

Female Hormone Restoration

Few topics have attracted as much attention in recent years as hormone replacement therapy (HRT) among postmenopausal women. For decades, physicians have been prescribing HRT to combat the symptoms of menopause as well as protect patients against osteoporosis and heart disease. The rationale behind heart disease prevention was simple: during their reproductive years, women enjoy lower rates of heart disease than men do, primarily because of the protective effect of estrogen hormones. It seemed only logical that by replacing the estrogens lost at menopause, women would retain some of their protection against heart disease. To offset the increased risk of certain cancers caused by unopposed estrogen therapy, doctors frequently added progestins to the therapy (Andrade et al 2002; Formby 1998). Progestins are synthetic chemicals designed in a lab to mimic natural progesterone.

Unfortunately, the logic of conventional HRT turned out to be faulty. In 2002, the results of the Women's Health Initiative were released early. This landmark study followed more than 16,000 women and assessed the effects of conventional HRT, including estrogen-only therapy and therapy that combined estrogen and synthetic progestin. The findings were shocking: the estrogen/progestin arm of the study was discontinued early because the hormone therapy not only failed to protect against heart disease but was shown to increase the risk of heart attack and breast cancer (La Vecchia et al 2001). Long-term conventional HRT also increases risk for uterine cancer (Hulley et al 2002; Van et al 2002). Side effects include weight gain, premenstrual symptoms such as depression and bloating, and breast tenderness (Walsh et al 2001).

In 2004, the estrogen-only arm of the study was discontinued as well because estrogen-only HRT was found to increase the risk of stroke (Azoulay 2004). Based on these side effects, conventional HRT should not be prescribed for osteoporosis and cardiovascular disease prevention (Azoulay 2004; Rapp et al 2003).

These findings had an immediate impact on the millions of women taking conventional HRT. Up to 70 percent of women taking HRT stopped, and overall, women's trust in the medical establishment declined significantly (Schonberg et al 2005).

This situation was unfortunate—and unnecessary. This approach to conventional HRT reflects a basic and widespread misunderstanding of female hormone replacement. Among conventional physicians, menopause is considered an isolated event that occurs around age 50, when the ovaries cease to produce estrogen and progesterone. Menopause is associated with increased incidence of heart disease, osteoporosis, and various symptoms.

While this understanding of menopause is correct, it does not do justice to the finely tuned hormone system that operates throughout a woman's life. In reality, hormone levels may begin to change in the 30s, as a woman enters a period called perimenopause. In the decades leading up to menopause, small hormonal imbalances can exist, so by the time menopause sets in, a woman may have already experienced close to 20 years of hormonal imbalance.

Furthermore, it is impossible to consider estrogen and progesterone in isolation from other hormones. All steroid hormones are created from cholesterol in a hormonal cascade. The first in the chain is pregnenolone, which is converted into other hormones, including dehydroepiandrosterone (DHEA), progesterone, testosterone, and the various forms of estrogen. These hormones are interrelated, each performing a unique biological function. True hormone replacement focuses on a woman's overall hormone health and seeks to achieve an optimal balance.

The importance of balance cannot be overstated. Physicians are just now beginning to understand the danger of having too much estrogen, a condition referred to as "estrogen dominance" (Carr et al 2001). Estrogen dominance might explain many of the conditions that confront modern Western women, from increasingly early menstruation (as early as age 10) to fibrocystic breasts (Kubista 1990), and cancer (Ashby et al 2001; Bentrem et al 2003; Bradlow et al 1995; Ghosh et al 1999; Papaconstantinou et al 2000). Estrogen dominance can occur in any woman, but perimenopausal women, who typically experience a more rapid decline in progesterone than in estrogen, are especially at risk.

Considering the dangers of estrogen dominance, it is a wonder that it took conventional medicine so long to become alert to the dangers of traditional HRT. Traditional HRT relies on a very strong estrogen called conjugated equine estrogen (CEE), which is usually (but not always) given in combination with synthetic progestins. A typical dosage is .625 mg of CEE with 2.5 mg of progestin. As the name implies, CEE is synthesized from the urine of pregnant horses (Bhavnani 2003). The progestin component used a chemical version of progesterone that was invented in a laboratory and has a chemical structure different from natural progesterone.

We believe that women should begin to monitor and, if necessary, correct hormone imbalances long before menopause, when there is still time to reverse this imbalance by restoring youthful hormone levels. Among younger women, it may be possible to address

estrogen and progesterone levels with natural hormones, such as phytoestrogens or progesterones that can be found in plants. Among menopausal and postmenopausal women, who have dramatically reduced levels of hormones, it is often necessary to turn to specially formulated hormones that are bioidentical and supplied in approximately the same ratio found in the body. These natural hormones are often taken in conjunction with supplements that have been shown to reduce the side effects of menopause.

In addition to estrogen and progesterone, it's also important to monitor levels of pregnenolone, DHEA, and testosterone. The ideal goal of HRT therapy goes beyond the suppression of side effects caused by dropping hormone levels. The real goal of Life Extension's hormone restoration program is to restore hormone levels to those of a woman aged 20 to 29. Such an approach has wide-ranging benefits throughout the body, including psychological well-being and sex drive.

What You Have Learned So Far

- Conventional hormone replacement, which relies primarily on equine (horse) estrogen and synthetic progestin, is associated with increased risk of breast cancer and heart attack. Unopposed hormone replacement (estrogen only) is associated with increased risk of breast cancer. These forms of HRT should not be prescribed for the prevention of osteoporosis or heart disease.
- Women's hormone levels begin to change in their middle 30s, long before menopause sets in. At this time, progesterone and estrogen levels both decline. Progesterone declines more rapidly than estrogen, however.
- When the balance between estrogen and progesterone is thrown off in favor of estrogen, a woman may be "estrogen dominant," which is associated with a wide variety of female conditions, including endometriosis, uterine fibroids, polycystic ovaries, and breast cancer.
- Natural, bioidentical hormone restoration with estrogen and progesterone offers an alternative much safer than conventional HRT.
- Because all the levels of steroid hormones are interconnected, and many freely convert to one another, true hormone restoration also monitors for pregnenolone, DHEA, and testosterone.

FROM PUBERTY TO MENOPAUSE: A WOMAN'S JOURNEY

At around age 12, girls enter puberty, a time when increased estrogen production causes the start of menstruation and the development of secondary sex characteristics, such as breasts and pubic hair. For the next two decades or more, a woman's hormonal cycles ideally operate like a finely tuned machine. Each monthly cycle of menstruation is an orchestrated dance between two ovarian hormones, estrogen and progesterone. During the first half of the menstrual cycle, estrogen levels rise and the lining of the uterus builds up in preparation for a fertilized egg. In the second half of the menstrual cycle, progesterone levels rise, causing the uterine lining to be infused with a rich blood supply. If fertilization does not occur, progesterone levels fall, and the uterine lining sloughs off as the uterus prepares itself for another cycle.

This cycle helps us understand in simple terms why the proper balance between estrogen and progesterone is so important. Estrogen is a pro-growth hormone, which explains why high estrogen levels are associated with increased risk of certain cancers. Progesterone, by contrast, protects women from estrogen's growth effect, which makes clear why it is used to help prevent cancers in conventional HRT. The two hormones oppose each other in other ways as well. Estrogen, for instance, increases body fat (Mayes et al 2004), while progesterone decreases body fat.

Around age 35, many women enter perimenopause, characterized by gradually declining estrogen levels and more rapidly declining progesterone levels. These different rates of decline can result in an imbalance. Although still menstruating, a perimenopausal woman may begin to experience symptoms of hormone imbalance, including unpredictable menstrual cycles, headaches, engorged breasts, cramping, and bleeding problems.

Perimenopause is followed at around age 50 by menopause, medically defined as the cessation of menstruation for 12 successive months (McAllister 1998; Walsh et al 2001). Most women will spend about one-third of their lives in menopause or postmenopause (Damewood 1997). During this time, the ovaries fail completely, and estrogen and progesterone levels (as well as other sex hormone levels) decline rapidly. Besides uncomfortable side effects, menopause is associated with increased risk for cardiovascular disease, osteoporosis, and breast cancer in the United States and other Western countries (Lock 1994). It is also accompanied by changes in the endocrinological, psychological, musculoskeletal, neurological, and immune systems (Danilovich et al 2004; Khorram 1996; Walsh et al 2001).

For most women, menopause is known chiefly through its side effects. Up to 85 percent of Western women experience menopausal symptoms, including hot flashes, night sweats, disturbed sleep, fatigue, and related psychological changes, such as depression and anxiety (Burd et al 2001; Mahady et al 2002; Philp 2003; Soares et al 2003). Physical changes include urinary tract atrophy, vaginal atrophy and dryness with discomfort during sexual intercourse (Burger 2001; Coope 1996; Griffith 2004). These uncomfortable symptoms can last up to five years, with an average duration of two to three years (Samsioe 1995). Other symptoms

include the following:

- Strength, energy, muscle, and bone loss (Notelovitz 2002; Proctor et al 1998)
- Cognitive changes, such as decreased memory, lack of concentration, and decreased learning capacity (Bhavnani 2003; Duffy et al 2003; File et al 2001; Lephart et al 2002)
- Elevated cholesterol levels due to alterations in cholesterol metabolism, as well as hardening of the arteries (atherosclerosis) and increased blood pressure (Philosophe et al 1991). Estrogen deprivation is a contributing factor to cardiovascular disease, the leading cause of death of women (Brochier et al 1998). It has been hypothesized that elevated cholesterol may be connected to falling hormone levels because the body tries to compensate for lost hormones by increasing the supply of precursor cholesterol (Dzuga et al 2002).

Causes of Estrogen Dominance

Beginning in perimenopause and continuing through menopause, women's production of progesterone tends to decline more rapidly than their estrogen production does. Between puberty and perimenopause, estrogen levels can be raised by external influences, such as birth control pills or chemicals and toxins. If the ratio between progesterone and estrogen is altered in favor of estrogen, a condition may result that is known as "estrogen dominance," which is associated with increased risk of cancer and other health risks (Kubista 1990; Ashby et al 2001).

Causes of estrogen dominance include the following:

- Environmental pesticides, including those found on commercially grown fruits and vegetables, which have an estrogen-like effect in the body (Tapiero et al 2002)
- Exposure to xenoestrogens (external estrogens) such as those found in herbicides and in petrochemicals found in cosmetics, glue, plastic, and other modern materials (Tapiero et al 2002)
- Unopposed conjugated equine estrogen (CEE)
- Obesity, in which fat cells cause the conversion of other hormones into estrogen
- Increased intake of sugar and processed food, which is linked to magnesium deficiency

Estrogen dominance often produces the following symptoms:

- Menstrual cramps and migraines
- Bloating
- Breast tenderness
- Hot flashes
- Weight gain
- Fatigue
- Depression
- Hair loss
- Fibroid tumors
- Endometriosis

UNDERSTANDING ESTROGEN

To fully understand HRT, it's important to understand the various forms of estrogen and their effects in the body. More than 20 forms of estrogen have been identified. The three major ones are estrone, estradiol, and estriol.

Estradiol is the strongest form of estrogen; it is the kind used in conventional HRT. It converts to estrone, which is produced to some extent in the ovaries but most often in other tissues. The weakest estrogen is estriol. It is the form of estrogen least associated with hormone-related cancers (Head 1998; Kano et al 2002).

These three estrogens convert into many metabolites. Estrone, for example, may convert into three different forms:

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

Scientists have identified 2-hydroxyestrone as a "good estrogen," while 16-alpha-hydroxyestrone and 4-hydroxyestrone have been

associated with the development of cancer (Bradlow et al 1996; Muti et al 2000). The relationship between 2-hydroxyestrone and 16-alpha-hydroxyestrone is sometimes expressed as the 2:16 ratio.

By increasing the ratio of 2-hydroxyestrone to 16-alpha-hydroxyestrone, it may be possible to reduce the risk of hormone-related cancers (Bradlow et al 1986). A cancer that requires estrogen to grow and multiply is known as an estrogen receptor positive (ER+) cancer. Estrogen replacement therapy is generally discouraged in women who have estrogen positive cancers.

The most important ratio to watch, however, is the relation of the three major estrogens to each other. In a young, healthy woman, the estrogen ratio generally averages as follows:

90 percent estriol:7 percent estradiol:3 percent estrone.

While these levels vary individually, the goal of hormone restoration therapy is to recreate a more natural balance while balancing the levels of estrogen against all the other sex hormones. Again, maintaining a youthful balance is key.

One of the major problems with conventional HRT should now be clear. The average ratio of estrogens in CEE is 52 percent estrone, 4 percent estradiol, and 43 percent equilenin, a horse estrogen. Although this therapy may reduce the symptoms of menopause, it clearly is not natural.

The Dangers of Hormone Loss

By the time a woman enters menopause, she may have already experienced two decades of hormonal imbalance and estrogen dominance. After menopause, when all hormone levels decrease significantly, aging women are at increased risk of major diseases, including the following:

Heart disease. Rates of heart disease in postmenopausal women gradually climb until they equal the rates typically seen among men. According to the American Heart Association, heart disease is the leading killer of American women (American Heart Association 2004). A number of negative changes in cardiovascular health are provoked by menopause, including elevations in blood pressure, low-density lipoprotein (LDL) cholesterol, total cholesterol, and triglycerides. At the same time, high-density lipoprotein (HDL) cholesterol levels drop significantly. Elevated levels of homocysteine, C-reactive protein, and interleukin-6 (an inflammatory cytokine) are all associated with estrogen deficiency (Cushman 2003; Davison et al 2003; Dijsselbloem et al 2004)

Osteoporosis. Hormone deficiencies are clearly associated with bone loss and osteoporosis, beginning even in the third decade of life. By the time women reach 50, they are at 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 (Lian et al 2001). Estrogen and androgen therapy increases bone mineral density (BMD), and estrogen/androgen replacement therapy has been shown to increase BMD more than estrogen therapy alone (Notelovitz 2002).

Alzheimer's and dementia. Loss of hormones is associated with neurodegeneration and increased risk of dementia, such as Alzheimer's disease and Parkinson's disease (Danilovich et al 2004; O'Suilleabhain et al 2004). 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 (Yao et al 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 (Maurice T et al 1999).

PROGESTERONE'S BALANCING ACT

Estrogen is only part of the hormone restoration picture. Equally important is progesterone. In a healthy young woman, progesterone serves as a counterpoint to estrogen. While estrogen builds up in the first half of a menstrual cycle, progesterone levels don't start rising until the middle of the cycle. Progesterone's job is to prepare the uterus for implantation with a healthy fertilized egg and to support the early pregnancy. If no implantation occurs, progesterone levels drop, and another cycle begins.

One of progesterone's most valuable functions is its ability to fight cancer. Whereas estrogen is pro-growth (causing the cells in the uterus to multiply early in a menstrual cycle), progesterone is antigrowth. Studies have shown that progesterone has antiproliferative effects on at least two different types of breast cancer cells (Formby et al 1998). Breast cancer is 5.4 times more common in women with low progesterone than in women who have favorable progesterone levels (Cowan et al 1981). Recent studies have also shown that natural progesterone does not affect breast cancer risk, but the synthetic progestins used in conventional HRT raise the risk of breast cancer (Campagnoli et al 2005).

Natural progesterone has also demonstrated neuroprotective properties. One recent 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). Progesterone deficiency has also been linked to migraine (Colson et al 2005).

Wild Mexican yam is a safe, natural source of progesterone (Bagur et al 1996; Komesaroff et al 2001; Uchibayashi 2001). Other

sources of natural progesterone include thyme, oregano, turmeric, verbena, damiana, and red clover (Bagur et al 1996).

Most natural progesterone products that can be purchased over the counter use progesterone derived from soybeans and yams. A common form of natural progesterone is dispensed in a cream that is rubbed into appropriate areas of the body (Komesaroff et al 2001; Uchibayashi 2001). This route of administration bypasses the liver (where the majority of oral progesterone is metabolized) and allows more hormone delivery to where it is needed.

This method provides the closest possible approximation to the natural production of progesterone by the ovaries, provided the dosages are properly timed. Once again, it's important that progesterone therapy mimic the natural cycle as much as possible. To accomplish this, many physicians recommend progesterone therapy be used only during the last half of the month to simulate a young, healthy progesterone cycle.

BEYOND ESTROGEN AND PROGESTERONE: THE TOTAL HORMONE PICTURE

The final step to total hormone restoration is to look at all the hormone levels. Because the steroid hormones are all related to one another, and because many convert into other hormones, it is very important to strive for balance.

DHEA is a natural steroidal hormone secreted by the adrenal gland, the gonads, and the brain (Williams et al 2001). Although women usually have less DHEA than men, both sexes lose DHEA at about the same rate, suggesting that its decline is age related (Khorram 1996; Wilder 1996). Peak levels are typically reached when women are in their 30s, after which they begin to lose approximately 2 percent per year. Decreased levels of DHEA are associated with cancer, diabetes, lupus, and psychiatric illness (Berkman et al 1993; Salek et al 2002). Low levels of DHEA are also associated with higher levels of insomnia, pain, and disability (Morrison et al 1998).

DHEA has been shown to improve mood, neurological functions, immune system functioning, energy, feelings of well-being, and to maintain muscle and bone mass (Kroboth et al 1999; Proctor et al 1998; Yen et al 1995). A study has demonstrated memory-enhancement effects by DHEA and pregnenolone (Rupprecht et al 1999). DHEA may also improve insulin sensitivity and lower triglyceride levels (Casson et al 1995).

Testosterone levels also gradually decrease with age (Schneider 2003). Loss of testosterone affects libido, bone and muscle mass, vasomotor symptoms, cardiovascular health, mood, and well-being (Burd et al 2001; Watt et al 2003). Testosterone therapy, combined with estrogen therapy, has been shown to improve quality of life, vigor and mood, ability to concentrate, bone mineralization, libido, and sexual satisfaction (Bachmann 1999; Braunstein 2002; Cameron et al 2004; Davis et al 2003; Sarrel 1999). This combination therapy also produces improvements with hot flashes, sleep disturbances, night sweats, and vaginal dryness. Because DHEA converts into testosterone, it may be possible to raise testosterone levels with DHEA supplements (Cameron et al 2004; Schneider 2003).

An observational study suggests that testosterone may protect against breast cancer (Slayden 1998). Studies also demonstrate that testosterone replacement alone may protect against breast cancer (Dimitrakakis et al 2003; Dimitrakakis et al 2004; Zhou et al 2000). In addition, testosterone is effective for the treatment of decreased libido (Davis 1999).

Pregnenolone levels also decline with age. As the primary steroid hormone in the cascade, pregnenolone is the first product of cholesterol. Like other hormones, there is a significant reduction occurring in women at about age 32 (Havlikova et al 2002). Reduced pregnenolone levels result in decreased amounts of all other hormones, and pregnenolone deficiencies have been associated with diminished brain function and dementia (Yao et al 2002; Maurice T et al 1999).

It is very important for women to check blood levels of hormones before beginning therapy, and again one and three months after initiating replacement therapy to ensure safe and adequate levels. If testosterone is still low after DHEA and pregnenolone therapy, talk to your physician about options. Always consult your physician before beginning HRT, especially if you are at high risk or have a family history of hormone-dependent cancer.

PHYTOESTROGENS: A NATURAL OPTION

It might seem like a stark choice: face aging and hormonal decline or rely on synthetic hormones that raise the risk of heart attack and breast cancer. Fortunately, there are other options. Progressive physicians throughout the United States, Europe, and Japan have begun to rely on natural bioidentical estrogens, or plant compounds that have estrogenic properties (called phytoestrogens).

Some of the best evidence for phytoestrogens comes from Asia. In Asia, women do not experience many of the diseases and symptoms associated with menopause and the loss of estrogen (Knight et al 1996; Park et al 2005; Sarkar et al 2003). Looking for answers, researchers examined whether there was a genetic difference or another explanation.

Phytoestrogens found in soy and other plant products may help protect aging Asian women (Park et al 2005; Sarkar et al 2003).

Phytoestrogens bind to estrogen receptors (Zittermann 2003). By competing for estrogen receptors, phytoestrogens help prevent the growth and spread of several hormone-dependent cancers (Adlercreutz et al 1992). They have also been shown to decrease the risk of some degenerative diseases, including cardiovascular disease, osteoporosis, and breast and uterine cancer (Badowski et al 2001; Fletcher 2003; Magee et al 2004; Park et al 2005; Valentin-Blasini et al 2003).

Heart Benefits of Phytoestrogens

Unlike conventional HRT, which was shown to raise the risk of heart attack among postmenopausal women, phytoestrogens

actually have a positive effect on the heart. In 1999, the US Food and Drug Administration authorized the use of food-label health claims connecting increased soy consumption with reduced risk of coronary artery disease (Vincent et al 2000). One study of more than 400 women demonstrated that phytoestrogens protect against arterial degeneration and atherosclerosis through their effect on the arterial walls, particularly in older women (van der Schouw et al 2002).

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

- Decreased blood pressure, LDL cholesterol, total cholesterol, and triglycerides (De Kleijn et al 2002; Ruiz-Larrea et al 2000).
- Increased HDL cholesterol and improved cardiovascular profile (De Kleijn et al 2002).
- Lowered the overall rate of cardiovascular disease among people with higher consumption of phytoestrogens (Ariyo et al 2002). Genistein and daidzein, two of the most extensively studied phytoestrogens, are effective at lowering lipids in people with high cholesterol (Anthony et al 1997; Teede et al 2001; Zittermann 2003). Increased levels of daidzein and genistein inhibit LDL oxidation and help reduce the risk of atherosclerosis (Exner et al 2001).
- A six-month study of more than 180 women confirmed that a soy-rich diet is as effective as conventional HRT for lipid lowering (Park et al 2005).

Furthermore, phytoestrogens have up to almost 3 times the radical scavenging activity of vitamin C and vitamin E and have protective effects on the arterial walls (Ruiz-Larrea et al 2000; van der Schouw et al 2002).

Osteoporosis and Phytoestrogens

Studies have shown that postmenopausal women with a habitually high intake of phytoestrogens have high bone mineral density of the spine and hip (Greendale et al 2002; Hanna et al 2004; Mei et al 2001). A number of studies have been conducted on phytoestrogens and bone homeostasis:

- Genistein, daidzein, and coumestrol increase bone mineralization (Clifton-Bligh et al 2001; Kanno et al 2004).
- Genistein and daidzein decrease bone resorption and inflammatory factors and increase bone-making proteins (Gao et al 1999; Gao et al 1999b; Harkness et al 2004; Jia et al 2003; Rassi et al 2002; Suh et al 2003; Yamaguchi et al 2000; Zhang et al 2004).
- An isoflavone mixture of daidzein, genistein, formononetin, and biochanin demonstrated significant increases in bone mineral density after six months of treatment. Women who took 57 mg/day of isoflavones had a 4 percent increase in bone mineral density (Clifton-Bligh et al 2001).
- A phytoestrogen preparation using daidzein, genistein, formononetin, and biochanin demonstrated protective effects on the lumbar spine (Atkinson et al 2004).
- Dietary supplementation with 54 mg/day of genistein “may be as effective as hormone replacement therapy in attenuating menopause-related bone loss without causing the associated side effects” (Cotter et al 2003).

Genistein: A Powerful Phytoestrogen

Genistein, together with daidzein, is one of the most extensively studied phytoestrogens. It has been shown to have beneficial estrogenic effects in bone, the brain and the cardiovascular system (Bang et al 2004). It is even being considered as an alternative to estrogen for the treatment of Alzheimer’s disease (Bang et al 2004).

Brain protection. Estrogen and estrogen-like compounds protect brain cells from degenerative changes due to aging and oxidative stress (Bhavnani 2003; Linford et al 2002). Genistein is a potential alternative to estrogen in the treatment of Alzheimer’s disease (Bang et al 2004).

Menopause symptoms. Several studies demonstrate that natural estrogens significantly decrease hot flashes and vaginal atrophy (Albert et al 2002; Baird et al 1995; Chiechi et al 2003; Clifton-Bligh et al 2001; Murkies et al 1995). Treatment with 54 mg/day of genistein safely decreases hot flashes up to 30 percent and should be considered as an alternative treatment for postmenopausal conditions (Crisafulli et al 2004).

Cancer. Studies demonstrate a significantly lower incidence of sex hormone-related cancer in Asian countries (Sarkar et al 2003; Vij et al 2004). This difference has been attributed to the traditionally high intake of soy isoflavones in the Asian diet because genistein has been shown to stop the growth and spread of breast cancer cells and significantly delay the progression of prostate cancer (Sarkar et al 2003; xon-Shanies et al 1999).

Daily soy isoflavone consumption is associated with decreased breast cancer risk (Lu et al 2001). A diet containing 113–202 mg/day (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 for breast cancer (Lu et al 2000). Genistein and daidzein also have an inhibitory effect on uterine cancer (Lian et al 2001). Most studies indicate that soy isoflavones are safe and

effective.

Naturally Suppressing Symptoms of Menopause

In addition to hormone restoration therapy, many supplements have been shown to suppress the symptoms of menopause and hormone loss. Folk and traditional healing therapies have successfully and safely used herbal medicines to treat gynecologic problems for more than 100 years (Hardy 2000; Mahady et al 2002). These herbal medicines include the following:

Black cohosh. Native American Indians have used black cohosh as a traditional medicine for many years, and Koreans have used it to treat pain and inflammation (Huntley 2004; Kim et al 2004; McKenna et al 2001). Today, it is used primarily for the treatment of menopausal symptoms, such as hot flashes, and menopausal depression and anxiety (Kennelly et al 2002). Black cohosh has also been used to treat younger women who have surgically induced hormonal deficits due to hysterectomy or ovariectomy and for menstrual disorders (McKenna et al 2001). It is effective for reducing hot flashes, night sweats, fatigue, and insomnia (Kronenberg et al 2002; Philp 2003; Pockaj et al 2004).

Black cohosh also has antiproliferative effects on breast cancer cells (Bodinet et al 2004; Einbond et al 2004; Hostanska et al 2004; Zierau et al 2002). Studies have shown it is as effective as Evista for preventing bone loss (Nisslein et al 2003).

Black cohosh is so effective that an extract called Remifemin® is commonly prescribed in Europe as an alternative to HRT for menopause (McKenna et al 2001). Several clinical studies demonstrate that black cohosh should be considered as an alternative therapy, especially for women who should not take HRT (Hardy 2000; Huntley 2004; Johnson et al 2003; Lieberman 1998; Lupu et al 2003).

Licorice root. Licorice root's many beneficial biological effects include estrogenic effects, body fat reduction, and reduction of testosterone (Armanini et al 2002). Similarly, licorice root has been shown to decrease serotonin reuptake by up to 60 percent, which may help alleviate menopausal depression (Ofir et al 2003). Licorice root also has the ability to lower the risk of cardiovascular disease by assisting with repair of blood vessel walls and preventing hardening of the arteries (Somjen et al 2004).

For more information on the safety profile of licorice root, please see "Safety Caveats" at the end of this chapter.

Dong quai. Dong quai is used in Chinese medicine to treat gynecologic conditions (Goh et al 2001; Hardy 2000). It is an effective remedy for alleviating menopausal symptoms without causing harmful changes in the uterus or vagina (Hirata et al 1997). A study demonstrated that a preparation with 60 mg of soy isoflavones, 50 mg of black cohosh, and 100 mg of dong quai reduced menstruation-related migraine headaches (Burke et al 2002). Most phytoestrogen preparations contain a small quantity of dong quai because of its various biological effects in the body.

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 and menopausal symptoms. Menopausal women report excellent symptomatic relief after using two essential oils from vitex (Chopin 2003).

BIODIDENTICAL HORMONE REPLACEMENT

Among younger women, phytoestrogens alone may be enough to correct small deficiencies. Menopausal and postmenopausal women, however, often require HRT with bioidentical estrogens and progesterone. As the name implies, these hormones have exactly the same chemical structure as biological hormones. Bioidentical hormones can be found at special pharmacies that will compound them in the correct ratio to naturally restore hormones to a youthful level. The use of bioidentical estrogens, which is gaining acceptance in the United States, has long been practiced in Europe and Japan (Kano et al 2002).

Estriol is the main component of Life Extension's recommended bioidentical estrogen replacement therapy, representing 90 percent of the content, with smaller proportions of estradiol (7 percent) and estrone (3 percent). Estriol offers many of the benefits of more conventional estrogen-replacement therapies, but without the harsh side effects or long-term dangers often encountered with conventional HRT, which has an unnatural balance of estrogens and contains almost 50 percent horse estrogen (Head 1998). This weak estrogen also slows the progression of atherosclerosis (Kano et al 2002).

Some popular prescription estrogen formulas are BiEst® and TriEst®. BiEst® consists of estradiol and estriol (Taylor 2001), while TriEst® contains all three estrogens in a ratio of 80 percent estriol to 10 percent each of estradiol and estrone (Taylor 2001). For a patient with a prescription, a compounding pharmacy can alter the proportion of each estrogen to achieve Life Extension's recommended ratio of 90:7:3. For referrals to physicians who are willing to prescribe bioidentical estrogens, or for information on obtaining a Female Hormone Profile, call 1-800-544-4440 or go to www.lef.org.

Bioidentical estrogens will often be prescribed after blood testing shows deficiencies in estrogen and can be part of a

comprehensive hormone restoration program that also includes progesterone cream or bioidentical progesterone, DHEA, pregnenolone, and perhaps testosterone.

Women should also discuss hormone cycling with their physicians. During their fertile years, women do not experience stable blood levels of estrogen and progesterone. Rather, estrogen and progesterone levels naturally rise and fall throughout the monthly cycle. Decades of this normal, natural flow of hormones has the effect of conditioning hormone receptors throughout the body to follow a rhythmic pattern.

To mimic nature and get the most benefit from hormone restoration, a woman should take estrogen in the first part of the month and taper the amount toward the end of the month, when her body is conditioned to receive less estrogen. Progesterone, on the other hand, should be taken in the latter half of the month, when her progesterone levels would be rising. Discuss this cycle with your physician because every woman's body and natural cycles are different.

LIFE EXTENSION'S HORMONE RESTORATION RECOMMENDATIONS

No program of hormone replacement should be launched without first undergoing a comprehensive female hormone profile blood test and 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 access to hormone blood testing can call 1-800-544-4440 or go to a special web site at www.lef.org.

Because of the wide variability of hormones within each woman, it is difficult to recommend standard doses for everyone. Instead, Life Extension recommends that women rely on regular blood testing to strive for ideal hormone levels. These ranges are based on a healthy 20- to 29-year-old woman:

| Hormone | Reference range |
|--------------------|-----------------|
| DHEA | 65-380 ug/dL |
| Pregnenolone | 0-230 ng/dL |
| Total estrogen | 61-437 pg/mL |
| Progesterone | .2 to 28 ng/mL |
| Total testosterone | 14-76 ng/dL |

Some women may be able to support their body's natural production of estrogen and progesterone levels and relieve some symptoms of menopause by consuming Life Extension products that are specially designed to address these needs. These products include the following:

Natural Estrogen, a product containing

- Genistein 25.81 mg
- Daidzein 24.97 mg
- Glycitein 4.69 mg
- Black cohosh extract: 20 mg
- Dong quai extract: 12.5 mg
- Licorice extract: 12.5 mg
- Vitex extract

Postmenopausal women can take it every day. Premenopausal women can take Natural Estrogen cyclically: three weeks on and one week off, beginning on the fifth day of the menstrual cycle. Do not take Natural Estrogen if you are pregnant or lactating or have a history or high risk of estrogen-dependent tumors. Always consult a physician before embarking on any hormone restoration program.

Mega Soy Extract with genistein 51.6 mg, daidzein 50 mg, and glycitein 9.4 mg. One capsule twice daily can be taken with meals.

Pro-Fem Cream, a natural progesterone cream. Pro-Fem Cream can be massaged into soft tissue areas such as the breast, underarm, abdomen, buttocks, and inner thighs and applied to a different area every application to avoid saturating the skin or fat cells in a particular area of the body. Discuss proper cycling and dosage with your physician.

Supplementation with additional hormones, including **pregnenolone**, **DHEA**, and **testosterone**, should be based on the results of blood tests. Women seeking more information on blood tests or who wish to speak to a knowledgeable health advisor can call 1-800-544-4440, or go to a special web site at www.lef.org.

FEMALE HORMONE SAFETY CAVEATS

Women who are at risk of hormone-dependent cancer should not begin hormone restoration therapy unless they are under the direct supervision of a qualified physician.

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Black Cohosh

- Do not take black cohosh if you could be pregnant; black cohosh can increase the chance of a miscarriage.
- Black cohosh can cause gastrointestinal symptoms such as nausea and diarrhea.
- Consult your doctor before taking black cohosh if you are taking medication to lower blood pressure. Black cohosh may amplify the blood pressure–lowering effects of blood pressure medications.

Daidzein

- Consult your doctor before taking daidzein/daidzin if you have prostate cancer.
- Do not use daidzein/daidzin if you have estrogen receptor–positive tumors.
- Daidzein/daidzin can cause hypothyroidism in some people.

DHEA

- Do not take DHEA if you could be pregnant, are breastfeeding, or could have prostate, breast, uterine, or ovarian cancer.
- DHEA can cause androgenic effects in woman such as acne, deepening of the voice, facial hair growth and hair loss.

Genistein

- Consult your doctor before taking genistein/genistin if you have prostate cancer.
- Do not take genistein/genistin if you have estrogen receptor–positive tumors.
- Genistein/genistin can cause hypothyroidism in some people.

Glycitein

- Consult your doctor before taking glycitein/glycitin if you have prostate cancer.
- Do not take glycitein/glycitin if you have estrogen receptor–positive tumors.

Licorice

- Do not take licorice extract if you have diabetes, high blood pressure, heart irregularities, abnormal muscle tension, poor kidney function, low blood potassium levels, or chronic hepatitis, cirrhosis of the liver, or any disease that impedes the flow of bile from the liver.
- Do not take licorice for more than 6 weeks in a row. High doses of licorice (more than 20 grams of licorice extract daily or 50 grams of licorice root daily) taken for extended periods may lead to excessive loss of sodium from the blood, water retention, high blood pressure, heart irregularities, fatigue, headaches, and muscle cramps.

Progesterone

- Do not take progesterone if you could be pregnant or are breastfeeding.
- Consult your doctor before taking progesterone if you have cancer of the reproductive organs.

Vitex (chasteberry)

- Vitex can cause rash.
- Consult your doctor before taking Vitex if you take dopamine-inhibiting medication. Vitex can make the dopamine inhibitor less effective.

For more information see the Safety Appendix

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.