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DHEA (dehydroepiandrosterone):

Is It Contraindicated in Prostate Cancer and BPH?

By Ward Dean, MD

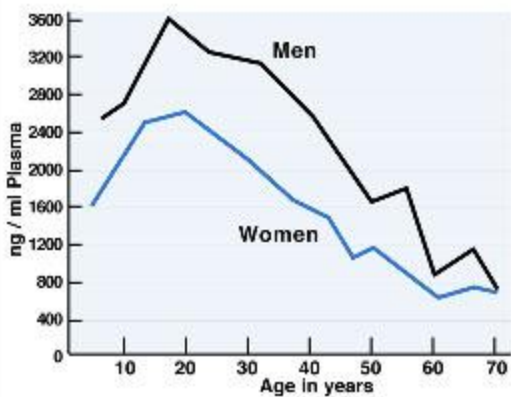


Fig 1. Decline of DHEA-S with age

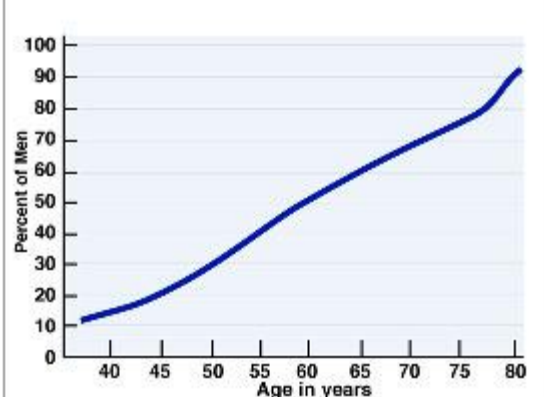


Fig 2. Incidence of BPH in men with age (redrawn from Guess, et al, 1994)

DHEA (dehydroepiandrosterone) is the most abundant steroid hormone in the body. It is also

one of the most significant age-related biomarkers, which predictably declines with age in even the healthiest of people (Fig 1). Abnormally low levels of DHEA have been reported to be related to a number of diseases, including cancer, diabetes, coronary artery disease, obesity, and Alzheimer's. Supplemental DHEA has been reported in study after study to have immunoregulatory, anti-diabetic, anti-cancer, anti-obesity and anti-stress activity, and to be involved in the prevention of atherosclerosis, hypertension, hypercholesterolemia, Alzheimer's disease and multiple sclerosis. (1,2)

Nevertheless, one controversy plagues many physicians, their patients, and consumers who are considering the addition of DHEA to their supplement regimens. This controversy involves whether men with prostate disease—either benign prostatic hypertrophy (BPH) or prostate cancer—should take DHEA. This question stems from the much-speculated possibility that DHEA could aggravate both conditions, based on the belief that DHEA is converted in the body into testosterone, and that testosterone, and/or its metabolite, dihydrotestosterone (DHT) causes or worsens BPH and prostate cancer. Let's examine each of these issues separately and review some of the laboratory and clinical studies that are relevant to these questions.

Prostate Size (and Incidence of BPH) Increases with Age

BPH is a common affliction of men over 50. The incidence of BPH progressively increases with age (Fig. 2). Symptoms that indicate the presence of BPH include (1) hesitation of urination, (2) a reduction in urinary force, (3) dribbling at the end of urination, and (4) nocturia (getting up one or more times during the night to urinate). In severe cases, BPH can cause complete urinary obstruction! These symptoms are due to compression of the urethra as it passes from the bladder through the gland. Large-scale autopsy studies confirm that prostate size increases significantly with age, in parallel with the severity of symptoms. (3)

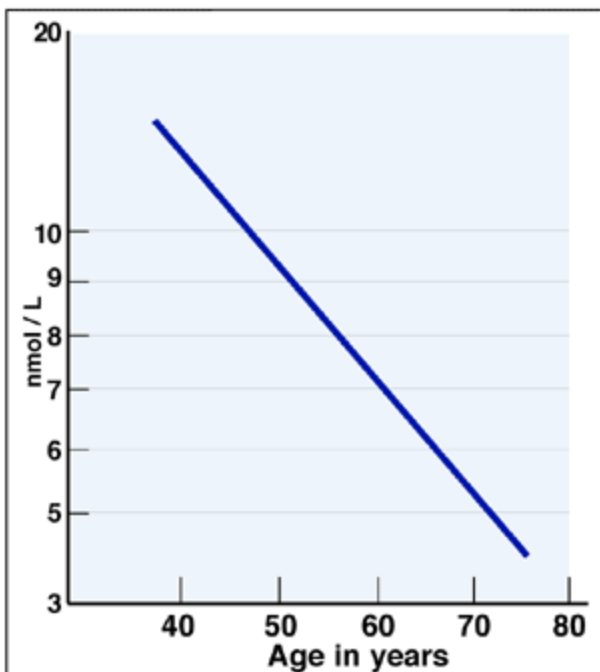


Fig. 3. Changes in total testosterone levels in men with age (redrawn from Belanger, et al, 1994).

Prostatic Hypertrophy or Prostate Cancer: Is it too Much or Too Little Testosterone?

Conventional medical wisdom holds that both prostatic hypertrophy and prostate cancer are due to or are promoted by testosterone and/or dihydrotestosterone. Consequently, standard medical therapy for these conditions includes blocking dihydrotestosterone formation by drugs, avoiding testosterone replacement, or (in the case of prostate cancer) orchiectomy (surgical removal of the testicles).

I am not yet convinced that testosterone is necessarily the bad guy. For example, it is clear that testosterone, like DHEA, drops progressively with age in both men and women (Fig 3). Consequently, it does not seem logical to me

that diseases which increase in incidence with age are caused by a hormone that progressively decreases with age. Dr. William Campbell Douglass, a pioneer in alternative medicine, agrees, writing ...testosterone has been proven to be protective against cancer...it has been suggested that testosterone is contraindicated in men with cancer of the prostate. In view of the hormone's protective effect in other cancers, I doubt the validity of this supposition. (4)

Dr. G. Debled, a European urologist, also believes that testosterone deficiency rather than excess DHT is a major causative factor of BPH. In fact, Dr. Debled uses testosterone to treat BPH. Furthermore, Dr Debled reports that in over 20 years of administering testosterone for patients with BPH, he has not had a single case of prostate cancer develop—despite the fact that approximately 50 cases should have been discovered, based on statistical averages. (5)

However, even the most mainstream of medical publications occasionally admits that the link between testosterone and prostate cancer is not that firmly established. For example, Dr. J.A. Jackson conceded that, The prostatic complications of testosterone replacement therapy have received little clinical attention, and that only three previous reports (of four patients) have described the simultaneous occurrence of prostate cancer and androgen replacement or abuse. (6) More recently, Dr. H.M. Behre admitted that little clinical information based on objective methods is available on the effect of testosterone substitution on prostate volume in hypogonadal patients, and that with regard to the increase in prostate volume with age, the relative roles of testosterone, DHT and estradiol are controversial. (4)

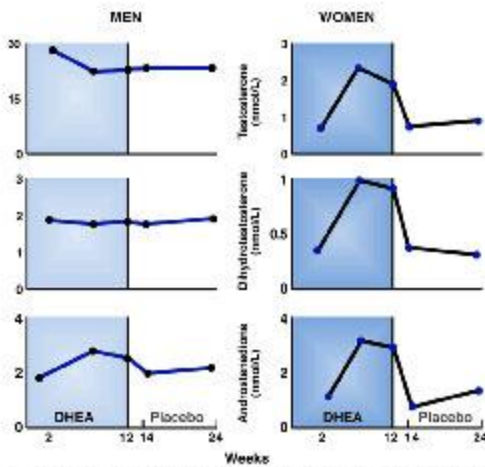


Fig. 4. Effect of nightly oral dose of 50 mg DHEA on androgen levels (testosterone, dihydrotestosterone (DHT), and androstenedione) in men and women, compared with placebo (redrawn from Morales, et al, 1994). Note the significant increases in androgen levels in women and the lack of effect on these levels in men.

prostate-related

Testosterone in Men

concern about DHEA that (1) testosterone causes (2) because DHEA is a consuming DHEA range could raise testosterone BPH or prostate cancer).

While DHEA may raise who very efficiently convert it appear to be true for men.

the findings of scientists at the University of California, San Diego, who performed a study on 13 men and 17 women, ranging from 40-70 years of age. These subjects were given 50 mg of DHEA orally every night for a six-month period. It was found that testosterone, dihydrotestosterone, and androstenedione were doubled in women —bringing these levels into the physiological range for young women. In men, however, only androstenedione levels increased slightly, while testosterone and dihydrotestosterone levels were unchanged (Fig 4). (8) Clearly, it appears that physiologic doses of DHEA (i.e., doses that restore DHEA and DHEA-S [DHEA-Sulfate] levels to those of youthful men and women) do not significantly elevate testosterone in men.

On the other hand, when pharmacologic doses of DHEA are administered (i.e., doses that are far in excess of those required to restore levels to those of healthy young adults), testosterone and DHT levels do increase significantly. For example, in one elderly man, to whom 400 mg of DHEA was administered, significant and rapid rises were noted in DHEA, DHEA-S, testosterone and DHT (Fig. 5).

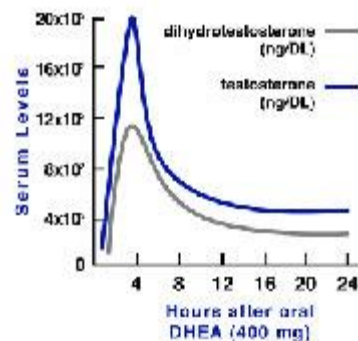
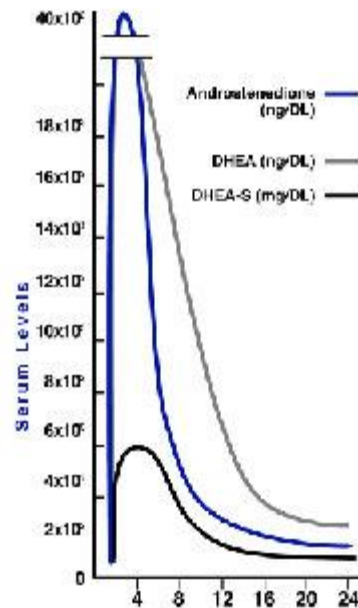


Fig 5. Changes in DHEA, DHEA-S, testosterone, dihydrotestosterone, and androstenedione after 400 mg oral DHEA in an elderly man (redrawn from Roberts and Fillen, 1990.)

Finally, Dr. B. de Lignieres conducted a nearly two-year survey of men aged 55-70 years of age who were treated with testosterone. He found that high levels of testosterone induced a number of clinical benefits, while reducing prostate size and symptomatology. (7)

DHEA is not Converted into

The major reason for the supplements in men is the belief BPH and prostate cancer, and precursor of testosterone, supplements in a physiological levels (and thus allegedly cause

testosterone levels in women, to testosterone, this does not

These statements are based on

Treatment of hypogonadal men with physiological doses of testosterone resulted in prostate size and PSA levels that were the same as normal men. The authors concluded that concern about testosterone-induced prostate growth should not preclude men with low testosterone levels from receiving testosterone therapy. (4) Most men over 40 have decreased output of testosterone and are hypogonadal (compared to what they were at 20). I think they are therefore candidates for testosterone replacement therapy.

DHEA Inhibits Prostate Cancer Cell Growth In Vitro

Scientists at the New York University Medical Center, Tuxedo, NY, studied the effect of DHEA on the proliferation of (1) three human prostate cancer cell lines, and (2) cell cultures of rat prostate carcinomas. They reported that DHEA inhibited growth of the human prostate cancer cell lines by approximately 10%, 25%, and 80% at concentrations of 1, 10, and 22.5 ug/ml, respectively. DHEA also inhibited growth of rat prostate carcinoma cultures (www.with 50 nM testosterone [T]), by 11-40% at 1 ug/ml, 25-54% at 10 ug/ml, and 55-77% at 22.5 ug/ml.

The scientists concluded that DHEA inhibits growth of human and rat prostate cancer cells in a dose-related fashion, that DHEA acts as a chemopreventive agent by direct growth inhibition of prostate cancer cells, and that DHEA should be considered for further research for prostate cancer chemoprevention in humans. (9,10)

DHEA Levels Decrease in Prostate Cancer Patients

Physicians at the Department of Urology, Institute of Experimental Endocrinology at Humboldt University Medical School in Berlin, Germany, found that DHEA levels in patients with prostate cancer were significantly lower than healthy controls. (11) Their findings confirmed Fehler, et al's previous report that DHEA-S levels were decreased in patients with prostate cancer.

Another interesting retrospective study conducted at Johns Hopkins University involved the analysis of DHEA and DHEA-S levels in blood serum that was collected and frozen in 1974 and the relationship of these levels to the subsequent development of prostate cancer. DHEA and DHEA-S levels for 81 men who were subsequently diagnosed with prostate cancer were found to have 11% lower levels of DHEA and 12% lower levels of DHEA-S compared to age-matched controls who did not develop prostate cancer. The authors concluded that it seems unlikely that serum levels of DHEA or DHEA-S are important risk factors for prostate cancer. (12) Similar findings were reported two years later by another group of researchers. (13)

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