

MALE HORMONE PROFILES

Why Profiles?

When patients have hormone-related symptoms, it is usually not a clear-cut case of one hormone level being abnormal, or even one hormone system. In fact, because of the role that hormones play as chemical messengers to wake up the genome in specific target tissues throughout the body, it makes sense that all hormone systems work in concert with each other to maintain a state of balance. This could be likened to the instruments in an orchestra playing together in harmony; when one instrument is off key or playing too loudly or softly (analogous to too much or too little hormone), the overall harmony is affected. In a similar manner, the adrenal, thyroid, and sex hormones work in harmony, and when one or more of the hormones in any one system become unbalanced, this affects the harmony or balance of the whole system. Symptoms common to hormonal imbalances in the endocrine systems are seen as the body struggles to maintain balance, but does not succeed. Without an overall picture of which hormone systems are affected, it is often difficult to know the best clinical course of action for correcting the imbalance.

Hormone “Profiles” at ZRT are multiple hormone tests bundled into one convenient kit. Priced lower than the sum of the individual tests, these provide a more economical method to assess a patient’s overall hormonal status, giving a better picture of the hormone imbalances that are causing symptoms. Instead of treating a secondary hormonal imbalance caused by an abnormality in only one of the hormonal systems (e.g., low libido caused by low testosterone), you can address the underlying issues that lie at the root of the problem, and therefore, better guide your patients towards overall wellness.

The Problem – Andropause and Low Testosterone

As men age, their levels of testosterone begin to decline, usually beginning around the mid-40s. This heralds what is commonly known as andropause, the male counterpart to menopause. While this is a natural part of aging, the decline in testosterone production by the testes can be more precipitous in some men than others. Excessive weight gain, stress, lack of exercise, and many medications further contribute to a man’s ability to manufacture testosterone, resulting in even lower testosterone levels and leading to symptoms of andropause. These symptoms may include low libido, irritability, depression, loss of muscle mass and strength, weight gain, metabolic syndrome, erectile dysfunction, sleep disturbances, osteoporosis, and adverse changes in the blood lipid profile. Symptoms of androgen deficiency and low testosterone levels are used to establish a diagnosis of hypogonadism. This low testosterone condition was found to increase significantly with age in the Massachusetts Male Aging Study¹. In the Hypogonadism in Males (HIM) study, hypogonadism was diagnosed in 38.7% of men over 45 years old who presented to primary care offices².

However, while this is certainly an option, the solution to the problem may not be a simple case of restoring testosterone levels. For example, some practitioners find that testosterone therapy may be of little benefit unless problems affecting cortisol production are addressed first. The body’s response to stress is mediated by increased cortisol production, and this prepares the body for “fight or flight” by shutting down other processes, including testosterone production. Correcting disorders such as adrenal fatigue or chronic stress may therefore lead to improved testosterone levels and resolve symptoms, without requiring testosterone therapy. Increasing cortisol levels, along with several other endocrine changes, have been reported in men³, highlighting the need to obtain a complete hormone profile before initiating any hormone replacement.

Saliva and Dried Blood Spot Testing.

Minimally-invasive home test kit.

Testosterone therapy is also not recommended for patients with signs of benign prostatic hypertrophy (BPH) or prostate cancer. While it is now known that testosterone itself does not cause either of these, it is thought to have the potential to exacerbate the problem when already present. This may in fact be a result of local aromatase production in prostate tumors, which increases local conversion of testosterone to estradiol, which in turn stimulates tumor growth⁴. Research now indicates a complex relationship between estrogens and androgens in the etiology of prostate cancer⁵, while serum levels of individual endogenous sex hormones have been found to be unrelated to prostate cancer risk⁶. Studies show that estrogens play both adverse and beneficial roles mediated by different types of estrogen receptor⁷. Testosterone's effects on the prostate are mediated by its more active metabolite, dihydrotestosterone (DHT), produced by the action of 5-alpha reductase type II (5-alpha reductase type I is the predominant form in the skin, and is responsible for the local action of DHT on hair follicles leading to the development of male pattern baldness). Prostate growth can be controlled by 5-alpha reductase inhibitors, and these may also have a role in prostate cancer prevention and treatment⁸.

The Hormones Tested in our Male Profiles and Why

Estradiol is tested because too much of it, relative to testosterone levels, suppresses testosterone receptors in target tissues and eventually leads to feminizing effects in men, such as breast enlargement. In healthy young men, testosterone is at its highest level and estradiol is very low. However, as men age, this shifts to a higher estradiol/testosterone ratio. Even if testosterone levels are normal, symptoms can indicate a functional testosterone deficiency because of the effects of higher than normal estradiol levels.

There are several mechanisms by which relative levels of estradiol and testosterone can change. Weight gain, whether or not this results from low testosterone, results in increased production of aromatase in fat

cells, which converts testosterone to estradiol. Rising estradiol levels also cause the liver to produce more SHBG, which has a greater affinity for testosterone than estradiol. This acts to suppress further the amount of circulating free testosterone. Estradiol also decreases luteinizing hormone (LH) production by negative feedback on the pituitary gland, which in turn acts to decrease testicular testosterone production. High estradiol levels can be controlled by weight reduction to decrease the amount of aromatase-producing adipose tissue. There are nutritional and pharmaceutical approaches to aromatase inhibition.

Progesterone is present in men but at a much lower level than found in premenopausal women. Some men supplement with topical progesterone to help with sleep, to support adrenal cortisol production (progesterone is a cortisol precursor), and to counterbalance the effects of estrogens on the prostate. It has also been used as a mild antiandrogen in patients with BPH and to reduce male pattern baldness, because of its competition with testosterone and DHT for androgen receptors. Salivary progesterone levels can, therefore, be useful to monitor supplementation.

Testosterone is the primary indicator of male hypogonadism and andropause. Many things can contribute to low testosterone levels, including high cortisol levels and high estrogen levels, as described above. Testosterone production in the testes is controlled by the hypothalamic-pituitary-testicular axis, and so dysfunctions of the hypothalamus or pituitary can affect levels, as well as the negative feedback effect of estradiol on LH levels to suppress testosterone production.

SHBG binds and transports both testosterone and estrogens in the bloodstream, and it therefore regulates the relative amounts of free and bound hormone and consequently their bioavailability to target tissues. SHBG is a protein produced by the liver in response to exposure to any type of estrogen. Testosterone binds about three times more tightly to SHBG than does estradiol, so this increase in SHBG as a result of estrogen exposure causes the relative proportion of

bioavailable testosterone to estradiol to decrease even further, exacerbating the symptoms of testosterone deficiency.

Many factors, in addition to estrogen exposure, can affect SHBG levels⁹. Thyroid hormone increases SHBG production, whereas insulin, on the other hand, decreases SHBG levels. In young men, testosterone levels are usually high and SHBG low, making most of the testosterone bioavailable. However, as men age, gain weight, and their estrogen levels increase, SHBG also rises, decreasing bioavailable testosterone. Measuring SHBG in blood provides an indication of the overall exposure to estrogens, as well as the bioavailable (free) fraction of testosterone (calculated from the ratio of testosterone to SHBG).

PSA is a measure of prostate health and high levels can indicate the presence of BPH or advancing prostate cancer. As prostate cells start to become crowded, they produce PSA, which acts to suppress angiogenesis and therefore reduce the blood supply to the surrounding tissue to prevent it from further growth. High levels are therefore seen only as a result of growth that is fairly rapid. It is important to test PSA levels prior to starting testosterone therapy, as a sharp increase in PSA can indicate prostate problems.

DHEA is a precursor for the production of estrogens and testosterone, and is therefore normally present in greater quantities than all the other steroid hormones. It is mostly found in the circulation in its conjugated form, DHEA sulfate (DHEA-S). Its production, which occurs in the adrenal glands, declines gradually with age. Like cortisol, it is involved with immune function and a balance between the two is essential. Low DHEA can result in reduced libido and general malaise.

Cortisol is an indicator of adrenal function and exposure to stressors. Under normal circumstances, adrenal cortisol production shows a diurnal variation and is highest early in the morning, soon after waking, falling to lower levels in the evening. Normal cortisol production shows a healthy ability to respond to stress. Low cortisol levels can indicate adrenal fatigue (a reduced ability to respond to stressors), and can leave the body more vulnerable to poor blood sugar regulation and immune system dysfunction. Chronically high cortisol is a consequence of high, constant exposure to stressors, and this has serious implications for long-term health,

including an increased risk of cancer, osteoporosis, and possibly Alzheimer's disease¹⁰.

Free T4, free T3, TSH, and TPO tests can indicate the presence of an imbalance in thyroid function, which can cause a wide variety of symptoms, including feeling cold all the time, low stamina, fatigue (particularly in the evening), depression, low sex drive, weight gain, and high cholesterol.

Which Profile?

Comprehensive Saliva and Blood Spot Profiles

For an initial evaluation of overall hormonal status, we strongly recommend the most comprehensive profiles using both saliva and blood spot collection, which give you the “big picture” of where the hormones may be unbalanced.

Comprehensive Male Profile I

Saliva tests: E2, T, DS, Cx4

Blood spot tests: PSA, fT4, fT3, TSH, TPO

Comprehensive Male Profile II

Saliva tests: Cx4

Blood spot tests: E2, T, SHBG, DS, PSA, fT4, fT3, TSH, TPO

Saliva Profiles

Saliva Profile I

E2, Pg, T, DS, morning C

Saliva Profile II

E2, Pg, T, DS, Cx2 (morning and night)

Saliva Profile III

E2, Pg, T, DS, Cx4 (diurnal)

Note: Saliva profiles do not include thyroid hormones or PSA and are not recommended for sublingual hormone users.

Blood Spot Profiles

Male Blood Spot Profile I

E2, T, SHBG, DS, PSA, C

Male Blood Spot Profile II

E2, T, SHBG, DS, PSA, C, fT4, fT3, TSH, TPO

Note: Blood spot profiles assess only waking cortisol - only a single a.m. sample is collected. Best choice for sublingual hormone users or individuals having problems collecting saliva, and for assessment of PSA levels

References

1. Araujo AB, O'Donnell AB, Brambilla DJ, Simpson WB, Longcope C, Matsumoto AM, McKinlay JB. Prevalence and incidence of androgen deficiency in middle-aged and older men: estimates from the Massachusetts Male Aging Study. *J Clin Endocrinol Metab.* 2004;89:5920-6.
2. Mulligan T, Frick MF, Zuraw QC, Stemhagen A, McWhirter C. Prevalence of hypogonadism in males aged at least 45 years: the HIM study. *Int J Clin Pract.* 2006;60:762-9.
3. Elmlinger MW, Dengler T, Weinstock C, Kuehnel W. Endocrine alterations in the aging male. *Clin Chem Lab Med.* 2003;41:934-41.
4. Risbridger GP, Bianco JJ, Ellem SJ, McPherson SJ. Oestrogens and prostate cancer. *Endocr Relat Cancer.* 2003;10:187-91.
5. Carruba G. Estrogen and prostate cancer: an eclipsed truth in an androgen-dominated scenario. *J Cell Biochem.* 2007;102:899-911.
6. Endogenous Hormones, Prostate Cancer Collaborative Group, Roddam AW, Allen NE, Appleby P, Key TJ. Endogenous sex hormones and prostate cancer: a collaborative analysis of 18 prospective studies. *J Natl Cancer Inst.* 2008;100:170-83.
7. Risbridger GP, Ellem SJ, McPherson SJ. Estrogen action on the prostate gland: a critical mix of endocrine and paracrine signaling. *J Mol Endocrinol.* 2007;39:183-8.
8. Tindall DJ, Rittmaster RS. The rationale for inhibiting 5alpha-reductase isoenzymes in the prevention and treatment of prostate cancer. *J Urol.* 2008;179:1235-42.
9. Selby C. Sex hormone binding globulin: origin, function and clinical significance. *Ann Clin Biochem.* 1990;27:532-41.
10. Magri F, Cravello L, Barili L, Sarra S, Cinchetti W, Salmoiraghi F, Micale G, Ferrari E. Stress and dementia: the role of the hypothalamic-pituitary-adrenal axis. *Aging Clin Exp Res.* 2006;18(2):167-70.

Useful Resources

American Thyroid Association – www.thyroid.org

Shawn M. Talbott. *The Cortisol Connection: Why Stress Makes You Fat And Ruins Your Health – And What You Can Do About It.* Hunter House Inc.; 2002.

Cherie Carter-Scott. *If Life Is A Game, These Are The Rules.* Broadway Books; 1998.

Richard Shames, Karilee Shames. *Feeling Fat, Fuzzy or Frazzled? A 3-Step Program to: Beat Hormone Havoc, Restore Thyroid, Adrenal, and Reproductive Balance, and Feel Better Fast!* Hudson Street Press; 2005. www.feelingfff.com

www.endotext.org

Relevant ZRT Provider Data Sheets:

About Dried Blood Spot Testing

About Saliva Testing

Cortisol Testing for Adrenal Function

Thyroid and Elements Profiles