of American women (CDC 2012). The risk for postmenopausal women is equal to that seen in men. Menopause can cause elevations in blood pressure, low-density lipoprotein (LDL) cholesterol, total cholesterol, triglycerides, as well as homocysteine levels, C-reactive protein, and interleukin-6 (an inflammatory cytokine), which are all associated with estrogen deficiency (Cushman 2003; Davison 2003; Dijsselbloem 2004). At the same time, high-density lipoprotein (HDL) cholesterol levels drop significantly. Estrogenic activities are vital for maintaining the integrity of the vascular endothelium, where atherosclerotic changes begin (Arnal 2009). Finally, lack of estrogen replacement in the postmenopausal state may predispose women to forms of cardiac muscle disease that are only now beginning to be understood (Kuo 2010).

Osteoporosis. Hormone deficiencies (beginning as early as age 30) are clearly associated with bone loss and osteoporosis. By the time women reach age 50, they are at a significantly increased risk of an osteoporotic bone fracture. Estrogen deficiency results in increased production of pro-inflammatory cytokines, which cause increased bone breakdown and inflammation (Weitzmann 2006). Combined estrogen and androgen (i.e., natural or synthetic) therapy has been shown to increase BMD more than estrogen therapy alone (Notelovitz 2002).

Alzheimer's and dementia. Hormone loss is associated with neuronal degeneration and increased risk of dementia, Alzheimer's disease, and Parkinson's disease (Amtul 2010; Rocca 2008). Estrogen stimulates degradation of beta-amyloid protein (noted to accumulate in the brain of Alzheimer's disease patients) by up-regulating production of protective proteins (Liang 2010). Deficiencies in pregnenolone and DHEA, which are both neuroprotective hormones, are also linked to reduced memory and brain cell death associated with Alzheimer's disease (Vallée 2001; Yao 2002). These two hormones play an important role in regulating neurotransmitter systems that are involved in learning, stress, depression, addiction, and many other vital functions (Vallée 2001).

PROGESTERONE'S BALANCING ACT

In a healthy young woman, progesterone serves as a counterweight to estrogen during the menstrual cycle. Estrogen levels rise during the first half of the cycle and progesterone levels rise in the middle. Progesterone's job is two-fold: 1) to prepare the uterus for implantation with a healthy fertilized egg, and 2) to support the early stage of pregnancy. If no implantation occurs, progesterone levels drop until another cycle begins.

Studies have shown that progesterone has anti-proliferative effects on breast cancer and leukemia cells (Formby 1998; Hayden 2009; Hilton 2010). Breast cancer is 5.4 times more common in pre-menopausal women with low progesterone levels than with favorable levels (Cowan 1981). Data suggest that while bioidentical (i.e., natural) progesterone does not increase risk of breast cancer, synthetic progestins used in conventional HRT do (Campagnoli 2005).

Natural progesterone has also demonstrated neuroprotective properties. One study called for more attention to progesterone as a "*potent neurotrophic agent that may play an important role in reducing or preventing motor, cognitive, and sensory impairments [in both men and women]*" (Stein 2005).

Bioidentical Hormone Replacement Therapy

Bioidentical hormone formulations in measured doses (i.e., tailored to individual patients) can be obtained from a compounding pharmacy with a physician's prescription. Bioidentical estrogen therapy has been utilized extensively in Europe and Japan for several years (Kano 2002).

Estriol. Estriol (E3) has shown beneficial effects in women at risk for cardiovascular disease.

Japanese scientists found that a group of menopausal women treated with E3 for 12 months had a significant decrease in both systolic and diastolic blood pressure (Takahashi 2000). Another placebo-controlled study demonstrated that E3 replacement for 30 weeks improved flow-mediated dilation (a measure of arterial relaxation) (Hayashi 2000). E3 accomplishes these effects by strongly activating nitric oxide signaling systems and stabilizing atherosclerotic plaques (Kano 2002).

E3 may further reduce cardiovascular risk through its beneficial effects on lipid profiles. One Japanese study found that E3 prevented a postmenopausal rise in total cholesterol while not inducing elevated triglyceride levels, a side effect frequently seen after treatment with conventional estrogen therapy (Itoi 2000). E3, in combination with a statin drug, can reduce carotid artery intima-media thickness (a measure of atherosclerosis) in postmenopausal women with elevated blood lipids (Yamanaka 2005).

E3 also increases bone mineral density, a vital parameter in post-menopausal women at risk for osteoporosis. In one study, women treated with E3 exhibited an increase in bone mineral density and improved climacteric (i.e., menopausal) symptoms with no increased risk of endometrial hyperplasia (Minaguchi 1996). In a second study, researchers treated postmenopausal and elderly women with either a combination of E3 and 1,000 mg/day of calcium lactate or 1,000 mg/day of calcium lactate alone. Bone mineral density significantly increased in women receiving E3 versus a decrease in those not receiving E3 (Nishibe 1996). In a summary statement, the researchers wrote, "*the acceleration of bone turnover usually observed after menopause was prevented by treatment with E3 [estriol]*" (Nozaki 1996).

E3 also supports sexual and urinary health. For example, one study showed that E3-treated women reported a 68% reduction in symptoms of incontinence compared to 16% in the placebo group (Dessole 2004). Women with recurrent urinary tract infections experienced a 91% reduction in infections following treatment with an intravaginal estriol cream compared to the placebo group (Raz 1993). Another study demonstrated that locally administered E3 therapy significantly increased the number of blood vessels surrounding the urethra, thereby improving its ability to maintain urine in the bladder until the desire to void the bladder is reached (Kobata 2008). The addition of E3 to standard therapy for prevention of urinary tract infections reduced the number of recurrences

11-fold, and the days of antibiotic therapy more than 12-fold in another study (Davidov 2009).

Stress incontinence refers to intermittent loss of urine with pelvic floor stress from laughing, coughing, etc. Pelvic floor muscle exercises are effective in reducing stress incontinence, and studies suggest that E3 adds substantially to the beneficial effect(s) (Ishiko 2001).

E3 can offer relief for women suffering from atrophic vaginitis, the symptoms of which include vaginal dryness, vaginal burning, and painful intercourse. After 4 weeks of treatment with an intravaginal estriol cream, researchers noted that *"atrophy of vaginal epithelium and chronic vaginitis stopped or significantly decreased… The subjective complaints relating to the estrogen deficiency (vaginal burning and dryness, itching, dyspareunia [painful sex] and urinary dysfunctions) ceased. Side-effects and complications during the treatment were not found"* (Koloszar 1995). More objective improvements to vaginal dryness and acidity have been demonstrated in recent studies (Chollet 2009).

Topical estriol creams applied to the face and neck can reduce many symptoms of aging skin (e.g., dryness and wrinkling). Animal studies demonstrate that estriol cream promotes collagen production and enhances skin's elasticity (Ozyazgan 2005).

Studies have also shown E3 to be effective in the treatment of menopausal symptoms. In one study, women being treated with varying doses of E3 for six months had decreased vasomotor symptoms of menopause (e.g., hot flashes). The improvements were found to be dose-dependent. There were no detrimental effects on uterine or breast tissue (Tzingounis 1978). Other studies have shown similar results with up to 71% of patients reporting elimination of hot flashes and sweating and 21% reporting a substantial reduction (Lauritzen 1987).

Progesterone. Progesterone complements and balances the impact of estrogen in aging women. Combined with estrogen, progesterone substantially improved the amount of time women with a history of heart attack or coronary artery disease could work out on a treadmill before reducing blood flow to the heart. Use of non-bioidentical progesterone produced no effect (Rosano 2000). Another mechanism by which progesterone enhances cardiovascular health is its ability to maintain or even increase HDL levels in women receiving estrogen replacement therapy (Bernstein 2010; Ottosson 1985; Jensen 1987).

Progesterone has a major role in relieving menopausal symptoms as well. Four head-to-head studies comparing progesterone to non-bioidentical synthetic progestogen (progestin) reported that women experienced greater satisfaction, improved quality of life, and fewer side effects when switched from progestin to progesterone (Hargrove 1989; Montplaisir 2001; Ryan 2001; Lindenfeld 2002). The beneficial effects of progesterone compared to non-bioidentical progestin included a 30% reduction in sleep problems, 50% reduction in anxiety, 60% reduction in depression, 25% reduction in menstrual bleeding, 40% reduction in cognitive difficulties, and 30% improvement in sexual function. Eighty percent of women in the study reported overall satisfaction with the bioidentical progesterone formulation (Fitzpatrick 2000).

What You Need to Know: Bioidentical Hormones

- Non-bioidentical hormones are chemically different than natural hormones produced within the body. The use of non-bioidentical estrogen and synthetic progestin in the WHI trial was associated with an increased risk of breast cancer, heart attack, venous blood clot and stroke.
- Non-bioidentical, oral conventional hormone replacement therapy is associated with an increased risk of uterine cancer.
- Bioidentical hormones have the same molecular structure as the hormones produced naturally within the body. The body does not distinguish between supplemental bioidentical hormones and the hormones produced within the body. As a result, bioidentical hormones are properly utilized, and are able to be naturally metabolized and excreted from the body.
- Current literature suggests that bioidentical progesterone is associated with a decreased risk of breast cancer.
- A scientific literature review suggests that bioidentical progesterone may be superior to progestins in treating menopausal symptoms. Estriol (see below) is also highly effective in the treatment of menopausal symptoms.
- Research on bioidentical progesterone has shown beneficial effects (e.g., decreasing the risk of blood clots, protecting against atherosclerosis, and maintaining healthy HDL levels) on cardiovascular health.
- Three major types of estrogen are produced naturally in a woman's body: estrone (E1), estradiol (E2), and estriol (E3).
- Estriol has been shown to improve bone density, promote youthful skin, enhance urinary health, and improve sexual function.

Beyond Estrogen and Progesterone: The Complete Hormonal Picture

In addition to estrogen and progesterone, it is important to monitor levels of the hormones pregnenolone, DHEA, and testosterone. Ideal bioidentical HRT goes beyond the mere suppression of symptoms caused by declining ovarian hormone levels. The real goal of Life Extension's approach to female hormone restoration is to restore hormones to youthful levels. Such an approach has wide-ranging benefits throughout the body and significantly enhances physical and psychological well-being.

DHEA. DHEA is a natural steroidal hormone secreted by the adrenal gland, gonads, and brain (Maninger 2009). Although women usually have less DHEA than men, both sexes lose DHEA over time, suggesting an age-related decline (Labrie 2010). Peak levels are typically reached when women are in their 30s, after which they begin to lose approximately 2% per year. Decreased levels of DHEA are associated with cancer, diabetes, lupus, psychiatric illness (Genazzani 2010), insomnia, pain, and disability (Morrison 2000).

DHEA has been shown to improve mood, neurological function, immune function, energy, feelings of well-being, and the maintenance of muscle and bone mass (Kenny 2010; Weiss 2009). A combination of DHEA and pregnenolone has been shown to improve memory (Ritsner 2010). DHEA may also improve insulin sensitivity and triglyceride levels (Genazzani 2010; Casson 1995).

Life Extension suggests that maturing women strive to keep their DHEA-sulfate (DHEA-s) levels in a range of 275 – 400 µg/dL to promote optimal health and vitality.

Testosterone. Like DHEA, testosterone levels in women gradually decrease with age (Schneider 2003). Loss of testosterone affects libido, bone and muscle mass, vasomotor symptoms, cardiovascular health, mood, and well-being (Simon 2001; Watt 2003). Testosterone in conjunction with estrogen has been shown to improve quality of life, vigor, mood, concentration, bone mineralization, libido, and sexual satisfaction (Al-Azzawi 2010; Simon 2001; Braunstein 2002; Cameron 2004). The combination has also been shown to reduce hot flashes, sleep disturbances, night sweats, and vaginal dryness (Guillermo 2010). Because DHEA converts into testosterone, it is possible to raise testosterone levels with DHEA (Cameron 2004; Schneider 2003).

Studies also suggest that testosterone, in the context of hormone restoration, may prevent or reduce estrogenic cancer risk in the treatment of women with ovarian failure (Dimitrakakis 2003; Zhou 2000). In addition, testosterone is effective in the treatment of low libido in women (Guillermo 2010).

Life Extension encourages females to maintain a total testosterone level of 35-45 ng/dL and a free testosterone level of 1-2.2 pg/mL.

Pregnenolone. As is the case with other hormones, a significant reduction of pregnenolone begins when women reach their early 30s (Havlikova 2002). As the initial hormone in the overall steroid hormone cascade, pregnenolone is derived from cholesterol. Pregnenolone deficiencies have been associated with diminished brain function and dementia (Mellon 2007).

Aging women should maintain a pregnenolone blood level of 130 -180 ng/dL for optimal performance.

It is very important that women have their hormone levels checked before beginning bioidentical hormone restoration therapy. To ensure safe and adequate levels, testing should occur one month after commencing HRT and then again two months later. Those women who wish to enhance their sexual desire and have already tried DHEA and pregnenolone therapy should consult with their physician about alternative options (e.g., small amounts of testosterone). Women should always consult a physician before beginning HRT, especially if they have had or are at high risk (e.g., first-degree relative with a diagnosis) of having hormone-responsive cancer (e.g., breast or endometrial).

Moving Forward with Bioidentical HRT

Given the wealth of data demonstrating the superiority of bioidentical HRT, a noted researcher in hormone replacement therapy proclaimed, *"Physiological data and clinical outcomes demonstrate that bioidentical hormones are associated with lower risks, including the risk of breast cancer and cardiovascular disease, and are more efficacious than their… animal-derived [non-bioidentical] counterparts. Until evidence is found to the contrary, bioidentical hormones remain the preferred method of HRT"* (Holtorf 2009).

Compounded prescription bioidentical estrogen formulas include *Bi-Est* and *Tri-Est*. Bi-Est consists of 20% estradiol (E2) and 80% estriol (E3). Tri-Est contains 10% E2, 10% estrone (E1), and 80% E3 (Taylor 2001). In some situations these ratios do not meet individual needs. In one study, the amounts observed naturally in reproductive age women were 90% E3, 7% E2, and 3% E1 (Wright 1999). In this case, a prescription (based upon the results of hormone tests and assessment of symptoms) is tailored to the needs of the patient by an experienced physician. A comprehensive hormone restoration program should also include progesterone, DHEA, pregnenolone, and perhaps testosterone.

There are two different philosophies regarding the dosing of hormones. The first encourages using the lowest possible dose that will

ameliorate the symptoms. This more conservative approach is unlikely to cause a menstrual cycle in menopausal woman. However, it is also unlikely to bring hormones back to what Life Extension considers optimal levels.

The second approach involves significantly higher hormone dosages. The idea here is to “trick” a woman’s brain into thinking she is still of reproductive age. The goal is to achieve levels that mimic the hormonal fluctuations of a menstruating woman, thereby restoring the menstrual cycle.

Utilizing the results of hormone testing and clinical evaluation(s), physicians with experience in bioidentical hormone replacement can help women find an optimal dosing strategy. Most women find they respond desirably to bioidentical HRT when based upon this combined approach. To obtain contact information for physicians in your area who are knowledgeable about bioidentical hormone replacement therapy, or to request information about Life Extension’s Female Comprehensive Hormone Profile blood test, call 1-800-226-2370 or visit our blood testing section.

Women taking any kind of estrogen replacement therapy (including bioidentical) should refer to the Breast Cancer Prevention protocol in order to understand the importance of making healthy lifestyle choices that could reduce the risk of breast cancer.

HOW BIOIDENTICAL ESTROGEN-PROGESTERONE IS PRESCRIBED

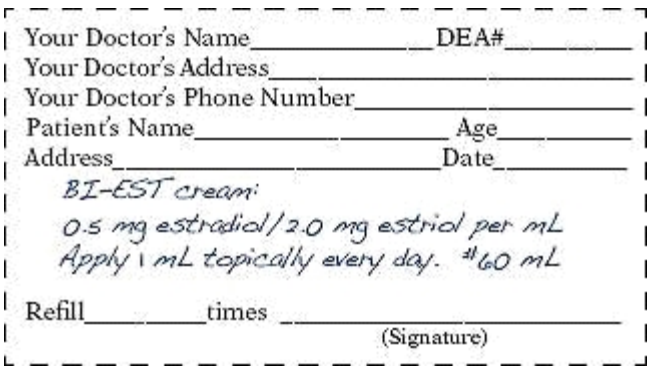
The commercial availability of individually tailored bioidentical hormone products is limited. As a result, many physicians utilize compounding pharmacies to prepare and dispense bioidentical hormone prescriptions to their patients. To obtain the phone number of a compounding pharmacist in your area, call 1-800-226-2370.

In order to gauge the initial dose of bioidentical estrogen, the estradiol (E2) and/or total estrogen blood levels should be considered in conjunction with other hormones levels (e.g., progesterone).

A menopausal woman typically has an E2 blood level of 0-19 pg/mL. With the use of bioidentical estrogen cream (e.g., compounded E3 and E2), the blood E2 level may increase to 100 pg/mL or higher, which would indicate to the prescribing doctor that the formula is being *absorbed* and has increased the patient’s E2 to a more youthful level.

If the patient reports that her menopausal symptoms have been resolved, most practitioners will continue the current dosage and conduct periodic follow-ups.

If, however, the patient is still having symptoms, the dose of bioidentical estrogen cream can be increased. In addition, a urinary hormone profile might be ordered to assess other estrogens and their associated metabolites. Based on the results of these tests, a more precise dose of E3, E2, progesterone, and occasionally, testosterone can be prescribed. A typical starting dose for bioidentical estrogen cream might read as follows:


Your Doctor's Name_____DEA#_____
Your Doctor's Address_____
Your Doctor's Phone Number_____
Patient's Name_____ Age_____
Address_____Date_____
BI-EST cream:
0.5 mg estradiol/2.0 mg estriol per mL
Apply 1 mL topically every day. #60 mL
Refill_____times _____
(Signature)

Please note this is a general suggestion for an initial prescription. A physician experienced in bioidentical hormone replacement will tailor the prescription to the individual woman’s needs.

The dose can be increased when severe symptoms of estrogen deficiency are present.

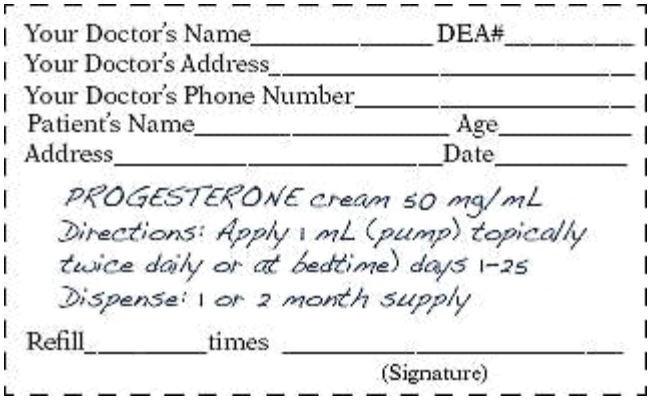
Women on an estrogen replacement regimen should also be prescribed *natural progesterone* (in contrast to synthetic progestin drugs like Provera®) in a dose that achieves a youthful balance. Natural progesterone produces many benefits when properly balanced with estrogen. The typical dose for topical progesterone cream may vary between 50-200mg, depending upon a woman’s individual biochemical needs.

Typically, progesterone cream should be applied twice daily to different parts of the body. Specific dosing instructions are as

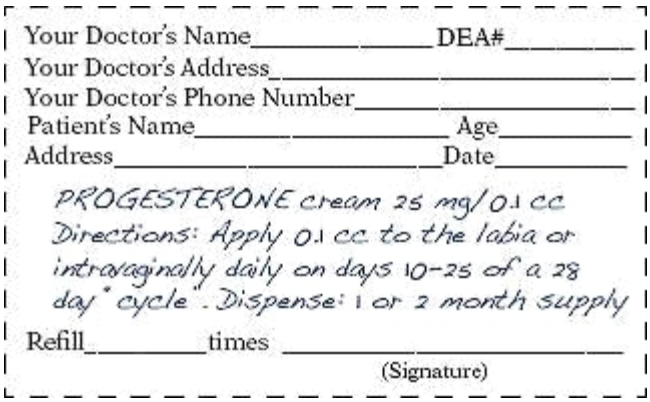
follows:

- Premenstrual and perimenopausal women: 1/4 tsp. of a 2.5% progesterone topical cream (approximately 30 mg natural progesterone) twice daily, starting on day 12 of the menstrual cycle and continuing up to day 28.
- Menopausal women: 1/4 tsp. twice daily for 21 days, followed by 7 days off.

The dose can be adjusted up or down depending on a woman's symptoms and her response to treatment. If using natural progesterone cream from a pharmacy, a prescription for a postmenopausal woman might be written as follows:


Your Doctor's Name_____DEA#_____
Your Doctor's Address_____
Your Doctor's Phone Number_____
Patient's Name_____ Age_____
Address_____Date_____
PROGESTERONE cream 50 mg/mL
Directions: Apply 1 mL (pump) topically twice daily or at bedtime) days 1-25
Dispense: 1 or 2 month supply
Refill_____times _____
(Signature)

A prescription for a premenopausal woman might read:


Your Doctor's Name_____DEA#_____
Your Doctor's Address_____
Your Doctor's Phone Number_____
Patient's Name_____ Age_____
Address_____Date_____
PROGESTERONE cream 25 mg/0.1 cc
Directions: Apply 0.1 cc to the labia or intravaginally daily on days 10-25 of a 28 day cycle. Dispense: 1 or 2 month supply
Refill_____times _____
(Signature)

Some physicians prescribe topical progesterone similarly to estrogen, i.e., in milligrams per fraction of a cubic centimeter (cc). These are applied via a syringe onto the skin, and have the dual advantage of more precise dosage adjustment and smaller volume of cream (which is less likely to make a mess on clothing).

The blood level targets in aging women might be:

- Estradiol: 90-211 pg/mL
- Progesterone: 2.0-6.0 ng/mL
- Free testosterone: 1.0-2.2 pg/mL

Before a prescription for bioidentical hormones can be written, it is important to have a baseline blood test to determine the doses of bioidenticals that might be needed. To order a comprehensive Female Panel that includes estradiol, progesterone, and free testosterone, call 1-800-226-2370**.**

In order to achieve optimal hormonal balance, it is important to also address testosterone levels. Although testosterone is thought of as a male hormone, it plays an important role in women's health. Testosterone levels decrease in women as they age. Low testosterone in postmenopausal women can have a negative impact upon sex drive, mood, psychological well-being, bone and muscle mass, and cardiovascular health (Ling 2009; Stuckey 2008; Maia 2009; Martin-Du Pan 2007). A physician experienced in bioidentical hormone therapy will measure testosterone levels in women and prescribe bioidentical testosterone if needed. Correcting low testosterone in women usually requires a 150-300 mcg patch or an individually prescribed testosterone cream (Davis 2008).

Since DHEA (dehydroepiandrosterone) can convert to testosterone in a woman's body (i.e., naturally), a woman with low testosterone might be able to increase her level by taking 15 to 25 mg daily of DHEA, which is available as a low cost dietary supplement (Weiss 2009).

THE PROS AND CONS OF THE DIFFERENT HORMONE TESTING METHODS

There is continuing debate regarding the best testing methods for hormones. Hormones can be analyzed in the blood, urine or saliva. There are benefits and drawbacks to each of these methods. Life Extension Foundation® currently offers blood and 24-hour urinary testing.

Saliva Testing:

Pros- This easy, at home collection process is a measurement of bioavailable hormone levels.

Cons- Accuracy and testing variability are issues to consider. Hormone levels in saliva are significantly less than in blood, which can affect the accuracy of the test. In addition, saliva flow rate as well as gum disease (even if subclinical) will alter the results of the test. There are limited laboratories available for this type of testing.

Note: Although Life Extension does not utilize saliva testing at this time, some experienced physicians use this type of testing, in conjunction with clinical symptoms, to successfully evaluate and treat hormone deficiencies.

Urine Testing:

Pros- This method provides a 24-hour picture of hormone levels rather than a snapshot in time. It allows for testing of not only the three main estrogens— estrone, estadiol and estriol—but also metabolites like 2- and 16- hydroxyestrone.

Cons- Inconvenient and more costly for a full hormone profile.

Blood Testing:

Pros- This method has been used consistently for decades. There is typically good correlation with symptoms. The testing is inexpensive, routine, and readily available through blood draw centers.

Cons- Blood draw involves a needle stick. Estrone and estradiol can be evaluated. This test, however, is not sensitive enough to assess estriol levels in menopausal women because the estriol test used by traditional laboratories is for the purposes of evaluating fetal growth in pregnancy, during which time levels of this hormone are much higher. Finally, there is no blood estrogen metabolite testing available.

Phytoestrogens and Nutritional Support

Phytoestrogens are natural compounds found in some plants. They exert estrogen-like activity in the body and may be an effective alternative to bioidentical HRT for some women.

Some of the best evidence to support the use of phytoestrogens comes from Asia, where women do not typically experience many of the diseases and menopausal symptoms associated with the loss of estrogen. One explanation for this may be the phytoestrogens found in soy and other plant products consumed in Asian diets (Aso 2010; Cho 2010; Sarkar 2003).

Phytoestrogens bind to estrogen receptors and help modulate estrogen activity (Zittermann 2003). When estrogen levels are too low, their very mild estrogenic effect raises total estrogenic activity. Alternatively, when estrogen levels are too high, they compete with estrogen at cellular receptor sites, thus reducing endogenous estrogenic impact. By competing with endogenous estrogen for estrogen receptors, phytoestrogens may help prevent the growth and spread of several hormone-dependent cancers (Adlercreutz 1992). They have also been shown to decrease the risk of some degenerative diseases including cardiovascular disease, osteoporosis, breast and uterine cancer (Baber 2010; Bawa 2010; Cho 2010; Messina 2008; Miyake 2009).

Dietary and supplemental phytoestrogens present a way for women to obtain limited hormonal support without the use of hormone therapy.

Cardiovascular Benefits: Unlike conventional HRT, which has been shown to raise the risk of heart attack among postmenopausal women, phytoestrogens have a positive effect on the heart. In 1999 the United States Food and Drug Administration authorized the use of health claims on food labels that link increased soy consumption with a reduced risk of

coronary artery disease (Vincent 2000). One study of more than 400 women demonstrated that phytoestrogens, through their effect on the arterial walls (particularly in older women), protect against arterial degeneration and atherosclerosis (van der Schouw 2002).

A scientific review of studies on phytoestrogens found they offer the following cardiovascular benefits:

- Improvements in lipid disturbances as a result of activating beneficial estrogen receptor sub-types (Okamura 2008)
- Decreased blood pressure, LDL cholesterol, total cholesterol, and triglycerides (De Kleijn 2002)
- Increased HDL cholesterol and improved cardiovascular profile (Bairey Merz 2006; De Kleijn 2002)
- Lowering the overall rate of cardiovascular disease among people with higher consumption of phytoestrogens (Ariyo 2002)
- Lowering of lipids in people with high cholesterol via genistein and daidzein, two of the most extensively studied phytoestrogens (Teede 2001; Zittermann 2003)
- Reduction in the risk of atherosclerosis due to increased levels of daidzein and genistein, which inhibit LDL oxidation (Exner 2001)

In addition, a six-month study of more than 180 women confirmed that a soy-rich diet is as effective as conventional HRT for lowering lipid levels (Park 2005).

Furthermore, phytoestrogens have almost 3 times the radical scavenging activity as vitamins C and E, as well as help protect arterial walls (Ruiz-Larrea 2000; van der Schouw 2002).

Brain protection: Estrogen and estrogen-like compounds protect brain cells from degenerative changes due to aging and oxidative stress (Bhavnani 2003; Linford 2002).

- The phytoestrogen genistein protects animal subjects from the effects of brain ischemia, the kind of injury seen in stroke (Schreihofer 2009; Donzelli 2010; Ma 2010).
- Genistein has anti-apoptotic activity, protecting cultured brain cells from self-destructing over time (Yu 2009).

Osteoporosis and bone health: Studies have shown that postmenopausal women with a habitually high intake of phytoestrogens have high bone mineral density of the spine and hip (Bawa 2010; Hanna 2004). A number of studies have been conducted on phytoestrogens and bone health, and their conclusions are as follows:

- Genistein and daidzein increase bone mineralization (Taku 2010; Clifton-Bligh 2001; Kanno 2004).
- Genistein and daidzein decrease bone resorption and inflammatory factors while increasing osteogenic (bone-forming) proteins (Ma 2008; Jia 2003; Rassi 2002; Yamaguchi 2000; Zhang 2004).
- An isoflavone mixture of daidzein and genistein demonstrated significant increases in bone mineral density after six months of treatment. Women who ingested 57mg daily of isoflavones had a 4% increase in bone mineral density (Clifton-Bligh 2001).
- A phytoestrogen preparation containing daidzein and genistein demonstrated protective effects on the lumbar spine (Atkinson 2004).
- Dietary supplementation with 54mg daily of genistein "*may be as effective as hormone replacement therapy in attenuating menopause-related bone loss without causing the associated side effects*" (Cotter 2003).

Cancer Protection: Studies demonstrate a significantly lower incidence of sex hormone-related cancer in Asian countries (Sarkar 2003; Vij 2004). These studies, which attribute this result to the traditionally high intake of soy isoflavones in the Asian diet, have concluded the following:

- Daily soy isoflavone consumption is associated with decreased breast cancer risk (Lu 2001). A diet containing 113–202 mg daily (depending on body size) of genistein and daidzein can increase the production of the protective 2-hydroxylated estrogen, decrease estradiol and its harmful metabolites, and lower the long-term risk of breast cancer (Lu 2000).
- Genistein and daidzein have an inhibitory effect on uterine cancer (Lian 2001).
- Genistein intake is linked with lower rates of stomach cancer (Ko 2010).

Menopause symptoms: Several studies have demonstrated that natural estrogen significantly decreases hot flashes and vaginal atrophy (Albert 2002; Chiechi 2003). Treatment with 54mg daily of genistein safely decreased hot flashes up to 30% and should be considered as an alternative treatment for postmenopausal conditions (Crisafulli 2004). Subsequent studies showed a decrease in hot flushes of more than 56% (D'Anna 2009). Another study concluded that "*genistein can be used for the management of hot flushes in postmenopausal women not treated with hormone replacement therapy due to their superior efficacy to placebo and very good safety profile"* (Ferrari 2009).

ADDITIONAL NATURAL INGREDIENTS TO TARGET THE SYMPTOMS OF MENOPAUSE

Black cohosh. Black cohosh has been used in the treatment of climacteric symptoms such as hot flashes, mood disturbances, diaphoresis, palpitations, and vaginal dryness (Donnelly 2007; Oktem 2007; Shams 2010). Additionally, black cohosh conveys antiproliferative effects on breast cancer cells (Fang 2010; Al-Akoum 2007; Hostanska 2004). Data suggests it is comparable to some pharmaceutical prescription medications for preventing bone loss (Nisslein 2003).

Dong quai. Dong quai, based on its use in Chinese medicine for gynecological disorders (i.e., painful menstruation or pelvic pain, recovery from childbirth or illness, and fatigue/low vitality), is referred to as "female ginseng" (Goh 2001; Hardy 2000). It is an effective remedy for alleviating menopausal symptoms without proliferative changes in the uterus or vagina (Hirata 1997). A study demonstrated that a preparation of soy isoflavones, black cohosh, and dong quai reduced menstruation-related migraine headaches (Burke 2002).

Licorice root. Licorice root exerts estrogen-like effects and has been shown to reduce body fat, positively impact testosterone metabolism (Hu 2009; Armanini 2002; Josephs 2001), and decrease serotonin reuptake by up to 60% which may help alleviate menopausal depression (Ofir 2003). Licorice root also assists with repair of blood vessel walls and supports arterial health, thus reducing the risk of cardiovascular disease (Somjen 2004).

Vitex agnus-castus. Extracts from the fruit and leaves of vitex agnus-castus (vitex), also known as chasteberry, contain chemicals with diverse beneficial effects for the treatment of premenstrual symptoms (Dante 2010). In one study, menopausal women reported excellent symptomatic relief after using two essential oils from vitex (Chopin 2003).

NUTRIENTS TO COMPLEMENT BIOIDENTICAL HRT

Vitamin D. Vitamin D confers significant protective effects against breast cancer. In a study, women with higher vitamin D levels had a nearly 70% reduction in their risk of breast cancer compared to women with the lowest levels (Abbas 2008). Laboratory studies have shown that vitamin D suppresses growth of breast cancer by:

- blocking signals that stimulate cancer cell growth
- enhancing signals that inhibit cancer cell growth
- favorably altering genetic regulators of the cell cycle (Ben-Shoshan 2007; Lee 2007; Jamshidi 2008; Crew 2009)

Vitamin D helps prevent mutated cells from becoming malignant and even induces cancer cell death (apoptosis). Human studies show that doses of 1100 IU vitamin D daily plus calcium result in a 60% risk reduction for developing any cancer, compared with placebo (Lappe 2007).

Cruciferous Vegetables. Cruciferous vegetables such as broccoli, cauliflower, cabbage, kale, and Brussels sprouts can help detoxify dangerous estrogen breakdown products that promote cancer growth (Lampe 2009; Ambrosone 2004). When estrogens are metabolized via certain biochemical pathways, they become more likely to trigger cancer (Fowke 2000; Muti 2002). Aging adults suffer from a high prevalence of cancers associated with an imbalance in estrogen metabolism (Fowke 2000; Muti 2002). Cruciferous vegetables contain compounds that promote a healthier pathway for the breakdown of estrogens in the body, thus protecting against cancer (Muti 2000; Michnovicz 1997; Michnovicz 1998; Kall 1997; Bradlow 1996; Dalessandri 2004).

A chief component of cruciferous vegetables, indole-3-carbinol (I3C), prevents the conversion of estrogen to its breast cancer promoting *16-alpha-hydroxyestrone* form, while increasing conversion to its cancer-fighting *2-hydroxyestrone* form (Acharya 2010; Weng 2008; Muti 2000).

Lignans. Lignans can slow the growth of breast cancer in women. Thirty-two women awaiting surgery for breast cancer were randomized to receive a muffin either with or without (control group) 25 grams of flaxseeds. Analysis of the cancerous tissue after surgery revealed that markers of tumor growth were reduced by 30%-71% in the flaxseed group, with no change noted in the control group (Thompson 2005).

A recently published study found that a combination of lignans, I3C, and calcium-d-glucarate along with other supportive herbs favorably altered the 2/16-hydroxyestrone ratio in pre- and post-menopausal women. The researchers remarked, "*Supplementation with a mixture of indole-3-carbinol and… lignan in women significantly increased estrogen C-2 hydroxylation. This may constitute a mechanism for the reduction of breast cancer risk as well as risk for other estrogen-related cancers*" (Laidlaw 2010).

A comprehensive review of 21 studies found that postmenopausal women with higher lignan intake were significantly less likely to get breast cancer. The investigators concluded that "*high lignan exposure may be associated with a reduced breast cancer risk in postmenopausal women*" (Buck 2010).

Fish oil. Fish oil, with its high omega-3 fatty acid content, reduces cancer risk by a number of mechanisms. Fish oil reduces oxidative stress and suppresses production of many inflammatory mediators that contribute to cancer development (Kansal 2010). It can sensitize tumor cells to chemotherapy effects (even when metastases are present), potentially reducing the doses of chemotherapy required for treatment (Bougnoux 2009).

A study revealed that fish oil, through its effect on oxidative stress and induction of apoptosis, can prevent the progression of colon cancer (Sarotra 2010). In an animal model of breast cancer, fish oil supplementation was shown to reduce bone metastasis by blunting the expression of a protein called CD44, which drives cancer cell migration (Mandal 2010).

Green tea. Green tea polyphenols, particularly one called epigallocatechin gallate (EGCG), suppress the growth and reproduction of human breast cancer cells. They have reduced the number of breast cancer tumors in animal models of the disease (Thangapazham 2007a; Thangapazham 2007b; Leong 2008). Green tea also reduces the production of vascular endothelial growth factor (VEGF), helping to starve tumors of their blood supply while down-regulating cancer-promoting estrogen receptors and increasing apoptosis (Leong 2008; Masuda 2002; Farabegoli 2007; Hsuuw 2007).

Pomegranate. Pomegranate has been extensively studied for its antioxidant properties as well as its cancer-fighting capacity. With respect to breast cancer, pomegranate is an especially promising phyto agent due to its ability to both inhibit the cancer-promoting enzyme aromatase and suppress angiogenesis, which is the process by which tumors gain new blood vessels (Toi 2003; Sturgeon 2010).

SUMMARY

Equine estrogens and synthetic progestins remained the staple of menopausal care until 2002, when the Women's Health Initiative (WHI) revealed the dangers associated with these *unnatural* hormone replacement methods. As women learned that conventional hormone replacement therapy was closely tied to an increased risk of certain cancers, many abandoned their trust in mainstream medicine and turned to natural bioidentical hormones as well as scientifically-validated phytoestrogens for menopausal symptom relief.

Emerging science continues to undermine conventional hormone replacement therapy in favor of bioidentical hormone replacement. Studies confirming the estrogen receptor modulating abilities of the natural estrogen *estriol* provide reassurance for women who seek relief from the ravages of age-related hormone loss without the fear of increased cancer risk.

By coupling healthy diet and lifestyle habits with regular blood testing and bioidentical hormone replacement therapy, women today have a means to look and feel their best at any age.

Given the preponderance of evidence, women should feel confident that bioidentical hormone replacement, when appropriately prescribed, offers a safer and potentially more effective alternative to conventional HRT to help relieve menopausal symptoms and optimize long-term health. The addition of several proven nutrients to a bioidentical hormone regimen may help optimize estrogen metabolism and reduce cancer risk even further, offering an optimal, balanced approach to health maintenance.

Life Extension Suggestions

A hormone replacement regimen should start with a comprehensive female hormone profile blood test and a consultation with a qualified, knowledgeable physician. Once a baseline hormone profile is established, periodic blood testing is recommended to monitor hormone levels. Women interested in hormone blood testing can call 1-800-226-2370 or visit Life Extension's Blood Testing and Laboratory Services online.

Life Extension recommends that women strive for the following optimal hormone levels.

Hormone	Optimal Range
DHEA-s:	275 - 400 µg/dL
Total estrogen:	Day 01 – 10: 61 – 394 pg/mL Day 11 – 20: 122 – 437 pg/mL Day 21 – 30: 156 – 350 pg/mL
	Menopause & post-menopausal: 75 – 200

	pg/mL
Estradiol:	Lowest dose to ameliorate symptoms: 30-50 pg/mL Typical replacement such as with a Bi-Est cream/gel: 80-100 pg/mL Higher end replacement/ restoration of menstrual cycle: 90-211 pg/mL
Progesterone:	18 -- 28 ng/mL (pre-menopause); 2 -- 6 ng/mL, but up to 15 for some women, especially if they are treated with higher doses of estrogen replacement (menopause & post-menopause)
Total testosterone:	35 -- 45 ng/dL
Free testosterone:	1 – 2.2 pg/mL

Nutrients to Support Hormonal Balance and Healthy Hormonal Metabolism

- **Genistein**: 25 – 75 mg daily
- **Daidzein**: 20 – 50 mg daily
- **Black cohosh; standardized extract**: 40 – 80 mg daily
- **Pomegranate; standardized extract**: 400 – 800 mg daily
- **Green tea; standardized extract**: 725 – 1450 mg daily
- **Vitex; standardized extract**: 20 – 40 mg daily
- **Broccoli; standardized extract**: 400 – 800 mg daily
- **Indole-3-carbinol (I3C)**: 80 – 160 mg daily
- **3,3'-Diindolylmethane (DIM)**: 14 – 28 mg daily
- **Licorice root extract**: 25 – 50 mg daily
- **Lignan extract (flax or Norway spruce)**: 25 – 50 mg daily
- **Vitamin D3**: 5000 – 8000 IU daily
- **Omega-3 fatty acids (from fish)**: 2000 – 6000 mg daily
- **Calcium D-glucarate**: 200 – 600 mg daily
- **DHEA**: 15 – 50 mg daily, followed by blood tests in 3-6 weeks; consider starting at a lower dose and increase as indicated. For additional information on DHEA, refer to the DHEA Restoration Therapy protocol.
- **Pregnenolone**: 50 – 100 mg daily (depending on blood test results)
- **Progesterone cream**: Per label directions

In addition, the following **blood testing resources** may be helpful:

- **Female Comprehensive Hormone Panel**
- **Female Basic Hormone Panel**
- **Urinary Hormone Profile (24 hour)**

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This information (and any accompanying material) is not intended to replace the attention or advice of a physician or other qualified health care professional. Anyone who wishes to embark on any dietary, drug, exercise, or other lifestyle change intended to prevent or treat a specific disease or condition should first consult with and seek clearance from a physician or other qualified health care professional. Pregnant women in particular should seek the advice of a physician before using any protocol listed on this website. The protocols described on this website are for adults only, unless otherwise specified. Product labels may contain important safety information and the most recent product information provided by the product manufacturers should be carefully reviewed prior to use to verify the dose, administration, and contraindications. National, state, and local laws may vary regarding the use and application of many of the treatments discussed. The reader assumes the risk of any injuries. The authors and publishers, their affiliates and assigns are not liable for any injury and/or damage to persons arising from this protocol and expressly disclaim responsibility for any adverse effects resulting from the use of the information contained herein.

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