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REPORT

Hormone Testing for Optimal Health

By Penny Baron

Hormones are life-sustaining chemical messengers that regulate growth and development, sexual function, metabolism, and well-being. Blood levels of these crucial hormones diminish with age, contributing to age-related disease and decline.

Many conventional physicians dismiss the importance of restoring youthful hormone levels in their aging patients, accepting diminished hormone levels as an inevitable consequence of aging. However, research indicates that low hormone levels contribute to many conditions such as osteoporosis,¹⁻³ depression,⁴ diabetes,⁵ excess weight,⁶ and heart disease.^{7,8} Optimizing hormone levels can benefit these and other conditions, including migraine headaches⁹⁻¹¹ and menopausal symptoms.¹²

Fortunately, people interested in attaining optimal health and preventing the common diseases of aging have access to cutting-edge hormone-testing technology. For many years, the Life Extension Foundation has stressed the importance of bioidentical hormone restoration in promoting optimal health and longevity.

Among the most important hormones to monitor and balance are free testosterone, estradiol, and DHEA-S (dehydroepiandrosterone sulfate), as well as progesterone in women. These tests are included in Life Extension's popular Male and Female Panels. Additionally, testing should often include pregnenolone and thyroid stimulating hormone (TSH), as well as total estrogens in women and dihydrotestosterone (DHT) in men.

In this article, we will discuss hormone testing and why optimizing hormone levels is such a critical part of an integrative strategy for living a long and healthy life.

GENERAL SCREENING TESTS

DHEA-S

DHEA, a hormone produced by the adrenal glands, serves as a precursor to estrogen and testosterone. Serum levels of DHEA sulfate measure adrenal cortical function. Levels of DHEA-S peak in our twenties and then decline dramatically with age.

DHEA may support immune function, which diminishes with age and puts older adults at increased risk for infections such as pneumonia and influenza. A study published in the *Journal of Immunology*, using rats as test subjects, found that DHEA administration supported specific immune function known to be lacking in elderly people. These findings suggest that "age-related loss in immunological responses, linked to defective pathways of signal transduction, are partially under hormonal control and can be restored by appropriate replacement therapy."¹³

DHEA may also have mood-elevating effects. At the University of California at San Diego, scientists studied the relationship between hormone levels (of estradiol, testosterone, estrone, androstenedione, cortisol, DHEA, and DHEA-S) to depressed mood in 699 women between the ages of 50 and 90. Low levels of DHEA-S (but not of other hormones) were associated with depressed mood, independent of age, physical activity, and weight change. The researchers concluded, "These results add to the evidence that [DHEA-S] is a neuroactive steroid and point to the need for careful long-term clinical trials of DHEA therapy in older women with depressed mood."⁴

DHEA may help optimize bone mineral density. At the UCLA School of Medicine, researchers found that DHEA was positively associated with bone mineral density of the arm, spine, and hip in older women but not in men. Bioavailable estrogen was strongly associated with bone mineral density in both men and women. The study enrolled 457 women and 534 men, aged 50-



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89, who were not taking corticosteroids or hormones. Investigators noted that “individual variation in age-related bone loss may be partially accounted for by alterations in sex steroid levels with aging.”¹⁴

DHEA-S may also influence libido levels in women. An Australian study identified DHEA-S as a marker of low libido in women under the age of 45. Investigators found that a significant proportion of participants reported little or no sexual desire or arousal, and that “low [DHEA-S] makes an independent contribution to low levels of sexual interest, but not of sexual behavior, in young women.” According to the authors, “[DHEA-S] is the most abundant sex steroid and is an important precursor for intracellular androgen production. We propose that [DHEA-S] is a useful marker of low androgen status.”¹⁵

A recent study published in the *Journal of the American Medical Association* found that DHEA supplementation may help reduce abdominal fat, which is associated with insulin resistance. Twenty-eight men and 28 women, aged 65-78, supplemented with 50 mg per day of DHEA or placebo for six months. Compared to placebo, DHEA therapy induced significant decreases in visceral and subcutaneous fat. Insulin action was also improved. The authors concluded, “DHEA replacement could play a role in prevention and treatment of the metabolic syndrome associated with abdominal obesity.”⁶

Finally, recent animal studies suggest that DHEA has neuroprotective properties. At the University of California at San Diego, investigators found that DHEA treatment in mice significantly enhanced their recovery of coordination and fine motor control following spinal cord injury. The authors suggested that DHEA helps promote functional recovery following nerve injury.¹⁶



Photomicrograph of human testosterone hormone, magnified 130 times.

Free and Total Testosterone

Testosterone is produced in the testes in men, in the ovaries in women, and in the adrenal glands of both men and women. Testosterone promotes the building of tissue and is considered an anabolic steroid hormone. Approximately 50% of testosterone is bound to sex hormone binding globulin (SHBG) and the remainder to albumin. Less than 2% of testosterone is typically found in the “free” (uncomplexed) state in the serum of both men and women.

In men, total testosterone (complexed and uncomplexed) is useful for assessing gonadal, adrenal, and pituitary function. In women, total testosterone can help in the evaluation of polycystic ovarian syndrome, testosterone-producing tumors of the ovary, tumors of the adrenal cortices, and congenital adrenal hyperplasia.

In men, free testosterone levels may be used to evaluate whether sufficient bioactive testosterone is available to protect against abdominal obesity, mental depression, osteoporosis, and heart disease. In women, high levels of free testosterone may indicate hirsutism, which causes excessive growth

of hair on the face and chest, and is often indicative of polycystic ovaries. Increased testosterone in women also may indicate low estrogen levels.

Importance of testosterone in men

Testosterone levels normally decline with age, contributing to the physiological changes seen in aging men. Low testosterone is associated with many adverse health conditions, including diminished libido, erectile dysfunction, loss of muscle tone, increased abdominal fat, low bone density, depression, Alzheimer’s disease, and heart disease.

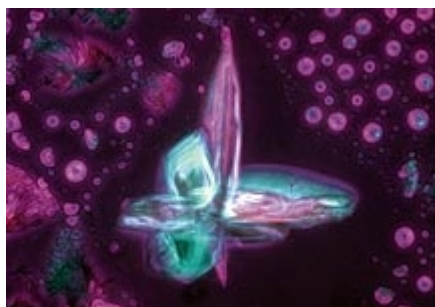
Researchers in Finland linked low testosterone levels to the development of metabolic syndrome. They measured testosterone levels in men who did not have metabolic syndrome or diabetes and followed the subjects for 11 years. Men with lower levels of total testosterone more than doubled their risk of developing metabolic syndrome. The researchers noted, “hypoandrogenism is an early marker for disturbances in insulin and glucose metabolism that may progress to metabolic syndrome.”¹⁷ Another investigation by the same research group found that in obese men with metabolic syndrome, weight loss increases total and free testosterone levels.¹⁸

Diminished testosterone levels may also be implicated in the development of diabetes. In a Japanese-American male cohort, lower baseline total testosterone levels independently predicted an increase in intra-abdominal (belly) fat. Investigators suggested that by “predisposing to an increase in visceral adiposity, low levels of testosterone may increase the risk of [type II] diabetes mellitus.”⁵ In addition to increasing diabetes risk, greater visceral adiposity increases the risk for hypertension, a risk factor for heart disease and stroke.¹⁹



Testosterone may protect cardiovascular health through anti-inflammatory and lipid-lowering effects. British investigators found that testosterone replacement therapy in men with symptomatic androgen insufficiency decreased levels of the proinflammatory cytokines tumor necrosis factor-alpha (TNF- α) and interleukin-1 beta (IL-1 β), and increased expression of the anti-inflammatory cytokine interleukin-10 (IL-10). Proinflammatory cytokines mediate the onset of atherosclerosis. Moreover, the researchers found

a significant reduction in total cholesterol in the testosterone-supplemented patients.⁷ In a recently published study, researchers found that testosterone replacement therapy in hypogonadal men improves mood and is associated with potentially beneficial reductions of total cholesterol and serum TNF- α .⁸



Photomicrograph of estrogen (female hormone) crystals, magnified 50 times.

A recent report in the journal *Neurology* found that older men with lower levels of free (unbound) testosterone may be at increased risk of developing Alzheimer's disease. For each 50% increase in the free testosterone index, the risk of developing Alzheimer's decreased by approximately 26%. The study, which began following subjects in 1958, showed that men diagnosed with Alzheimer's disease had approximately half the levels of free testosterone as men who did not develop disease. According to the investigators, "Our finding that low free testosterone might be associated with an increased risk of developing Alzheimer's disease is a step forward in helping to understand the possible effects of sex hormones on the aging brain and other parts of the body." The authors also indicated that future research "may determine whether higher endogenous free testosterone levels offer protection against a diagnosis of Alzheimer's disease in older men."²⁰

Importance of testosterone in women

Although women produce only small quantities of testosterone, mounting evidence indicates that this important hormone helps women maintain muscle strength, bone mass, and sexual function. Testosterone levels decrease following menopause, and restoring testosterone levels may help improve well-being and libido.

A study published in the *New England Journal of Medicine* examined the effects of transdermal testosterone patches on 75 women, aged 31-56, with diminished testosterone levels due to hysterectomy and removal of both ovaries. Investigators found a significant improvement in sexual function, mood, and general well-being in the women who received the 300-mcg patch compared to those using the 150-mcg patch or placebo.²¹

Estradiol

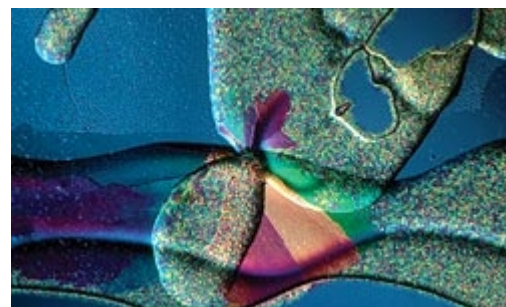
Estradiol is the primary circulating form of estrogen in men and women, and is an indicator of hypothalamic and pituitary function. Men produce lesser amounts of estradiol than do women, with a fraction of estradiol produced directly by the testes and most from testosterone and adrenal steroid hormones. In women, estradiol is produced in the ovaries, adrenal glands, and peripheral tissues.

In men, estradiol levels help in assessing gynecomastia and feminization syndromes. In women, estradiol helps in evaluating menopausal status and sexual maturity. Estradiol levels play a role in healthy bone density in both men and women.

Importance of estradiol in men

At the University of California at San Diego, researchers showed that low levels of estradiol, but not of other hormones, increased the risk of vertebral fractures in older men. Among 352 men with a median age of 66, "age-adjusted hormone levels differed by fracture status only for total and bioavailable estradiol." The researchers concluded, "estrogen plays a critical role in the skeletal health of older men."¹

Other scientists also found an association between suboptimal estradiol levels in men and osteoporosis risk. Researchers measured total testosterone, total estradiol, and luteinizing hormone in 405 men aged 68-96. The study results linked decreases in bone mineral density with declining levels of estradiol. The researchers noted, "The difference in mean mineral bone density between men in the lowest and highest estradiol quartile levels was similar to the effects of 10 years of aging on bone mineral density." The authors concluded that in elderly men, low testosterone related to aging "has little influence on bone mineral density, but serum estradiol levels have a strong and positive association with bone mineral density."²



Photomicrograph of estradiol crystals. Estradiol, the most potent of the natural estrogens, is used in its natural or semisynthetic form to treat menopausal symptoms.

Importance of estradiol in women

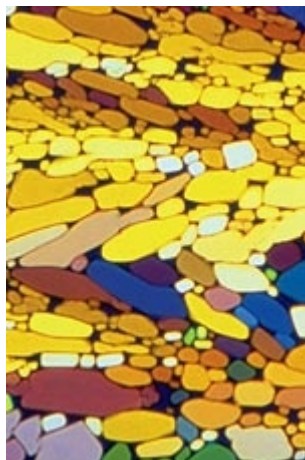
At the Creighton University School of Medicine in Omaha, NE, researchers observed that in women aged 65-75, low levels of serum total and bioavailable estradiol correlate with low levels of bone mineral density in the femur, spine, and total body. Women with low levels of bioavailable estradiol also experienced an increased rate of bone loss in the spine and throughout the body. The researchers found that "small variations in endogenous serum estradiol . . . determine differences in bone mineral density and rate of bone loss in elderly women," and suggested that women with low serum estradiol levels are optimal candidates for estrogen therapy to help prevent osteoporosis.³

Estradiol may improve quality of life in menopausal women. Italian scientists tested the effects of six months of transdermal estradiol therapy in women who were experiencing uncomfortable symptoms of early menopause. Eighty percent of the treated women reported improvement of hot flashes, insomnia, and irritability, and 61% reported an improved sense of well-being.¹²

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Photomicrograph of progesterone hormone crystals, magnified 40 times.

Progesterone (women)

Progesterone, a hormone that is synthesized in a biochemical pathway from cholesterol, is a precursor to other hormones, including cortisol, estrogen, and testosterone. In women, progesterone is produced in the corpus luteum of the ovary, in smaller amounts by the adrenal glands, and in copious amounts by the placenta during pregnancy.

Progesterone levels, which decline with increasing age, may be used to track cycles of ovulation and menstruation, evaluate corpus luteum function in infertility patients, and assess placental function during pregnancy. In women, progesterone is responsible for maintaining a normal pregnancy.

According to a recent study, a single serum progesterone measurement may be a useful indicator of pregnancy outcome in women undergoing in-vitro fertilization or intracytoplasmic sperm injection. Investigators measured serum progesterone levels 14 days after egg retrieval and performed ultrasound at eight weeks of gestation. In women with normally progressing pregnancies, progesterone levels remained high. Women with abnormal pregnancies or who could not conceive had significantly lower progesterone levels, despite progesterone supplementation.²²

At the University of Adelaide Exercise Physiology Laboratory in Australia, researchers reported that progesterone may boost fat metabolism in women. Women who exercised during times of peak (mid-month) progesterone and estrogen levels had increased rates of fat metabolism as well as lower perceived exertion levels. These findings suggest that progesterone and estrogen improve exercise performance, possibly by promoting the use of fats as energy sources to support physical activity.²³

All of the blood hormone tests discussed so far are included in the popular Male and Female Panels. The only exception is progesterone, which is included only in the Female Panel.

SPECIALIZED TESTS

Pregnenolone

Pregnenolone functions mainly as a hormone intermediate in the body. Made directly from cholesterol, pregnenolone is the precursor for DHEA and other hormones, including testosterone, estrogen, cortisol, and aldosterone. The body produces pregnenolone primarily in the adrenal glands, liver, testes (in men), and ovaries (in women), as well as in the brain. Pregnenolone levels tend to diminish with age, leading to a decline in the “downstream” hormones for which it acts as a precursor. Pregnenolone levels tend to be elevated in congenital adrenal hyperplasia and idiopathic hirsutism (increased hair growth in women).

Investigators have shown that pregnenolone may help reduce fatigue while enhancing endurance.²⁴ In an experimental model, pregnenolone promoted the growth of brain cells.²⁵

In an animal study, pregnenolone administration helped to enhance memory. While DHEA and testosterone yielded similar effects, the hormones estradiol, estrone, and progesterone did not benefit memory. The investigators suggested that pregnenolone may exert its effects by acting as a precursor for numerous neurosteroid hormones. They concluded, “low serum levels of pregnenolone in aging and the increases of cancer and behavioral disorders in individuals receiving drugs that block synthesis of cholesterol, the immediate precursor of pregnenolone, suggest possible clinical utility for pregnenolone.”²⁶ Testing one’s blood to measure pregnenolone levels is becoming very popular, as low pregnenolone can cause a wide range of hormone imbalances.





Total Estrogens (women)

The total estrogens test measures the sum of three estrogens: estradiol, estriol, and estrone. Women produce estrogens mainly in the ovaries (and in the placenta during pregnancy). The adrenal glands also produce small amounts. These hormones shift over the course of a woman's life, strongly influencing her health and well-being.

Estradiol is the most commonly measured type of estrogen. Its level varies throughout the menstrual cycle and falls to a low but constant level after menopause. Increased levels of estradiol in woman suggest an increased risk of breast or endometrial cancer. Low levels may

increase risk for bone fractures.

Estriol is considered the "weakest" of the three primary estrogens, yet women with higher levels of estriol may have far lower risks of breast cancer.²⁷ European doctors routinely prescribe estriol to menopausal and postmenopausal women in place of more potent estrone and estradiol drugs. If a blood test reveals low estriol levels, then a woman may ask her doctor for a prescription estriol drug (2-8 mg/day). Estriol drugs are available through compounding pharmacies.

Estrone, the major source of estrogen in postmenopausal women, may help assess adrenal or ovarian conditions. The body manufactures small amounts of estrone in most tissues, especially in fat and muscle.

Doctors use the total estrogen laboratory assessment to evaluate fertility problems, menstrual disorders, menopausal status, and sexual maturity in women. It is also used to help detect fetal birth defects during pregnancy and fetal distress in high-risk pregnancies. Occasionally, doctors use the test in men to assess abnormal sexual characteristics such as enlarged breasts (gynecomastia).

Hormone imbalance may be a cause of migraine headaches in women. Declining estrogen levels during menstruation and menopause may trigger migraine headaches. By contrast, sustained high levels of estrogen, as occur during pregnancy, frequently provide relief from headaches. Estrogen produces changes in body levels of prostaglandins and opioids, which may account for its effects in relieving headaches.^{9,10}

Researchers at the North Central Mississippi Regional Cancer Center in Greenwood, MS, and later at the Life Extension Foundation, used an innovative treatment to correct hormone imbalances associated with migraine headaches. They administered hormone restorative therapy to 23 women suffering from migraine. In 100% of cases, hormone restoration resolved headaches, and the headaches did not recur. Additionally, symptoms associated with migraine, such as body pains, insomnia, depression, and fatigue, also resolved entirely. (See "An Innovative New Treatment for Migraine," *Life Extension*, September 2004.)¹¹

Thyroid Stimulating Hormone (TSH)

The thyroid stimulating hormone (TSH) test assesses thyroid gland status. Thyroid hormones play a crucial role in regulating growth, development, and metabolism. Thyroid hormones increase oxygen consumption and heat production, which are measured as resting metabolic rate. Elevated TSH is associated with hypothyroidism, a condition marked by lethargy, weakness, slow speech, constipation, dry skin, and weight gain. Low TSH suggests hyperthyroidism, a condition characterized by increased heart rate, hyperactivity, nervousness, palpitations, and heat intolerance.

While overt hypothyroidism can increase cardiovascular disease risk, a possible risk from subclinical hypothyroidism is controversial. Scientists investigated the relationship of thyroid status and cardiovascular health in women participating in the Rotterdam Study. Women with subclinical hypothyroidism, as determined by a high-normal TSH level and normal serum free thyroxine level, had a greater prevalence of aortic atherosclerosis and myocardial infarction. Adjustment for body mass index, total cholesterol, HDL (high-density lipoprotein), and blood pressure did not affect these results. The study authors concluded, "subclinical hypothyroidism is a strong indicator of risk for atherosclerosis and myocardial infarction in elderly women."²⁸

Dihydrotestosterone (DHT)

DHT is an activated form of testosterone generated by the enzyme 5-alpha reductase. Scientists estimate that DHT is 2-10 times more potent than testosterone.²⁹⁻³¹ DHT is responsible for the development and maintenance of the male external genitalia and the prostate gland. Elevated DHT levels may indicate hypergonadism or hirsutism. Additionally, elevated DHT may increase the risk of prostate enlargement or cancer.

Agents that block the conversion of testosterone to dihydrotestosterone by inhibiting the 5-alpha reductase enzyme are being studied as therapeutics for managing benign prostatic enlargement. Such agents improve urinary flow and reduce the risk of acute urinary retention or the necessity for surgical management of an enlarged prostate.³² In addition, researchers are studying 5-alpha reductase inhibitors for their potential role in reducing prostate cancer risk.³³



CONCLUSION

Men and women no longer need suffer the effects of diminished hormone levels and the accompanying onset of degenerative decline and disease. Blood testing is a powerful tool for assessing hormone status and implementing appropriate therapeutics. By restoring optimal hormone levels, you can reduce your risk for many of the most common diseases of aging, including life-threatening conditions such as osteoporosis, Alzheimer's disease, heart disease, and depression.

View information on obtaining blood tests

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