Overview

Increasingly, women at mid-life are assuming greater control over their health care. Although women experience significant changes in their health with the ending of menstruation, many of the conditions associated with this period of a woman’s life can be overcome or modulated with hormone replacement and/or nutritional therapies. Effective assessment can provide important information to practitioners and patients to avoid the negative side effects associated with hormone replacement therapies and to help determine nutritional changes and/or supplementation.

The **Menopause Profile** examines hormone levels in three salivary samples (collected over five days). Test results include three estradiol assays, three estrone assays, three estriol assays, three progesterone assays, and one testosterone assay. Reference ranges for the **Menopause Profile** are based only on non-supplementing post-menopausal women. Transdermal and sublingual forms of hormone replacement, in particular, may cause significant elevations in salivary hormone levels. For these reasons, this assessment is recommended for use only as a baseline analysis of hormone levels in non-supplementing women.

For the comprehensive version of this profile, an additional four saliva samples are collected at designated times. This comprehensive profile includes the **Adrenocortex Stress Profile** (DHEA and cortisol) and the **Comprehensive Melatonin Profile** with standard interpretation. Since menopause and its aftermath can affect cortisol, DHEA, or melatonin activity, the **Comprehensive Menopause Profile** provides the most clinically relevant information. The Menopause panel may be ordered separately if desired.

The Comprehensive Menopause Profile is indicated for postmenopausal women when fatigue, sleep disorders, or depression are part of the clinical presentation. These tests will reveal estradiol, estrone, estriol, and progesterone levels, as well as the degree of fluctuation between each day. In addition they can illuminate the roles that adrenal dysfunction and melatonin imbalances play in hormonal dysequilibrium. This assessment establishes a clinical baseline for designing customized therapy to optimize hormonal health. In addition, bone resorption analysis is suggested for women who are postmenopausal and/or at risk for osteoporosis.

The test report includes commentary which discusses the clinical significance of individual test results. The Interpretive Guidelines help physicians design an appropriate therapeutic protocol.

### Collection of Samples: Saliva vs. Serum

The collection of female sex hormones in saliva is a convenient, non-invasive, and stress-free procedure. Saliva testing is cost-effective, because the samples can be collected by the patient at home or in the workplace, without the assistance or supervision of medical personnel. Patient instructions are simple and contain few precautions.

In addition, salivary hormone levels correlate extremely well with free levels in plasma for most steroid hormones analyzed. Salivary hormone concentrations reflect the bioactive, unbound fraction of total serum levels. Saliva levels display a linear correlation to free serum levels independent of saliva flow rate. The correlation of salivary estradiol and progesterone to that of their serum levels were \( r^2 =0.93 \) and \( r^2=0.97 \), respectively. Salivary testosterone has a 1 to 1 correlation to free serum testosterone. Saliva has been deemed a reliable medium for determining estrone and estriol levels as well, providing good correlations with free serum levels. Salivary assays of cortisol, measured by radioimmunoassay, have also been recommended by numerous studies. In general, scientific literature demonstrates excellent circadian plotting obtained by salivary hormone analysis.

### What this test does:

Analyzes Melatonin secretion pattern for imbalances that can lead to sleep disorders, SAD, infertility and compromised immune function.

### Turn-around Time 7 days
The “Sex” Hormones: Estrogen, Progesterone, Testosterone

Hormones are powerful chemical messengers that circulate throughout the bloodstream to specific target cells, where they generate biological responses. Principal players in the body’s process of homeostasis, hormones mediate such a prodigious array of physiological functions that they have become critical indicators for diagnosis and treatment of numerous health conditions.

Three steroid hormones—estradiol, estrone, and estriol—are known collectively by their function as estrogens. In postmenopausal women, following the decline of ovarian function, these estrogens are produced primarily in the adrenal glands.

The estogenic potency of estradiol is 12 times that of estrone and 80 times that of estriol. Estradiol is synthesized from testosterone and androstenedione. Due to its potency, it plays a critical role in female sexual development, menstrual function, protein synthesis, cardiovascular function, bone formation and remodeling, cognitive function, emotional balance, and other important health factors. It also may be the most stimulatory estrogen for promoting cell growth and proliferation.

After menopause, estrone becomes the primary estrogen as the ovary loses its ability to manufacture estradiol. Estrone is synthesized from androstenedione in the adrenal glands and from peripheral tissues by aromatization. Fat cells are especially rich in the aromatase enzyme that converts androstenedione to estrone. This explains why obese postmenopausal women often have higher circulating levels of estrogens.

Estriol is considered to be the mildest and briefest-acting of the three estrogens. Estradiol is formed in the liver by conversion of either estradiol or estrone. Although there is evidence that a certain amount of estriol can be recirculated into the body via the liver or gut hydrolysis, its conversion is believed to be more fixed than the other two estrogens, with a reduced ability to reconvert into more potent forms of estrogen.

Progestins are comprised of progesterone and 17-alpha hydroprogesterone, and they exhibit similar potency. Because 17-alpha hydroprogesterone is produced in minute quantities compared to progesterone, the latter is considered as the sole progestin.

In postmenopausal women, progesterone is produced mainly in the adrenal cortices. Both progesterone and testosterone are formed from cholesterol. Before menopause, in the follicular phase of the menstrual cycle, most of these steroids are converted to estrogens.

Conversion of estradiol to a less potent estrone or estriol lessens the potency of circulating estrogens, and further functional degradation occurs as formation of glucuronides and sulfates in the liver takes place. Similarly, progesterone is functionally degraded to less potent steroids in the liver.

Following menopause, a decrease in estrogen levels produces several distinct changes in female physiology. For sexually active women, intercourse can become uncomfortable or painful because vaginal lubrication is reduced with the decrease in estrogen and the epithelium becomes progressively thinner, potentially leading to a condition known as atrophic vaginitis. Hormone replacement therapy or the use of water soluble lubricants can sometimes provide relief in such cases. Lower levels of estrogens can also influence skin aging, affect memory, alter lipid metabolism, trigger changes in mood and cognition, and accelerate rate of bone loss. Vasomotor symptoms, at least among women in the industrialized western countries, include hot flashes, which may also be ameliorated by estrogen replacement.

Progestin also decreases at this point in the female life cycle. Lower levels of this hormone have been associated with dysfunctional uterine bleeding, and may play a role in osteoporosis and other age-associated conditions. To reduce some of the side effects of estrogen replacement therapy, especially the increased risk of endometrial hyperplasia or adenocarcinoma, progesterone is often combined in hormone replacement therapy.

For women as well as men, testosterone helps maintain libido. Imbalances of testosterone in postmenopausal women are associated with various forms of coronary heart disease and cardiovascular events, including myocardial infarction. In addition to influencing muscle mass and weight loss, testosterone also plays a role in the production of several other hormones.
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Cortisol and DHEA

Cortisol and DHEA are major hormones produced in the adrenal glands. The balance between these hormones plays a major role in modulating the body’s adaptive response to physiological and psychological stress. Changing amounts of DHEA and cortisol can profoundly affect energy levels, coping abilities, fat and carbohydrate metabolism, disease resistance, sleep patterns, immune response, and general sense of well-being in postmenopausal women.

As women (and men) age, the loss of the inner zone of the adrenal cortex, the zona reticularis, can cause levels of DHEA to decline steadily, a waning process likened to that of menopause. In contrast, levels of cortisol may increase slowly with time, while its natural circadian rise and fall becomes blunted. These hormonal shifts have important implications for women both at menopause and in its aftermath, and can strongly affect their risk of developing degenerative conditions as they age.25

A higher ratio of cortisol to DHEA has been linked to climacteric symptoms such as fatigue, insomnia, and depression. In fact, one recent study showed that the ability of red ginseng to help alleviate menopausal symptoms may rest largely in its ability to decrease the cortisol/DHEA-S ratio.26

Adrenal hormone levels can also be influenced by changing levels of sex hormones. Certain types of estrogen replacement therapy have been shown to affect levels of androgens such as DHEA and testosterone, which may further complicate menopause symptoms.27-29

Over time, chronic elevations of cortisol can force the body to function in “overdrive,” causing high circulating glucose levels, increased bone loss, hypertension, and other potentially degenerative processes. Adipose tissue in the abdomen is especially sensitive to high cortisol; this can lead to increased fat deposits around the waist in response to stress.30,31 Chronic obesity, osteoporosis, type-2 diabetes, dementia, and cardiovascular disease are just a few of the many age-related clinical conditions associated with the loss of optimal adrenal function.

By accurately assaying levels of cortisol and DHEA, the Comprehensive Menopause Profile reveals unsuspected imbalances that may be subtly or dramatically influencing a postmenopausal women’s current and future health. For more information about the biochemistry, physiology, and clinical effects of adrenal hormones, see the Adrenocortex Stress Profile and the Metabolic Dysglycemia Profile Application Guides.

Melatonin

Melatonin is the major neuroendocrine modulator of annual and circadian rhythms in the body, including the sleep-wake cycle. Operating much like an internal aging clock, melatonin exerts antioxidant and regenerative influences that can strongly affect immune response, cardiovascular function, and mood-related neuronal mechanisms. Melatonin is the primary substance secreted by the pineal gland in the brain. It has access to a rich supply of blood, and its hormonal products affect virtually every organ system in the body. As one of the few antioxidants in nature that is both fat- and water-soluble, melatonin has the potential to protect diverse parts of the cell.

The interdependent relationship between pineal function and sex hormone levels has been borne out by several studies. One possible explanation is that sex hormones regulate melatonin production by modifying β-adrenergic mechanisms.32

Relatively sudden shifts in nocturnal melatonin production—both increases and decreases—have been reported in women during the perimenopausal period.33,34 Thereafter, a “steep, age-related decline in nocturnal melatonin secretion” has been observed during the 15 years following menopause, tapering to a more gradual decline thereafter.34

This pattern has prompted researchers to explore the benefits of melatonin therapy in many menopause-associated conditions, such as sleep disorders, breast cancer, depression, and degenerative aging.33,34 For example, in postmenopausal women with low baseline levels of melatonin (as detected in saliva), replacement therapy has been shown to significantly restore pituitary and thyroid function, leading to improved mood and well-being.37
Estrogen replacement therapy (ERT) in postmenopausal women appears to affect melatonin production in different ways depending on the individual, either suppressing or stimulating secretion. ERT can also modulate melatonin’s influence on catecholamine levels. Such an individualized response supports the importance of hormone testing to design effective, customized interventions.

Great Smokies’ assay of saliva provides a noninvasive method for assessing melatonin circadian secretion patterns, revealing abnormal levels that may be significantly affecting physical and psychological disorders in postmenopausal women, including:

- Insomnia
- Depression
- Stress/Axiety
- Immunological Disorders
- Delayed Sleep Phase Syndrome
- Cardiovascular Disease
- Seasonal Affective Disorder
- Cancer

For more information on the biochemistry, physiology, and clinical effects of melatonin, see the Comprehensive Melatonin Profile Application Guide.

Using the Comprehensive Menopause Profile to Enhance Women’s Health

By identifying deficiencies (or excesses) of important hormones, the Comprehensive Menopause Profile can provide clinical guidance for therapeutic intervention in numerous conditions:

Menopause

For women in the U.S., the cessation of menstruation (i.e., menopause) normally occurs between 40 and 60 years of age. The initial symptoms may include irregular menstrual cycles, anovulation, and hot flashes. A dramatic decline in the levels of progesterone and estrogen occurs at this time. Estradiol values decline to subfunctional levels after menopause, and the less potent estrone becomes the most dominant estrogen.

Maintaining adequate estrogen levels may help alleviate symptoms of menopause. Addressing imbalances of related hormones such as melatonin, cortisol, and DHEA can also provide relief. However, estrogen replacement therapy may also increase a woman’s risk of developing breast or endometrial cancer. In addition, a decrease in progesterone levels prior to menopause may also result in a reduced anti-estrogenic effect.

The Comprehensive Menopause Profile provides clinical guidance in determining which women may benefit most from hormone replacement therapy. Because the stimulatory potency of the three major estrogens differs, each woman may require customized therapy based on her unique health status, hormone levels, and disease risks. Testing can pinpoint specific hormonal deficiencies, and help to avoid excess levels (both estrogens and androgens) associated with health risks.

Menopausal bleeding can develop in women with or without hormone replacement therapy. Because of the increased incidence of endometrial adenocarcinoma, endometrial sampling should be performed as soon as possible. Cyclic courses of progestogens have been used to arrest heavy menopausal bleeding and reverse hyperplasia of the endometrium.

Breast Cancer

Elevated levels of bioavailable estrogens and androgens—including estradiol, estrone, DHEA, and testosterone—are generally considered to increase the risk of breast cancer in women after menopause. This increased risk is theorized to stem from the ability of these steroids to stimulate the growth and proliferation of cells in breast tissue.

Estriol, the weakest estrogen fraction, is often viewed as a “safer” form for relieving symptoms of the climacteric. Some preliminary evidence suggests estriol may help reduce breast cancer risk by blocking more potent estrogens from attaching to cell receptors and by reducing stimulatory mechanisms on breast tissue; it has, however, also exhibited mild proliferative effects in vitro.
Melatonin has shown clinical promise in breast cancer prevention and treatment through its ability to influence estrogen receptor expression and inhibit breast cancer cell growth and proliferation. Numerous studies have reported an inverse correlation between melatonin levels and the growth of estrogen-receptive positive tumors.

Hypertension and Heart Disease

Combined estrogen/progestin therapy may improve lipid profiles in postmenopausal women, reducing LDL, raising HDL, lowering fibrinogen and Lp(a). Estrogen replacement has been shown to improve endothelium-dependent vasodilation of coronary arteries in women with risk factors for atherosclerosis, perhaps due to its antioxidant properties. Other positive cardiac effects cited for estrogen/progestin include increased blood flow, reduced stress response, and decreased clotting tendency. However, not all studies show consistent benefit; the impact of estrogen replacement on cardiovascular risk factors, including insulin sensitivity and lipid balance, may also depend on the dose and type of therapy used (oral vs. transdermal) as well as each woman’s unique metabolic and genetic make-up. This underscores the importance of monitoring the safety of replacement therapy with testing for lipid imbalances, glycemic dysregulation, and other cardiac risk factors.

Excess levels of androgens (DHEA and testosterone), as well as the adrenal hormone cortisol, are increasingly being recognized as strong coronary disease risk factors in postmenopausal women. Left unchecked, such elevations can fuel chronic, synergistic metabolic imbalances that underlie abdominal obesity, dysglycemia, insulin resistance, and hypertension.

Adequate levels of melatonin may reduce the risk of blood vessel damage and heart attack in various ways: reducing sympathetic activity; improving cholesterol balance; and inhibiting the build-up of blood clotting factors. Melatonin has also been shown to relax arteries and reduce blood pressure in postmenopausal women on hormone replacement, and prevent the oxidation of LDL cholesterol in healthy postmenopausal women.

Osteoporosis

Because estrogen modulates the functioning of osteoclasts and osteoblasts in bone tissue, the hormone also influences the rate of resorption and deposition of calcium. Estrogen deprivation following menopause results in increased activity of osteoclasts which exceeds the capacity of osteoblasts to deposit needed calcium. For this reason, declining levels of estrogen after menopause have been directly correlated with a progressive decrease in bone mineral density. Under these conditions osteopenia and osteoporosis often develop.

Some research suggests that testosterone enhances the ability of estrogen to increase bone mineral density. DHEA also appears to boost bone formation and reduce bone turnover in postmenopausal women, although androgen replacement therapy can adversely affect their lipid levels.

Both endogenous and exogenous cortisol excesses are well-established causes of accelerated bone loss that increase the risk of osteoporotic fractures. As researchers at Cornell University Medical College noted, “The clinical presentation of cortisol excess is one of progressive [bone] demineralization... resulting in fractures of the vertebral bodies and ribs.”

Melatonin plays a role in regulating calcium metabolism. Declining levels of this pineal hormone after menopause may be an important contributory factor in osteoporosis. One investigator has even suggested using oral doses of melatonin combined with light therapy for prophylaxis and treatment of postmenopausal osteoporosis.

Obesity

Steroid hormone dysfunction can play a pivotal role in the dynamics of metabolic obesity. Increasingly, research shows that chronic imbalances may perpetuate a self-sustaining cycle of weight gain in postmenopausal women.

Because fat cells are rich in the aromatase enzyme that converts the precursor androgen, androstenedione, into estrone, obesity (particularly increased thigh fat mass and intrabdominal fat mass) in postmenopausal women often leads to higher circulating estrogen levels. Obesity also significantly lowers levels of SHBG, the carrier protein.
that binds to sex hormones and renders them biologically inactive. Together, these two tendencies can trigger higher circulating levels of unbound, bioactive sex steroids in obese, postmenopausal women, increasing their risk of breast cancer.85

Androgen and adrenal excess is associated with central obesity in postmenopausal women. Oversecretion of cortisol is known to promote increased fat deposition—particularly in the abdominal region.85,86-88

**Stress**

Stress has been shown to decrease the production of sex steroids, which can lead to reduced libido, depression, and accelerated aging. Maladaptation of the adrenocortex is, at least in part, responsible for the reduction of sex steroid levels, since the body must create excess cortisol at the expense of synthesizing many sex steroid hormones.

Stress initially causes elevated cortisol levels (hypercortisolism). During stress, negative HPA feedback for cortisol is overridden. High levels are maintained as long as the stressor is present and may flare up if it reappears.89

Experimentally-induced hypercortisolism has been shown to damage cells in the hippocampus (glucocorticoid receptors), which are normally responsible for mediating cortisol-induced suppression of corticotropin releasing hormone.90 The damage to the receptors may thus permit higher cortisol levels.

Eventually, prolonged stress can cause the adrenal cortex to hypertrophy, leading to adrenal exhaustion and chronic fatigue.

**Aging**

Estrogen and androgens are wellknown for their pivotal roles in promoting muscle and bone formation. This relationship becomes even more vital as the body ages and tissue breakdown accelerates. Growing evidence also suggests that these hormones may be critical for slowing or preventing certain forms of dementia and cognitive decline.

Estrogen deficiency in the postmenopause is believed to accelerate brain aging and increase the risk of neurodegenerative disease.91 Significantly lower levels of estradiol have been reported in women with Alzheimer’s disease.92 Most studies associate postmenopausal estrogen therapy with roughly a 50% reduced risk of developing Alzheimer’s disease.93

Various mechanisms have been cited to explain estrogen’s positive impact on brain function, including its ability to preserve the brain’s “neural plasticity”, to act as an anti-inflammatory, and to increase cerebral blood flow.94

Chronic stress can also accelerate the aging process, by causing inappropriately elevated cortisol levels. While cortisol levels generally rise steadily with age, the resiliency of the HPA-axis may decrease, causing the normally steep circadian secretion pattern (morning rise and nocturnal fall) to become blunted.95-97 Besides promoting bone loss, dysglycemia, and depression, chronic cortisol elevation—especially when combined with DHEA deficiency—may damage the hippocampal region of the brain, accelerating age-related memory loss.98-100

**Depression**

Mounting studies point to the importance of steroid hormones in modulating emotional states. Estrogen receptors have been identified in the specific brain regions that regulate mood. Estrogen is believed to act as a neuroexcitatory agent; it can boost levels of neurotransmitters, increase synaptic connections, and spark electrical activity in the cerebellum, hippocampus, and cerebral cortex regions of the brain.101

These mechanisms may partly explain why estrogen replacement often improves well-being in postmenopausal women with depressive symptoms.102-104 However, because overstimulation can lead to irritability and anxiety states, research also suggests that estrogen excess be avoided. Optimum well-being may be achieved when estrogen is kept in balance with progesterone, which acts like a sedative, shutting down the neuronal firing system in the brain, and decreasing the number of excitatory synaptic connections.101, 105

Adrenal and pineal dysfunction can also play important roles in postmenopausal depression.
Elevated cortisol, as well as disrupted circadian secretion rhythm, is a common finding in depressed individuals. Abnormalities of melatonin circadian function are closely linked to a variety of behavioral changes and mood disorders, including depression, Seasonal Affective Disorder, and panic disorder.

**Chronic Fatigue**

Fatigue is a common symptom that often manifests in women during or after menopause. Feelings of chronic energy depletion can be triggered by adrenal hormone imbalances. Treatments that re-establish a healthy balance of DHEA and cortisol have been shown to improve fatigue symptoms in many postmenopausal women.

Chronic Fatigue Syndrome (CFS) is characterized by persistent or relapsing debilitating fatigue for at least 6 months in the absence of any other definable diagnosis. Symptoms of CFS may include depression, hypotension, weight loss, and inability to endure stress.

Researchers have proposed that CFS is actually a disease of the hypothalamic pituitary-adrenal axis. Patients with CFS typically show low free cortisol levels and adrenal insufficiency.

**Sleep**

Insomnia and other sleep disturbances may surface in the menopause transition and continue into later years. Sometimes these sleep problems may stem from nocturnal vasomotor symptoms caused by estrogen deficiency. But estrogen also has a powerful direct impact on other factors that modulate sleep, such as body temperature and circadian rhythm.

Difficulty falling asleep, increased awakenings at night, more fragmented sleep and less deep sleep have been linked with the postmenopausal profile of sex steroid hormones. Replacement therapy with combined estrogen and progesterone often alleviates sleep disturbances in these women.

Sex steroid imbalances are also believed to play an important role in sleep apnea in postmenopausal women. Addressing this problem is important since apnea is linked with increased risk of cardiovascular disease and mortality.

Higher cortisol levels have been correlated with less restful stages of the sleep cycle, such as Wakefulness and Stage 1 (Short-Wave) sleep. Rapid eye movement (REM) sleep occurs primarily when cortisol levels are decreasing, with diminished or absent secretory activity of the adrenals.

Hormonal disruptions of the body's biological clock are often signalled by imbalances of melatonin. One study found that melatonin levels were significantly lower in postmenopausal women with insomnia compared to controls. Therapy to re-establish melatonin's circadian secretion pattern has been shown to benefit patients with delayed sleep phase insomnia, sleep deprivation, jet lag, and many other sleep disorders.

**Immune Function**

A shifting balance between cellular (Th1) and humoral (Th2) immunity is theorized to underlie the etiology of many autoimmune conditions.

In general, estrogens are considered to stimulate humoral immunity (Th2). Androgens such as testosterone are generally considered to suppress both cellular (Th1) and humoral (Th2) immunity.

Rheumatoid arthritis (RA) chiefly strikes women during the peri- and postmenopausal period. Mounting evidence suggests that RA may develop in response to the sudden drop in adrenal and gonadal steroid hormones induced by menopause, which creates a shift towards the Th1 immune response.

Low levels of adrenal hormones (such as cortisol and DHEA) are typically reported in postmenopausal women with RA. These deficiencies may affect the production of downstream hormones and impair healthy anti-inflammatory feedback mechanisms, thus playing a critical role in RA onset and progression.
One recent study also suggests that diminished estrogen levels after menopause may disrupt the immune-brain barrier and incite inflammatory processes in the brain, accelerating brain aging.\(^{136}\)

Cortisol, like other glucocorticoids, is an anti-inflammatory agent that downregulates the production of IL-2 and interferon, creating strong immunosuppressive effects.\(^{137,138}\)

Melatonin has general stimulatory effects on immune system functions; its positive anti-cancer effects may stem from this strengthening of the immune response.\(^{139}\) One theory is that melatonin acts as an anti-stress hormone via the brain opioid system, with consequent up-regulation of the immune system.\(^{140,141}\)

Some researchers believe that T-derived cytokines are the main mediators of the immunological effect of melatonin. Specific high affinity binding sites for [I-125] melatonin have been discovered on T-helper-type 2 lymphocytes in the bone marrow and in various lymphoid tissues.\(^{142,143}\)

**Antioxidant**

Free radicals, especially the hydroxyl radical, can be extremely damaging to macromolecules in cells. Estradiol is a powerful antioxidant—as effective as alpha-tocopherol in guarding against the peroxidation of cholesterol.\(^{144}\) In postmenopausal women, estradiol replacement has been shown to help keep LDL cholesterol in a reduced antioxidant state by preserving alpha-tocopherol and beta-carotene in LDL particles.\(^{146}\) This may partly explain its ability to reduce cardiovascular disease risk in women.

Dehydroepiandrosterone (DHEA) is also believed to be a powerful endogenous antioxidant and an important protectant against degenerative aging.\(^{146-148}\) The free radical fighting abilities of DHEA and estrogen may make them important in the prevention and treatment of neural damage in Alzheimer’s disease.\(^{146-148}\)

Melatonin has both water and fat soluble properties, making it one of the only known antioxidants in nature that can protect all parts of a cell. Since melatonin has the unique ability to navigate any body barrier with ease—including the blood-brain barrier and the placental barrier—\(^{150}\) it can protect virtually every cell in the body.

Recent evidence suggests that melatonin plays a critical role in free radical scavenging activity, preserving macromolecules such as DNA, proteins, and lipids from oxidative damage.\(^{151,152}\) In fact, melatonin has been proven more powerful than both glutathione and mannitol in neutralizing hydroxyl radicals and may protect cell membranes more effectively than Vitamin E.\(^{153,154}\) Remarkably, it is five hundred times more efficient at protecting cells from radiation than dimethyl sulfoxide (DMSO).\(^{155}\)

**Glucose and Insulin**

Estrogen deficiency after menopause has been associated with increased central obesity, poorer glycemic control, and reduced insulin sensitivity.\(^{156}\) Estrogen replacement has been shown to improve glycemic control and insulin response, independent of body weight, in postmenopausal women with type-2 diabetes.\(^{157-160}\) However, different doses, preparations, and routes of administration may affect insulin sensitivity differently.\(^{62}\)

Estrogen's ability to shift lipid deposition away from the central abdominal region, toward hip and thigh areas, may partly explain its potential benefit in glycemic regulation.\(^{161}\)

A hyperandrogenic profile in postmenopausal women is associated with central obesity and insulin resistance. Elevated levels of DHEA-S and free testosterone have been positively correlated with higher glucose and insulin levels, as well as type-2 diabetes, in postmenopausal women.\(^{162}\)

Cortisol counterregulates the effects of insulin, stimulating gluconeogenesis, reducing glucose utilization in tissues, triggering the release of fatty acids from adipose tissues, and decreasing protein synthesis.\(^{163,164}\) Elevated cortisol levels promote fat deposits in the central abdominal region, and thus, a higher waist-to-hip ratio.

**Sexual Function**

Sexual function is an important factor affecting the quality of life of postmenopausal women. Lower circulating levels of estrogen after menopause can cause the vaginal epithelium to dry out and atrophy, leading to discomfort, itching, and dyspareunia.\(^{165,166}\)

Inadequate estrogen for periurethral tissues may also promote pelvic laxity and
stress incontinence. Both estradiol and estriol replacement (tablets and suppositories) have been shown effective in reducing vaginal atrophy and discomfort in post-menopausal women.167

Positive psychologic and sensory response also plays an important role in sexual function. Recent evidence suggests that adequate levels of DHEA and testosterone are critical for ensuring healthy libido, sexual sensitivity, sexual response and sexual satisfaction in women after menopause.165,166,168

**Lifestyle Considerations**

**Diet**

There is strong evidence that the foods consumed by women have an effect on hormone levels. Investigation into dietary habits and, in particular, vegetarian diets has established that certain foods can modify gonadal estrogen metabolism.170

Some studies have reported an association between higher levels of dietary fat, particularly animal fats, and increased estrogen levels.171,172 Increased fiber intake, on the other, may lower estrogen levels, possibly by decreasing the time available for estrogen to be reabsorbed from the colon.173

Preliminary evidence also suggests that soy products, which contain phytoestrogens, may reduce circulating estrogen levels.174 Consumption of caffeine-containing beverages has been correlated with rises in SHBG that may diminish bioavailable steroid hormone levels.175,176

**Exercise**

Exercise for menopausal women is very important. Circulation and bone strength, along with the balance necessary to avoid unnecessary falls, are enhanced by regular exercise.177

Exercise may also improve mood and reduce vasomotor and other symptoms of menopause in middle-aged women.178 A rise in androgen and adrenal hormone levels (DHEA and cortisol) has been reported in postmenopausal women in response to exercise.179 Research also suggests that timed exercise can be very effective for re-establishing a healthy secretion pattern of melatonin.180-83

By assisting in long-term weight reduction, regular exercise has been shown to reduce both estrogen and insulin concentrations in obese postmenopausal women.184 In normal healthy postmenopausal women, exercise may increase bioavailable levels of estrogen, thereby helping to guard against deficiencies associated with cardiovascular disease and osteoporosis.185

**A Final Word**

When we realize how recently menopause was named (the mid-nineteenth century) and how negatively men and women viewed this phase of female development until somewhat recently, it is truly remarkable how supportive most of the medical community has become. Women themselves, once they have accepted the changes in their bodies, frequently describe this period of their lives as one of empowerment and self-fulfillment. Danish author Isak Dinesen, for example, assumed her pseudonym to signify her birth as an artist following her menopause: all of her acclaimed novels and stories were written after she had experienced her climacteric and ended an abusive marriage. Gail Sheehy speaks for many mature women in her 1992 study, The Silent Passage: Menopause, when she writes of the self-assurance many women develop at this time of change. Others have rejoiced in their new freedom from child-bearing, and a number have assumed greater control of their sexuality.

Clearly, it is the obligation of the caring healer to help women through this change and to inform them fully of their many therapeutic options. If there were ever a time when a physician should treat the “whole” person, menopause is clearly it. The changes are physical, mental, and spiritual. The metamorphosis can be frightening, but the potential for a long and healthy life beyond menopause is great. And the healer can help in many ways to usher in this “new age” for women, the second half of life between the climacteric and death, when women can become wiser and stronger.
Comprehensive Menopause Profile Application Guide

Suggested Reading for the Patient


How do I order this test?

For Comprehensive Menopause Profile kits or information, please call a GSDL Accounts Receivable representative at 888-201-8333 or use our secure web contact center at www.gsdl.com/billing.
References


References


For comprehensive menopause profile application guide.

363 Zillicoa Street
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