

REPORT

The Death of Anti-Aging Supplements?



In 1513, at the age of 53, Juan Ponce de Leon began earnestly searching for the fountain of youth—a mythical spring fabled to possess the ability to restore health and vitality to all who bathed in its waters. Now, almost five centuries later, scientists continuing that ill-fated Spanish explorer's quest for youth may actually have found it—in the human body.

After decades of painstaking work, researchers worldwide have finally begun to unravel the mysteries surrounding the aging process. DHEA, one of the human body's most abundant hormones, has been proven not only to decline in direct proportion to aging, but also to be a major component in maintaining health and vitality. In just this past year alone, researchers have discovered that DHEA at increased levels effectively reduces the risk of heart disease, promotes brain cell growth and survival, reduces the symptoms of depression, lupus and arthritis and, perhaps most stunning of all, is an effective

chemopreventative agent against cancer!

But all of that work may come to nothing if Congress has its way. A new Bill introduced in October would seriously undermine the legitimate usage of certain over-the-counter anti-aging supplements, including DHEA. Known as H.R. 207 or the "Anti-Andro Bill," this legislation is designed to curtail the usage of certain muscle-building "andro" supplements by teenagers. The scope of H.R. 207, however, is so broadly written that it includes DHEA and other beneficial anti-aging supplements. This Bill could be interpreted to make DHEA a controlled substance, the possession of which is punishable under the Federal Controlled Substances Act of 1970. Although the Bill is not without its merits—such as keeping ignorant teens from abusing steroid hormone precursors—its myopic restrictions may result in incalculable harm to the nation's older citizens.

It appears that regardless of the valiant strides medical science has taken in its quest to overcome debilitating age-related disorders, and bring hope to millions of older Americans, the fountain of youth may be lost forever.

The following article provides a brief update on new findings about DHEA published over the past twelve months. In it, we examine some of the latest groundbreaking research that has propelled DHEA into the forefront of the anti-aging industry. (For more information about H.R. 207 and to find out what you can do to stop it, read the article titled "Anti-Aging Supplements May Soon Be Illegal!" in this issue.)

Since initially isolated by Nobel Prize winning biochemist Dr. Adolf Butenandt in 1931, dehydro-epiandrosterone, commonly known as DHEA, has been a controversial medical enigma whose anti-aging properties are as compelling as they are elusive.

Arguably one of the most popular and potentially effective anti-aging supplements, DHEA has recently become the subject of intense debate and scientific scrutiny, resulting in a surge of research whose goal has been to reveal—or refute—the life saving potential of this biomarker of aging.

DHEA: Biomarker of aging

DHEA and its sulfated metabolite, DHEA-S, are the most abundant circulating hormones in the human body.¹ Nicknamed the "mother hormone," DHEA is actually a prohormone-a neurosteroidal progenitor produced by the adrenal cortex, gonads and central nervous system (CNS)-whose offspring are converted into over 50 essential hormones including testosterone, estrogen and cortisone.² DHEA's ability to provide life-sustaining hormones is one reason why it is so critical to healthy metabolic functioning in aging humans. As we age, the endogenous level of DHEA is drastically reduced. Research has shown that optimal production is between the ages of 20 to 25, with each successive decade seeing diminished levels-dropping down to as low as 20% by the age of 70.³ Numerous studies have also indicated that this decrease in DHEA is directly associated with many age-related disorders including immune dysfunction, autoimmune disease, heart disease, mental disturbances, osteoporosis and blood sugar instability. These established correlations suggests that high levels of DHEA may be associated both with longevity and vitality.



Neurological benefits

As a partial product of the central nervous system, DHEA is especially abundant in the human brain.⁴ Consequently, many studies have reported that DHEA provides an appreciable level of defense against many of the neurodegenerative diseases commonly associated with advanced age. Alzheimer's patients, for example, have shown substantially lower levels of DHEA in comparison to healthy subjects as well as an associated reduction of blood flow to the hippocampus-the area of the brain believed to be associated with memory.⁵ Prior studies have also demonstrated that DHEA is a significant factor in restricting the damage associated with stroke, and is equally instrumental at lowering the autoimmune response during brain injury-thereby reducing the inflammation and protecting nearby healthy neurons.⁶ Evidence now suggests that in addition to having neuroprotective characteristics, DHEA may also be directly related to neurogenesis -the formation of new neurons.

A group working at the University of Cambridge has determined that treating rats with subcutaneous DHEA pellets actually increased the number of newly formed cells in the dentate gyrus of the hippocampus. Most notable, however, was the fact that the neurogenesis effect was especially prominent in older rats. These results prove that DHEA effectively regulates neurogenesis in the hippocampus and modulates the inhibitory effects of increased corticoids on both the formation of new neurons and their survival.⁷

The relationship between diabetes, a blood sugar disorder that often results in neural damage, and levels of circulating DHEA was recently a topic of study by doctors at the Diabetes Endocrinology Research Center and Department of Internal Medicine in Iowa. According to their findings, nutritional supplementation with DHEA may be a candidate for treating diabetes-induced vascular and neural dysfunction.

In their study, they found that supplementing the diet of streptozotocin-induced diabetic rats with 0.1%, 0.25%, or 0.5% DHEA caused a dose-dependent prevention in the development of motor nerve conduction velocity and endoneurial blood flow impairment-factors that are decreased in diabetes. They also determined that at 0.25%, DHEA significantly improved both vascular relaxation and sciatic nerve enzyme activity, and prevented oxidative stress damage inherent to diabetes. This suggests that at moderate dosage, DHEA is effective at treating both vascular and neural dysfunctions associated with diabetes.⁸

DHEA also shows promise in protecting against Alzheimer's disease. An article recently published in the Journal of Clinical Endocrinology and Metabolism described researchers' attempts to investigate the significance of neurosteroids in Alzheimer's disease.

The study focused on the individual brain regions of Alzheimer's disease (AD) patients, including hippocampus, amygdala, frontal cortex, striatum, hypothalamus and cerebellum, and found that a general trend toward decreased levels of all steroids was observed in all AD patients' brain regions compared with controls. The results concluded that pregnenolone sulfate (PREGS) and DHEA-S were significantly lower in the striatum and cerebellum, and that DHEA-S was also significantly reduced in the hypothalamus. The study further found that high levels of key proteins implicated in the formation of plaques were correlated with decreased brain levels of DHEA-S, suggesting it has a possible neuroprotective role in AD.⁹

Depression, cognitive abilities and DHEA

Depression is a common condition associated with aging. Often misconstrued as sadness or grief, depression is characterized by a lowered mood, feelings of worthlessness, difficulty concentrating and various somatic disorders.¹⁰ Far from simply being the result of neurotransmitter dysfunction, depression can be symptomatic of a variety of illnesses including degenerative disorders that damage vital neural tissue. Consequently, DHEA's role as an anti-depressant has been rigorously examined for years.

During these many trials, researchers routinely found that when taken daily, DHEA supplements effectively reduced depressive episodes and enhanced mood. In fact, according to one major study in the UK, as many as 67% of men and 82% of women reported a noticeable decrease in their depressive symptoms while taking as little as 25 mg/day of DHEA.¹¹ In addition, women suffering from adrenal insufficiency have reported an improved sense of well-being and an associated increase in both sexual interest and sexual satisfaction while taking DHEA.¹²



More recently, researchers at the University of Newcastle Upon Tyne, UK tested DHEA to see if it offered any protection against cortisol, a glucocorticoid known to be elevated in patients with depression.

In their study, cortisol and DHEA were measured in saliva taken from 39 patients with unipolar depression who had been medication free for at least six weeks. These samples were then compared with those of 41 non-depressed subjects. The results showed that the level of cortisol was significantly higher than that of DHEA in the depressed patients when compared to healthy subjects. This indicates that reduced DHEA levels may be a marker for depressive illness and a contributing factor to the associated deficits in learning and memory. These results also suggest that the administration of DHEA or other anti-

glucocorticoid treatments may reduce neurocognitive deficits in major depression.¹³

To further correlate the association of DHEA with depression, researchers from the Center for Torture and Trauma Survivors in Sweden examined the levels of DHEA-S in refugees suffering from post traumatic stress disorder (PTSD). According to their results, DHEA-S was observed to be higher in non-depressed PTSD cases than in non-PTSD without depression, suggesting an interaction between PTSD, depression and levels of DHEA-S.¹⁴

Although research into DHEA's ability to promote improved cognitive functioning in humans is still mired in the early stages of development, scientists at Open University, UK demonstrated that it does have the potential to increase memory retention. Their studies found that by administering intracerebral injections of DHEA and DHEA-S 15 minutes before or up to 60 minutes after training, one-day-old chicks showed enhanced recall ability for up to 24 hours. These findings provide evidence that neurosteroids such as DHEA and DHEA-S have memory-enhancing properties and may constitute therapeutic tools for the treatment of cognitive deficits.¹⁵

Continued on Page 2 of 2

[Back to the Magazine Forum](#)

REPORT

The Death of Anti-Aging Supplements?

The role of DHEA in cancer prevention



DHEA is recognized as one of the major adrenal androgens, and many of its abilities have been well-documented. We have learned through years of research that it enhances the immune system, fights osteoporosis, lowers hyperglycemia (high blood sugar) and may even help to mount a defense against HIV. But despite all that has been learned, its complete role in the human endocrine system continues to remain unclear. One of the prime areas yet to be fully examined is its effect on carcinogenesis.

To understand its role in cancer prevention and treatment, scientists in Japan performed a study to determine whether DHEA has a chemopreventative effect on the precursors of colon cancer. In the study, aberrant cryptic foci (ACF) were induced via azoxymethane into mice, which were then treated with DHEA. ACF is a precancerous condition. The results showed that mice treated with 0.4% and 0.8% DHEA had a significant decrease in the number of ACF, although there were no significant differences between DHEA-treated and control mice in terms of the ACF size, or level of dysplasia. This is the first study of colon cancer carcinogenesis demonstrating that DHEA treatment can decrease the number of ACF. These results strongly suggest that DHEA is a potential chemopreventative agent against human colon cancer.¹⁶

In another provocative cancer study, researchers at Peking Union Medical College in China used Dimethylbenz (alpha) anthracene (DMBA) to induce breast carcinoma in Sprague-Dawley rats, followed by 10 weeks of oral administration of DHEA. The results of this experiment showed significant inhibition of tumor development and a lower incidence of mammary carcinoma on daily doses of 25 mg/kg DHEA. In addition, the mean tumor volume per rat was remarkably reduced by 92%. Moreover, 25 mg/kg DHEA treatment significantly increased the carcinoma latency for about 3.5 weeks as compared with the control. These results prove that DHEA is a potent cancer chemoprophylaxis agent that exhibits inhibitory potential on mutation and chemical carcinogen in vivo and in vitro.¹⁷

Cardiovascular system

When most people hear the term "heart disease" they typically think about coronary artery disease-the narrowing of the arteries leading to the heart. But coronary artery disease is just one of a staggering number of conditions that fall under the heading of heart disease. Cardiomyopathy, cardiogenic pulmonary edema, aortic stenosis and myocarditis are all forms of this killer-and the list goes on.¹⁸

Owing to its dubious distinction of being the leading cause of death for men and women in the U.S., heart disease has been the subject of innumerable scientific studies. Not surprisingly, an impressive amount of this research has focused on the relationship between heart disease, age and the concurrent drop of DHEA-with results suggesting the need to re-establish youthful levels, especially in men

Men, it seems, are particularly receptive to the cardioprotective action of DHEA. Numerous studies that examined the relationship between DHEA and heart disease found that men with low serum levels of DHEA are as much as 1.6 times more likely to develop coronary artery disease than men with normal levels.¹⁹

Other studies revealed that DHEA is a crucial antioxidant that helps to protect blood vessels against atherosclerosis. Several years ago, researchers in Canada found that in elderly patients, vitamin E does not restore the resistance of LDL to oxidation back to the levels found in youth. DHEA, on the other hand, did increase LDL's resistance in a dose-dependent manner. Furthermore, they found evidence that DHEA is actually a part of both HDL and LDL cholesterol and at youthful concentrations its presence helps to reduce the degree of oxidation that occurs within cholesterol. The elderly, whose circulating levels of DHEA are diminished, have no such defense and subsequently suffer increased cholesterol oxidation-the primary suspect in the development of heart disease.²⁰

DHEA's anti-oxidizing properties were later confirmed by researchers in Poland who found that it effectively increases the activity of

the enzyme superoxide dismutase (SOD), one of the most important natural antioxidants and a major factor for preventing circulatory diseases.²¹

It is known from prior studies that serum apolipoprotein AI (apoAI) levels correlate with the risk of developing atherosclerosis. Researchers in Greece have now shown that there is a direct association between endogenous adrenal C19 steroid hormones (DHEA and androstenedione [ASD]) and serum lipoprotein levels. In that study, the serum concentrations of DHEA-S, ASD, LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), triglycerides, apolipoprotein AI (ApoAI) and apolipoprotein B100 (ApoB100) were measured in a sample of 88 healthy men. The results revealed that low DHEA-S is an independent factor for increased levels of atherosclerosis-inducing ApoAI, triglycerides, LDL-C, and ApoB100.²²

In the recent population-based Rotterdam Study, researchers investigated the relationship between levels of DHEA-S and aortic atherosclerosis among 1,032 nonsmoking men and women aged 55-years and over. Although no clear association between the levels of DHEA-S and the presence of severe aortic atherosclerosis was found, a protective effect against the progression of aortic atherosclerosis was clearly observed in subjects with the highest percentages of available DHEA-S. This report further bolsters the proposal that increasing the circulating levels of DHEA provides protection against circulatory disorders.²³

Chronic inflammatory disease

Chronic inflammation is yet another common ailment associated with aging. It is known that the levels of various chemical mediators of inflammation, such as interleukin-6 (IL-6) and tumor necrosis factor (TNF), increase with age, while levels of anti-inflammatory steroids, such as DHEA, decline.²⁴ Left uncorrected, this distorted ratio produces a host of inflammatory disorders whose net result is discomfort, increased physical limitations and premature death.

Years of research have shown that increased inflammation in the elderly is directly related to declining levels of DHEA. Several independent studies have also agreed that in cases of chronic inflammation (such as rheumatoid arthritis) where adrenal dysfunction resulted in low levels of DHEA, taking DHEA supplements is necessary to help overcome the inflammatory response.²⁵

Recently, a team of researchers from the University of Regensburg, Germany reaffirmed these conclusions in a study that examined the role of DHEA in reducing the damage produced by chronic inflammation. According to that study, DHEA and DHEA-S inhibit T-helper lymphocyte immune reactions and effectively exert anti-inflammatory control over the immune response. In cases of chronic inflammation where DHEA and DHEA-S are dramatically decreased there is only a limited ability to restrict inflammation. These new findings support previous studies suggesting that in cases of chronic inflammation, it is paramount to re-establish adequate levels of DHEA.²⁶



Another new study published in *Arthritis & Rheumatism* reported on the effects of low serum levels of DHEA in relation to other adrenal hormones in patients with early rheumatoid arthritis (RA) and reactive arthritis (ReA). In that study the authors found that levels of DHEA-S were relatively low in relation to levels of IL-6 and TNF in untreated patients with early RA and ReA when compared with healthy subjects. The study further demonstrated that there was a relative increase of cortisol—a potentially harmful steroid—in relation to DHEA-S.²⁷

Systemic lupus erythematosus (SLE), an inflammatory autoimmune disorder that affects approximately one in every 700 women, is another promising candidate for DHEA therapy. Researchers at the National Defense Medical Center in China evaluated the efficacy and tolerability of DHEA at high dosage in women with active SLE. In a multicenter, randomized double-blind, placebo-controlled trial, 120 adult women with active SLE received oral doses of DHEA at 200 mg/day for 24 weeks. After the therapy concluded, results showed that the number of patients with SLE flares receiving the DHEA supplement orally was decreased by 16% compared with the control group. In addition, no life-threatening reactions or serious safety issues were observed, indicating that DHEA was well tolerated and is effective in mitigating SLE and reducing disease activity.²⁸

The research continues



Whether or not DHEA proves to be the panacea of aging remains to be seen. Effective, prolonged research dealing with this potential biochemical miracle is still in its infancy—despite having been discovered over 70 years ago. However, within the past year alone scientists have taken enormous strides in unraveling the riddle of DHEA—proving not only its extraordinary benefit as a dietary supplement, but also its effectiveness for treating and preventing dozens of the most common, debilitating age-related disorders.

Already, new research is well underway to further define and explore DHEA's place in HIV treatment, cancer prevention, neurological trauma, osteoporosis and many other diseases that currently offer little or no hope for the afflicted.

References

1. Allolio B, et al. DHEA treatment: myth or reality? *Trends Endocrinol Metab* 2002 Sep;13(7):288-94.
2. Zdrojewicz Z, et al. Dehydroepiandrosterone (DHEA)-youth hormone? *Wiad Lek* 2001;54(11-12):693-704.
3. Corrigan B. DHEA and sport. *Clin J Sport Med* 2002 Jul;12(4):236-41.
4. Steckelbroeck S, et al. Characterization of the dehydroepiandrosterone (DHEA) metabolism via oxysterol 7 α -hydroxylase and 17-ketosteroid reductase activity in the human brain. *J Neurochem* 2002 Nov;83(3):713-26.
5. Murialdo G, et al. Hippocampal perfusion and pituitary-adrenal axis in Alzheimer's disease. *Neuropsychobiology* 2000;42(2):51-7.
6. Aragno M, et al. Dehydroepiandrosterone prevents oxidative injury induced by transient ischemia/reperfusion in the brain of diabetic rats. *Diabetes* 2000 Nov;49(11):1924-31.
7. Karishma KK, et al. Dehydroepiandrosterone (DHEA) stimulates neurogenesis in the hippocampus of the rat, promotes survival of newly formed neurons and prevents corticosterone-induced suppression. *Eur J Neurosci* 2002 Aug;16(3):445-53.
8. Yorek MA, et al. Effect of treatment of diabetic rats with dehydroepiandrosterone on vascular and neural function. *Am J Physiol Endocrinol Metab* 2002 Nov;283(5):E1067-75.
9. Weill-Engerer S, et al. Neurosteroid quantification in human brain regions: comparison between Alzheimer's and nondemented patients. *J Clin Endocrinol Metab* 2002 Nov;87(11):5138-43.
10. Almeida OP, et al. Sex hormones and their impact on dementia and depression: a clinical perspective. *Expert Opin Pharmacother* 2001 Apr;2(4):527-35.
11. Huppert FA, et al. Dehydroepiandrosterone (DHEA) supplementation for cognition and well-being. *Cochrane Database Syst Rev* 2000;(2):CD000304.
12. Arlt W, et al. DHEA replacement in women with adrenal insufficiency-pharmacokinetics, bioconversion and clinical effects on well-being, sexuality and cognition. *Endocr Res* 2000 Nov;26(4):505-11.
13. Young AH, et al. Elevation of the cortisol-dehydroepiandrosterone ratio in drug-free depressed patients. *Am J Psychiatry* 2002 Jul;159(7):1237-9.
14. Sondergaard HP, et al. Elevated blood levels of dehydroepiandrosterone sulphate vary with symptom load in posttraumatic stress disorder: findings from a longitudinal study of refugees in Sweden. *Psychother Psychosom* 2002 Sep-Oct;71(5):298-303.
15. Miguez PV, et al. Dehydroepiandrosterone and its sulphate enhance memory retention in day-old chicks. *Neuroscience* 2002;109(2):243-51.
16. Osawa E, et al. Chemoprevention of precursors to colon cancer by dehydroepiandrosterone (DHEA). *Life Sci* 2002 Apr 19;70(22):2623-30.
17. Yang S, et al. Anti-mutagenicity activity of dehydroepiandrosterone. *Zhonghua Zhong Liu Za Zhi* 2002 Mar;24(2):137-40.
18. Tierney L, et al. *Current medical diagnosis and treatment*. 40th ed., pp. 352-447. New York, NY: McGraw-Hill.
19. Feldman HA, et al. Low dehydroepiandrosterone and ischemic heart disease in middle-aged men: prospective results from the Massachusetts Male Aging Study. *Am J Epidemiol* 2001 Jan 1;153(1):79-89
20. Khalil A, et al. Age-related decrease of dehydroepiandrosterone concentrations in low density lipoproteins and its role in the susceptibility of low density lipoproteins to lipid peroxidation. *J Lipid Res* 2000 Oct;41(10):1552-61.
21. Bednarek-Tupikowska G, et al. Influence of dehydroepiandrosterone on platelet aggregation, superoxide dismutase activity and serum lipid peroxide concentrations in rabbits with induced hypercholesterolemia. *Med Sci Monit* 2000 Jan-Feb;6(1):40-5

22. Zofkova I, et al. Apolipoprotein E gene determines serum testosterone and dehydroepiandrosterone levels in postmenopausal women. *Eur J Endocrinol* 2002 Oct;147(4):503-6.
23. Hak AE, et al. Low levels of endogenous androgens increase the risk of atherosclerosis in elderly men: the Rotterdam study. *J Clin Endocrinol Metab* 2002 Aug;87(8):3632-9.
24. Straub RH, et al. Dehydroepiandrosterone in relation to other adrenal hormones during an acute inflammatory stressful disease state compared with chronic inflammatory disease: role of interleukin-6 and tumour necrosis factor. *Eur J Endocrinol* 2002 Mar;146(3):365-74.
25. Leowattana W, et al. DHEA(S): the fountain of youth. *J Med Assoc Thai* 2001 Oct;84 Suppl 2:S605-12
26. Straub RH, et al. The endotoxin-induced increase of cytokines is followed by an increase of cortisol relative to dehydroepiandrosterone (DHEA) in healthy male subjects. *J Endocrinol* 2002 Nov;175(2):467-74.
27. Straub RH, et al. Inadequately low serum levels of steroid hormones in relation to interleukin-6 and tumor necrosis factor in untreated patients with early rheumatoid arthritis and reactive arthritis. *Arthritis Rheum* 2002 Mar;46(3):654-62.
28. Chang DM, et al. Dehydroepiandrosterone treatment of women with mild-to-moderate systemic lupus erythematosus: a multicenter randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2002 Nov;46(11):2924-7.

[Back to the Magazine Forum](#)

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

LifeExtension[®]

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.