Is 5-Alpha Dihydrotestosterone (DHT) Evil?

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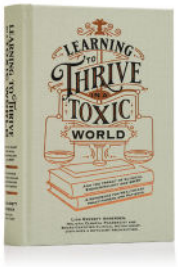

HFor the "hormonally savvy," DHT might be a hormone they have heard of, but more than likely in a negative connotation. It is the reason men lose their hair and have enlarged prostates, right? Well, there's a lot more to DHT and its absolutely essential duties regarding male development.

The quick answer is no, dihydrotestosterone is not evil. It is produced in peripheral target tissues and the liver and appears only in low amounts in the systemic circulation. It is the most potent androgen, and the only one that cannot be converted to estrogen. Along with testosterone and anti-mullerian hormone, it is required in the embryonic state to form male organs. The urogenital sinus, genital tubercle, urogenital fold, and labio-scrotal fold, which end up forming the penis, scrotum, and prostate are only possible due to the signaling of DHT. It is also necessary for testicular descent. So without DHT, there is no male expression.

As the male child goes through puberty, the growth and maturation of the penis and scrotum happen due to DHT, as does hair growth (facial, body, and pubic) and normal prostate growth. Sebaceous gland development is dependent on DHT. All of this, and yet it typically only makes up 10% of the circulating testosterone. It serves as an important exit strategy from the body for testosterone, via 5-alpha reductase, in regulating those levels.

Once the boy becomes a man, it is easy for many practitioners to say DHT is problematic or longer required. It is fair to say imbalanced DHT can create issues, but this happens when levels become elevated and therefore out of balance with other steroids, commonly due to increased 5-alpha reductase activity from low testosterone production and/or nutrient deficiency. This happens secondarily to the high consumption of meat, dairy, and eggs in the standard American Diet that are rich in powerful animal hormones and pesticides/herbicides (yes, even the organic) which disrupt our endocrine production, uptake, and utilization. When men have low testosterone, a greater percentage of it is converted to DHT, which in turn leads to inflamed prostates and hair loss. But it is also important to remember a reason DHT is still produced: testosterone is recycled or eliminated through DHT (via 5-alpha reductase) and estrogen (via aromatase) pathways. This crucial action generates hormonal balance and yields physiologic active molecules. When the conversion of DHT is blocked by 5-alpha reductase inhibitors, such as finasteride, then the body has no choice but to rid the testosterone through the estrogen pathways, increasing estrogen levels. If on the other hand aromatase inhibitors, such as anastrozole, are employed to block the conversion of testosterone to estrogen, then DHT becomes too high. If it is determined that either one of these pathways need to be mitigated, be it naturally or with pharmaceuticals, it is imperative to monitor the blood levels of estradiol, estrone, testosterone, and total testosterone, as well as DHT, and then to adjust dosages in order to promote balanced, physiologic levels.

Another reason we continue to produce DHT in adulthood is that higher levels are inversely associated with insulin resistance and risk of diabetes. This mechanism is independent of testosterone. In animal studies regarding Alzheimer's disease and cognition, DHT "positively modified synaptic structure and significantly delayed cognitive impairment." Other animal studies "suggest a role for DHT in adipose tissue that inhibits biochemical pathways involved in lipid synthesis and promotes several transcripts associated with apoptosis of adipocytes," definitely a helpful function of DHT, albeit that activity is much weaker than that of testosterone. There is a lack of evidence, either epidemiological or clinical, to blame DHT as an instigator or contributor to cardiovascular disease. In fact, studies have reported that higher DHT levels in older men were associated with decreased all-cause mortality and reduced ischemic heart disease mortality. More work is needed to confirm these observations in humans.

Other actions of DHT in men and women are to support normal cell function as it is fundamental for cell growth and death. This is exceptionally vital when it comes to prostate and breast cancer. It binds to intracellular androgen receptors (iAR) with 5 times the affinity of testosterone, which in turn down-regulates beta cell lymphoma 2 (BCL2) in prostate and breast cancer (prostate cancer cells contain high levels of iARs). BCL2 inhibits apoptosis (natural cellular death). High testosterone can increase BCL2 in prostate cancer, but in breast cancer higher testosterone levels lower BCL2, actually helping to prevent the formation of immortal breast cells. In this same situation, DHT up-regulates AS3, a protein that shuts off cell proliferation. Proper amounts of DHT in tissues increase apoptotic proteins and calcium influx while reducing calreticulin, all of which increase the rate of cellular death in cancer cells. High levels of testosterone increase apoptotic proteins and calcium influx in cancer cells, killing them. There are some prostate cancers whose growth is inhibited by testosterone, but stimulated by testosterone plus finasteride, which tells us that DHT is needed to balance cell growth and cell death.

Interestingly, circulating levels of DHT with testosterone replacement therapy do not correlate with those found in prostate, adipose, and muscle tissues which are rich in androgen receptors. This may be due to "local regulatory mechanisms that tightly control intracellular androgen homeostasis" as previously described. There can be a minimal increase or a significant decline in serum DHT levels, depending on the severity of testosterone deficiency and other health cormorbidities, after testosterone supplementation is initiated that are not only of little concern but in the context of clinical data, may actually be of benefit by improving DHT to testosterone ratios. Ronald S. Swerdloff, et al. in Dihydrotestosterone: Biochemistry, Physiology, and Clinical Implications of Elevated Blood Levels wrote, "While well-controlled, long-term studies designed to specifically examine the effects of androgen exposure on risk for prostate need to be conducted, the current clinical data base is relatively reassuring that circulating levels of androgens (or changes in such) apparently do not play as pivotal a role as once thought in the development of prostate disease."

So, it would seem that with balanced and physiologic testosterone, estrogen, and DHEA levels, DHT functions as it should, keeping cancerous cells and other physiological functions in check without instigating problems.

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