ANDROGEN METABOLITES

Urinary Androgen Metabolites

Androgens play an important role in increasing the anabolic status of both men and women. Androgens are important for strengthening structural tissues such as muscles, bone, connective tissue, and skin. They also play an important role in the brain to increase the level of neurotransmitters such as dopamine, which are important for mood elevation and sex drive. Androgens are also precursors to the estrogens, estradiol and estrone. The most potent of the androgens is dihydrotestosterone (DHT), which is created from testosterone via 5α reductase. Testosterone itself is derived mostly from androstenedione and DHEA. In premenopausal women about half of the testosterone is derived from androstenedione produced by the ovaries, and the other half from peripheral conversion of DHEA manufactured in the adrenals.

Low androgens, particularly the more potent androgens testosterone and DHT, are associated with many different adverse conditions (bone loss, thinning skin, vaginal dryness, incontinence, cardiovascular disease, insulin resistance/metabolic syndrome, breast cancer) and symptoms (fatigue, low stamina, depression, memory lapses, loss of sex drive, hot flashes, allergies). If testosterone and/or DHEA are low and some of the symptoms listed above are problematic, consider supplementing with DHEA or testosterone. Oral DHEA supplementation will increase both urinary DHEA and testosterone, and usually DHT. Oral testosterone (mostly testosterone esters such as testosterone undecanoate), testosterone injections, testosterone subcutaneous pellets, and sublingual testosterone result in dose-dependent increases in urinary, serum, capillary blood, and salivary testosterone (note salivary testosterone is not suitable for monitoring testosterone after sublingual dosing, because of its retention in the submucosal tissues and residual release into saliva). Testosterone is most commonly used in women as a compounded topical cream or subcutaneous pellet inserts. Testosterone is effectively monitored in urine after pellet inserts, but not with topical testosterone at any concentration.

IMPORTANT NOTE: Testosterone supplementation is usually delivered topically in women. Like other topically delivered hormones, topical testosterone at doses commonly used in women (0.3-2 mg) does not raise urinary or venipuncture serum testosterone levels significantly beyond baseline; however, this dosing does significantly increase salivary and capillary blood testosterone. Therefore, for those individuals supplementing with exogenous topical testosterone, saliva or capillary blood testing is recommended over urinary testosterone.

Guide to Results Interpretation

Epi-Testosterone & Relationship to Testosterone

Epi-testosterone (Epi-T) and testosterone (T) are created in about equal amounts from androstenedione and DHEA. The ratio of T/Epi-T is about 1. When testosterone is supplemented with any delivery system except topical, the T/Epi-T ratio increases, which reflects an increase in the exogenous testosterone, but not Epi-T, which represents endogenous production. When exogenous testosterone is excessive this results in a depression of LH (negative

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hypothalamic/pituitary feedback of excessive T and estrogens created via aromatization) and a lowering of both endogenous testosterone and Epi-testosterone. In those supplementing with exogenous testosterone this can result in very low Epi-T, high T, and a very high T/Epi-T ratio. The urinary T/Epi-T ratio is used to monitor Olympic athletes for exogenous testosterone use, and ratios above 6 can result in disqualification. Women and men on testosterone pellets will likely have a T/Epi-T ratio >6 and a suppressed LH. Synthetic androgens will also suppress LH when in excess, and suppress endogenous T and Epi-T levels. However, because the androgen used is synthetic, T levels do not rise. Unless methods are used to identify the synthetic androgen by LC or GC mass spectrometry, the only markers to indicate synthetic anabolic hormone use are low T, low Epi-T, and undetectable LH.

DHEA

DHEA is not androgenic per se, in that it does not bind to cellular androgen receptors like testosterone and DHT, but it is a precursor for androstenedione, which then converts to testosterone. The circulating level of the sulfated form of DHEA(S) is higher than any other steroid in adults. DHEA(S) levels generally begin to rise in the early teens (adrenarche), peak in the early twenties, and then begin to fall steadily with age.

HIGH ENDOGENOUS DHEA (NO SUPPLEMENTATION):
In young well-trained athletes the level of DHEA(S) can be slightly higher than reference ranges, which is normal. DHEA(S), as well as its down-stream metabolites, androstenedione and testosterone, is more commonly found to be elevated in women with insulin resistance and polycystic ovarian syndrome (PCOS). These individuals usually have higher levels of insulin and LH (LH/FSH ratio is usually > 2.5 in 75% of women with PCOS), which stimulates high adrenal synthesis of DHEA(S), and high ovarian synthesis of testosterone.

HIGH DHEA(S) (DHEA SUPPLEMENTATION):
DHEA(S) is also higher in the body fluids (serum, saliva, capillary blood, urine) of individuals supplementing with DHEA; however, the DHEA-supplemented level will depend on the starting baseline level of DHEA(S) and the type of delivery. Oral DHEA supplementation, which is the most common, results in a dose-dependent increase of DHEA(S) from baseline levels. DHEA dosing generally ranges from 5-200 mg daily. Topical DHEA supplementation, which is becoming more common, results in very little increase in urine and venipuncture serum DHEA(S), but dose-dependent increases in salivary and capillary blood DHEA (not DHEAS). Much less of the DHEA delivered topically is sulfated to DHEA(S), which is why tests that measure DHEA(S) see little increase.

LOW DHEA(S) AND BREAST CANCER:
Lower age-matched levels of DHEA(S) are associated with higher breast cancer risk. This is thought to be due to the direct effects of DHEA on the immune system in influencing the distribution of type 1 and type 2 helper T-cells. High-normal DHEA(S) and normal diurnal cortisol favor anti-cancer immunity. Low age-matched DHEA(S) and high cortisol, particularly high night cortisol, is associated with lower anti-cancer immunity and higher breast cancer risk.