

Hormonal Health The Uphill Battle of Modern Day Women

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Modern women face a lot of pressures that women decades ago never had to face. Dealing with working full time, job stress, carting the kids or grandkids off to various soccer games and other extracurricular activities leaves women in modern society feeling a lot of stress. The hectic lifestyle of today's woman, who is often sleep-deprived and stressed, is affecting hormone levels and impacting female health to an extent unheard of 100 years ago. Even oral contraceptives, another factor to which modern women are exposed, have been found to reduce levels of hormones such as DHEA, pregnenolone and estrogen,¹ further altering the female hormone balance.

Balanced levels of hormones play an important role in women's health. This article will review the ways in which stress, sleep loss and other lifestyle factors affect women's hormonal health and natural strategies to create optimal hormonal health.

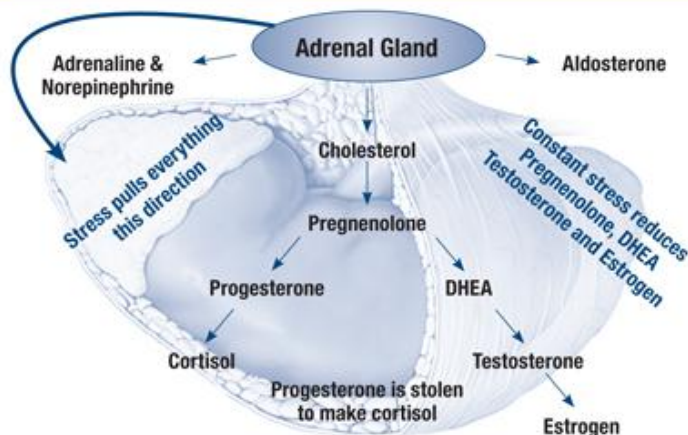
There are four hormones I will discuss in this article in regards to women's health: pregnenolone, progesterone, DHEA and melatonin.

Pregnenolone

Pregnenolone is the precursor (building-block) for all other steroid hormones. It is converted directly into DHEA and/or progesterone. DHEA converts to testosterone and estrogens; progesterone converts, cortisol and aldosterone.

Pregnenolone supports cognitive health and produces feelings of calm.² It's known to modulate at least two key nerve receptor systems in the brain: NMDA receptors and GABA receptors. NMDA receptors, which weaken with age, are involved in learning, memory and alertness.³ Pregnenolone enhances NMDA receptor function.³ GABA receptors promote relaxation, mental slowing, sedation and sleep. Pregnenolone inhibits GABA receptors. Thus, too little NMDA activity combined with excessive GABA activity could promote mental sluggishness and poor mood and affect. Since pregnenolone raises NMDA activity and lowers excessive GABA activity, pregnenolone seems to be a natural mood balancer.

The Pregnenolone/Cortisol Steal



The Pregnenolone Steal

In the body, cholesterol is converted into pregnenolone, which is then processed by one of two pathways. It can be converted into progesterone or DHEA. Progesterone is then converted into cortisol or aldosterone while DHEA is converted into the sex hormones such as testosterone, estradiol or estrogen breakdown products of estrone, estriol or testosterone. When an individual undergoes continual stress, the body will prefer the pathway where cholesterol is converted to pregnenolone then to

progesterone and cortisol. This process is known as either pregnenolone or cortisol steal. So the body de-emphasizes the DHEA-producing pathway and therefore doesn't make sex hormones. The results of this phenomenon can include effects on the normal menstrual cycle, libido, occasional fatigue and imbalanced mood.

Progesterone

Progesterone is made in the ovaries of menstruating women. It is produced by the corpus luteum at the time of ovulation (20-25 mg/day), and by the placenta during pregnancy (up to 300-400 mg/day). Progesterone is a precursor to most steroid hormones and performs different functions including supporting bone, breast and endometrial health and helping to burn fat for energy.⁴⁻⁸

According to progesterone researcher Dr. John Lee, many women suffer from a syndrome known as Estrogen Dominance, where estrogen is not balanced sufficiently by progesterone. When natural progesterone is present in normal levels, it supports balanced blood pressure, normal blood clotting mechanisms, healthy levels of body fat, thyroid, breast, liver, endometrial and gallbladder health.⁹

Estrogen dominance can occur at the age of menopause or significantly earlier in life during pre-menopause. During menopause, progesterone production virtually ceases, plummeting to approximately 1 percent of its premenopausal level. At the same time the production of estrogen only falls to about 50 percent of its premenopausal level.¹⁰ This dramatically alters the estrogen: progesterone ratio, and the estrogen becomes increasingly toxic to the body without progesterone to stop it. As a result, there is an effect on breast, uterine, ovarian, cervical and bone health.⁹ Estrogen dominance can contribute to low energy, mood imbalances, water retention, weight gain, low sex drive, irritability, occasional headaches, slow metabolism and cravings for sweets.⁹

DHEA

DHEA (dehydroepiandrosterone) is the most abundant steroid hormone in the body. DHEA reaches its highest levels in the blood at age 20-24, and drops progressively with age thereafter. This decline is so significant (the level of DHEA in 70-year-olds is only about 20 percent that of young adults) that it has been referred to as the "DHEA Deficiency Syndrome—A new term for old age."¹¹⁻¹²

DHEA supplementation has been shown to enhance lower extremity strength and function in older women also involved in a gentle exercise program of chair aerobics or yoga.¹³ Healthy levels of DHEA have also been found to be related to cardiovascular health,¹⁴ breast health,¹⁵ and cognitive function.¹⁶

Melatonin

The hormone melatonin, as discussed below, is important in the production of progesterone and helps promote restorative sleep.

Hormones and Anxiousness

Women today are facing an unprecedented amount of stress. It becomes a vicious circle with stress depleting levels of hormones that are known to increase feelings of relaxation, making women

even more stressed. Hormones such as pregnenolone and DHEA have been shown to help increase levels of calmness, when these hormones are insufficient. In an animal study, mice were exposed to footshocks and were then given DHEA-sulfate and pregnenolone-sulfate. The two hormones dose dependently attenuated the conditioned fear stress response the animals had felt prior to being given the hormones.¹⁷

In another animal study, mice were exposed to a mirrored chamber, a situation the animals find stressful. Pregnenolone-sulfate significantly reduced the latency to enter the chamber, and increased both number of entries and total time spent in the chamber in a dose-dependent manner. Progesterone also produced a clear dose-dependent relaxation effect in the mirrored chamber.¹⁸

Cognitive Health

Progesterone, pregnenolone and DHEA are produced in the nervous system, and are therefore referred to by scientists as neurosteroids.¹⁹⁻²⁰ As such, they play a role in cognitive health. Neurons and glia in the central nervous system express the necessary enzymes for the synthesis of neurosteroids.

Synthesis of brain neurosteroids declines with age, during stressful conditions (including with mood imbalances and nervous tension), and in inflammatory and neurological concerns. Reports in the medical literature have linked the decrease of brain neurosteroids to suboptimal neuronal functioning. DHEA, pregnenolone and progesterone have been found to affect neuronal survival, neurite outgrowth and neurogenesis. Scientists have therefore studied the effects of these hormones on age-related brain health.¹⁹

RESTorative Sleep

Due to hectic schedules, sleep has become something that modern women consider optional. However, restorative sleep is essential for good health, both physical and mental, and also for quality of life, performance and productivity. Although sleep challenges increase with age in both sexes, women are more susceptible to sleep issues at all ages. The decrease in both estrogen and progesterone that occurs during menopause has been shown to reduce sleep quality, but concerns about sleep quality often occur before menopause in midlife. Weight changes at midlife may also affect sleep quality.²¹

Melatonin, a hormone secreted from the pineal gland during sleep and sufficient darkness, plays a key role in progesterone production. As an antioxidant, melatonin protects luteinized granulosa cells from reactive oxygen species (ROS), enhancing progesterone production in the follicle during ovulation. Melatonin concentrations in follicular fluid positively correspond with progesterone concentrations and are negatively correlated with the concentration of an oxidative stress marker known as 8-hydroxy-2'-deoxyguanosine (8-OHdG).

Researchers studied 25 women who had low serum progesterone concentrations (less than 10 ng/mL) during the mid-luteal phase. The researchers divided the women into two groups. In one group, 14 women received melatonin (3 mg/day at 22:00 hr) throughout the luteal phase and in the other group 11 women who were not given melatonin served as controls. Melatonin treatment enhanced serum progesterone concentrations to greater than 10 ng/mL during the mid-luteal phase in nine of 14 women. In contrast, only two of 11 women showed normal serum progesterone levels in the control group.²²

The study authors wrote, “In conclusion, melatonin protects granulosa cells undergoing luteinization from ROS [reactive oxygen species] in the follicle and contributes to luteinization for progesterone production during ovulation.”

The fact that melatonin enhances progesterone production is important in that progesterone is known to improve the quality of sleep. Neuroactive progesterone metabolites possess sedative-like effects. In one randomized, double-blind, placebo-controlled study, researchers investigated the effects of three weeks of progesterone administration on sleep in 8 healthy postmenopausal women (48 to 74 years old). The women had no sleep complaints and weren't on hormone replacement therapy. During the last two nights of the study, researchers measured sleep using a polygraph, and blood samples were obtained at 15-minute intervals for the 24 hours including the last night of the sleep study. The blood sampling served to disrupt sleep.

During the first night (no blood sampling), sleep was similar in both groups. In the subjects given the placebo, the blood sampling procedure was associated with suboptimal sleep. In the subjects given progesterone, however, sleep quality was restored. In the subjects taking progesterone, mean duration of wake after sleep onset was 53 percent lower, slow-wave sleep duration almost 50 percent higher, and total slow-wave activity (reflecting duration and intensity of deep sleep) almost 45 percent higher under progesterone than under placebo. Furthermore, in the subjects on progesterone, nocturnal growth hormone secretion was increased, and evening and nocturnal thyroid stimulating hormone (TSH) levels were decreased under progesterone.²³

The researchers concluded that progesterone acts as a “physiologic” regulator of sleep. They suggested that progesterone might be used in aging to support more solid, high-quality, restorative sleep.

Hormonal Balancing

For any woman undergoing today's stressful, high-paced lifestyle, balancing hormones can lead to enhanced energy and optimal health. It's important to first “test not guess” by using a Comprehensive Hormone Panel to determine levels of hormones prior to supplementation with progesterone, pregnenolone and DHEA. In my patients, I will then determine proper supplementation levels based on the results of the test and then re-test after supplementation has been in effect for several months in order to determine if balanced levels have been restored. In women who want to support sleep quality, melatonin also can be added to the regimen. When looking to optimize hormone levels into the normal healthy range, keeping one's personal healthcare provider as part of the discussion is important, as he or she best knows your specific health and health considerations.

Conclusion

The lifestyle of today's modern woman is throwing off hormonal balance, which is affecting energy levels, mood, stress levels and sleep. For optimal health, it's important to determine hormonal levels and begin a supplement regimen based on the needs established in the test. Once this is done, excellent results can be achieved.

References:

1. Rapkin AJ, Morgan M, Sogliano C, Biggio G, Concas A. Decreased neuroactive steroids induced by combined oral contraceptive pills are not associated with mood changes. *Fertil Steril.* 2006 May;85(5):1371-8.
2. Reddy DS. Neurosteroids: endogenous role in the human brain and therapeutic potentials. *Prog Brain Res.* 2010;186:113-37.

3. Wu FS, Gibbs TT, Farb DH. Pregnenolone sulfate: a positive allosteric modulator at the N-methyl-D-aspartate receptor. *Mol Pharmacol.* 1991 Sep;40(3):333-6.
4. Goodman L & Gilman A. *The Pharmacological Basis of Therapeutics.* Toronto, McMillan, 8th edition, 1990, chapter 58.
5. Thomas J & Gillham B. *Wills Biochemistry Basis of Medicine.* Oxford, Butterworth-Heinemann Ltd. 1989.
6. Ellison PT, et al. The ecological context of human ovarian function. *Human Reproduction.* 1993;8:2248-58.
7. Elks ML. Peripheral effects of steroid hormones, implications for patient management. *JAMWA.* 1993;48(2):41-6, 50.
8. Tietz N, ed. *Textbook of Clinical Chemistry,* Philadelphia, W.B. Sanders Co., 1986, 1085-1171.
9. Lee JR. *What Your Doctor May Not Tell You About Menopause.* Warner Books, May, 1996.
10. Lee JR. *What Your Doctor May Not Tell You About Menopause.* Warner Books, May 1996.
11. Heaney JL, Phillips AC, Carroll D. Ageing, physical function, and the diurnal rhythms of cortisol and dehydroepiandrosterone. *Psychoneuroendocrinology.* 2011 Jul 28. Published Online Ahead of Print.
12. Hinson JP, Raven PW. DHEA deficiency syndrome: A new term for old age? *J Endocrinol.* 1999;163:1-5.
13. Kenny AM, Boxer RS, Kleppinger A, Brindisi J, Feinn R, Burleson JA. Dehydroepiandrosterone combined with exercise improves muscle strength and physical function in frail older women. *J Am Geriatr Soc.* 2010 Sep;58(9):1707-14.
14. Jansson JH, Nilsson TK, Johnson O. Von Willebrand factor, tissue plasminogen activator and dehydroepiandrosterone sulphate predict cardiovascular death in a 10-year follow-up of survivors of acute myocardial infarction. *Heart.* 1998;80:334-337.
15. Schwartz AG. Inhibition of spontaneous breast cancer formation in female mice by long term treatment with dehydroepiandrosterone. *Cancer Res.* 1979;39:1129-1132.
16. Merrill CR, Harrington MG, Sunderland T. Reduced plasma dehydroepiandrosterone concentrations in HIV infection and Alzheimer's disease, in: *The Biologic Role of Dehydroepiandrosterone (DHEA),* by Regelson, W., Kalimi, M., and Loria, R. (eds.), Walter de Gruyter, Inc., Hawthorne, NY, 1990.
17. Noda Y, Kamei H, Kamei Y, Nagai T, Nishida M, Nabeshima T. Neurosteroids ameliorate conditioned fear stress: an association with sigma receptors. *Neuropsychopharmacology.* 2000 Sep;23(3):276-84.
18. Reddy DS, Kulkarni SK. Differential anxiolytic effects of neurosteroids in the mirrored chamber behavior test in mice. *Brain Res.* 1997 Mar 28;752(1-2):61-71.
19. Charalampopoulos I, Remboutsika E, Margioris AN, Gravanis A. Neurosteroids as modulators of neurogenesis and neuronal survival. *Trends Endocrinol Metab.* 2008 Oct;19(8):300-7.
20. Torres JM, Ortega E. DHEA, PREG and their sulphate derivatives on plasma and brain after CRH and ACTH administration. *Neurochem Res.* 2003 Aug;28(8):1187-91.
21. Polo-Kantola P. Sleep problems in midlife and beyond. *Maturitas.* 2011 Mar;68(3):224-32.
22. Taketani T, Tamura H, Takasaki A, Lee L, Kizuka F, Tamura I, Taniguchi K, Maekawa R, Asada H, Shimamura K, Reiter RJ, Sugino N. Protective role of melatonin in progesterone production by human luteal cells. *J Pineal Res.* 2011 Mar 22. Published online ahead of print.
23. Caufriez A, Leproult R, L'Hermite-Balériaux M, Kerkhofs M, Copinschi G. Progesterone prevents sleep disturbances and modulates GH, TSH, and melatonin secretion in postmenopausal women. *J Clin Endocrinol Metab.* 2011 Apr;96(4):E614-23.