LIFE EXTENSION MAGAZINE

<< Back to March 2004 (/Magazine/2004/3)

The DHEA Debate

March 2004

COVER STORY

A critical review of clinical and experimental data

x) As I explain in my book, The Metabolic Plan, this is one of the most important keys to living a long and healthy life. As we age, most people lose muscle and gain fat. You have to understand the profound effect this has on quality of life. Beyond the aesthetic effect, which affects our self-esteem and outlook on life, the accumulation of fat and loss of muscle causes a progressive loss of functional ability and a dramatic alteration in glucose metabolism. More than 70% of obese individuals will become diabetic, and the diabetic state is like turbo-aging, producing rapid degeneration throughout the body and brain.

Naysayer: So now you're going to tell me that DHEA prevents diabetes?

Stephen Cherniske: Well, it prevents diabetes in animals[48] and there is compelling evidence that it reduces the risk for diabetes in humans. We all know that aging is associated with a decreased muscle-to-fat ratio and decreased insulin sensitivity, which often lead to type II diabetes. DHEA has been shown in human clinical trials to improve insulin sensitivity and to help restore muscle mass.[2,3] It has long been known that diabetics have reduced serum levels of DHEA compared to age-matched controls.[129,130] Importantly, new research shows that even in healthy individuals, low DHEA levels are correlated with high plasma glucose, suggesting that DHEA deficiency contributes directly to the diabetic state.[131] Here is a quote from one of many studies on DHEA and aging:

“Oral replacement of DHEA, which does not appear to cause important adverse effects, may prevent, or even reverse, some age-associated conditions.”[105]

Naysayer: If DHEA is safe and beneficial, why are there two bills in Congress that seek to ban it? One of the bills, H.R. 207, is aimed at keeping anabolic steroids out of the hands of teenage athletes. You don’t condone drug abuse in sports, do you?

Stephen Cherniske: Of course not, but it is absurd to put DHEA in the same category as the anabolic steroids that athletes and body- builders use. Those are synthetic testosterone analogs that produce abnormal muscle growth and have dangerous side effects. You simply cannot create abnormal muscle growth with DHEA. Because of this, there is no evidence whatsoever that athletes of any age are abusing DHEA. The USOC began testing for DHEA abuse in 1996. How many violations have they found? None. Regarding sports performance, a report in the journal Clinical Chemistry states:

“Performance benefits for athletes are neither documented nor proven. DHEA is ‘guilty’ by virtue of its position in the biochemistry of gonadal hormone production.”[132]

Naysayer: Well, some doctors are worried about interactions with prescription drugs.

Stephen Cherniske: Only two possible interactions have been identified. Women taking tamoxifen (an anti-estrogen) and men being treated for prostate cancer with testosterone blockade will not want to take DHEA. These are well-known and well-publicized caveats. On the other hand, studies show that many prescription drugs alter DHEA metabolism or reduce DHEA blood levels.[133] Unfortunately, no one seems to be concerned about this.

Remember that adverse interactions between prescription drugs are extremely common. Popular non-steroidal anti-inflammatory drugs (NSAIDs), including ibuprofen, have scores of adverse interactions that can be life threatening. Again, it is a matter of informed choice. You can’t champion informed choice everywhere else and then call for a ban on DHEA because someone, somewhere might be harmed someday.

I come back to the double standard that is being used to evaluate DHEA. More than 600 Viagra® users have died since that drug was approved. No one has died from taking DHEA and members of Congress are trying to ban it.

Naysayer: But that’s a good case in point. The effects and side effects of Viagra® are well known, whereas the long-term effects of DHEA are unknown.

Stephen Cherniske: You’ve fallen for the biggest myth in all of alth care—that the long-term effects of prescription drugs are known. thing could be further from the truth. A study published in the Journal of the American dical Association reports that “51% of approved drugs have serious adverse effects not ected prior to approval.”[134] Using Viagra® as an example, there are very troubling questions

regarding long-term use. Viagra® has been shown to trigger migraines in the vast majority of migraine sufferers.[135] This was unknown until 2003. How the drug affects cardiovascular health is a continuing debate. But whether or not you believe that Viagra® causes heart attacks, you can't ignore the vast number of reported adverse events associated with the drug. The Journal of the American College of Cardiology published an analysis of the first 13 months Viagra® was on the market. It found 1,473 major adverse reactions reported to the FDA, including 522 deaths, 517 heart attacks, 161 cardiac arrhythmias, and 119 strokes.[136] In reality, of course, this is most likely the tip of an iceberg, as only about 5% of serious adverse drug reactions are reported to the FDA.

Naysayer: Well, what about people on steroid therapy like prednisone?

Stephen Cherniske: DHEA does not reduce the efficacy of prednisone.[137] In fact, it appears to enhance the effectiveness of prednisone therapy by reducing the immune suppression associated with the drug.[138] For this reason, a growing number of researchers and clinicians are recommending that DHEA be used along with prednisone. Studies with lupus patients who are normally treated with prednisone show that supplemental DHEA can significantly reduce symptoms, and many are able to reduce or even eliminate the prednisone.[139]

And while we're talking about chronic inflammatory disease, please remember the Catch-22 of conventional corticosteroid therapy where the desired anti-inflammatory effect is often followed by adverse side effects, including immune suppression, osteoporosis, and the stimulation of pro-inflammatory cytokines including IL-6, nuclear factor-kappa B, and tumor necrosis factor (TNF). Recent research shows that:

1. IL-6 levels tend to increase with advancing age.[140]
2. DHEA is a potent inhibitor of IL-6 in animals and humans.[141]
3. In every chronic inflammatory disease tested, including systemic lupus erythematosus (SLE), rheumatoid arthritis, polymyalgia rheumatica, and inflammatory bowel diseases, DHEA and/or DHEAS levels in patients have been found to be lower than in healthy controls.[142-144]
4. Oral administration with DHEA shows significant promise in the treatment of chronic inflammatory diseases.[145,146]

Naysayer: What about people undergoing surgery?

Stephen Cherniske: Surgical stress has been shown to seriously deplete DHEA, leaving the patient in a more vulnerable state.[147,148] Post-surgical use of DHEA is one of the most appropriate uses of this repair and regenerative signaling molecule.

Naysayer: Who else would be a candidate for DHEA? Don't say, "76 million baby boomers." I want solid science.

Stephen Cherniske: How about 19 million Americans with depression?[149] That's nearly 10% of the adult population.

Naysayer: Studies do show that depressed individuals have much lower levels of DHEA compared to age-matched controls.[10] But that doesn't mean DHEA is a treatment for depression.

Stephen Cherniske: Yes, it is. Numerous studies show that DHEA has profound antidepressive benefits.[17,20,150] Here is one example:

"Elevated cortisol-DHEA ratios may be a state marker of depressive illness and may contribute to the associated deficits in learning and memory. Administration of DHEA may reduce neurocognitive deficits in major depression."[151]

We now know that the brain manufactures large amounts of DHEA. In fact, brain concentrations of DHEA are much higher than plasma concentrations. And just like blood levels, brain levels of DHEA fall dramatically with advancing age.[152] DHEA is now recognized as a critically important neurosteroid, playing an active role in neurotransmitter function, memory, and cognition. And while I am not suggesting that DHEA can treat Alzheimer's disease, it is certainly interesting to note that DHEA levels in the brains of Alzheimer's patients are far lower than in age-matched controls.[153] A study reported in the Journal of Endocrinology Investigations explores the mechanism by which DHEA may block the toxic effects of stress hormones, and concludes that because aging is associated with increasing stress, DHEA may well be of benefit to the normal aging brain.[154] A report in the World Journal of Biological Psychiatry concludes that restoring hormone balance in the brain via supplemental DHEA may significantly reduce risk for many psychiatric diseases.[20]

Importantly, the area of the brain most vulnerable to age-related degeneration is the hippocampus. In healthy elderly subjects, hippocampal volume has been found to correlate directly with DHEA levels,[155] and in animal studies, DHEA supplementation has been found not only to protect the hippocampus from stress hormone-related damage, but also to promote the anabolic repair of nerve tissue and even promote the formation of new neurons. A study just published in the European Journal of Neuroscience concludes:

"These results show that DHEA, a steroid prominent in the blood and cerebral environment of humans, but which decreases markedly with age and during major depressive disorder, regulates neurogenesis in the hippocampus and modulates the inhibitory effect of increased corticoids on both the formation of new neurons and their survival."[156]

In other areas of mental health, DHEA levels were found to correlate directly with better symptom scores in a group of izophrenic patients. The authors note:

“Higher DHEA levels were significantly correlated with lower symptom ratings, better performance on some measures of memory and lower ratings of Parkinsonian symptoms.” A follow-up placebo-controlled human trial published in the Archives of General Psychiatry reports that DHEA supplementation produced significant benefits in patients with schizophrenia.[157]

Etienne-Emile Baulieu, one of the world’s foremost hormone biochemists and a leading DHEA researcher, stated in the Journal of Clinical Endocrinology and Metabolism:

“Logic pleads in favor of oral administration of DHEA at a dose that provides so called ‘young’ DHEA levels in the blood and no T/DHT and E2 concentrations superior to those of normal people of 30 to 40 years of age. Calculations based on production rates, interconversion between DHEA and DHEAS, and metabolic studies suggest that replacement doses of 25-50 mg once daily are able to fulfill this double requirement.”[16]

Concluding statements

Naysayer: I have to say that all of the data that you’ve supplied have surprised me, especially the material relating to DHEA’s potential anticancer role. But there’s one fundamental issue that we haven’t addressed, which could be called the natural law argument. DHEA levels peak late in the third decade of life and then progressively decline. I believe that there is probably a good reason for this, and that manipulating levels of this powerful hormone could have unforeseen consequences, perhaps much later in life. Most of the doctors I know share this feeling and therefore recommend that patients wait until long-term, conclusive studies have been performed.

Stephen Cherniske: What you call “natural law” could also be called the “do nothing” argument, or the “don’t mess with Mother Nature” argument, both of which are more romantic than scientific. The doctors you refer to mess with Mother Nature every day. Mother Nature creates infections that kill people. Doctors prescribe antibiotics to keep them alive. Cholesterol is purely natural and blood levels rise with advancing age, but doctors last year wrote more than 80 million prescriptions to lower cholesterol. Diabetes is natural, but it is treated with a hormone called insulin. We are constantly messing with Mother Nature to prevent death and maintain quality of life. And by the way, a year-long review by the US Office of Technology Assessment found that only 10-20% of all procedures used in medical practice have been shown to be safe and effective by controlled clinical trials.[158]

In other words, health professionals are very comfortable with what is called the risk-reward ratio, or benefits versus possible side effects. This is easy to do when you’re treating a life-threatening infection or a fatal disease, or surgically removing a tumor. In these critical situations, messing with Mother Nature is of no concern.

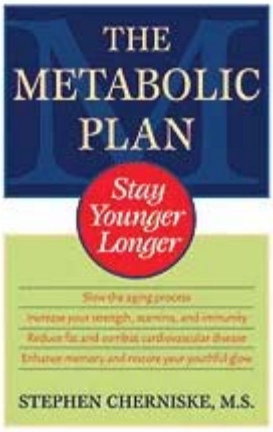
I simply want to suggest that, since aging contributes directly to virtually all disease states, it makes sense to treat aging before the signs and symptoms arise. This is not rocket science. Studies show that the hormone signal (ACTH) that produces a robust DHEA response in young people is significantly blunted in elderly men and women.[152] Restoring DHEA levels is not a magic bullet, but it should be an integral part of any sensible anti-aging effort. Naysayers tell us to wait for "more information" while they ignore the mountain of clinical and research data already in hand. To summarize:

1. DHEA is the most abundant circulating hormone in the human body, and influences more than 150 known anabolic (repair) functions throughout the body and brain.
2. Starting at about age 28, DHEA levels start to decline, and this loss of anabolic drive accelerates with advancing age, so that by age 70, most people are producing only 10-15% of the DHEA they were producing in their twenties.
3. High levels of DHEA are strongly associated with longevity.
4. Low levels of DHEA are associated with depression, dementia, obesity, diabetes, asthma, autoimmune disease, osteoporosis, and increased risk for cancer and cardiovascular disease.
5. Low levels of DHEA are also associated with increased mor- tality in a number of disease states, and one study found low DHEA to be associated with increased risk for death from all causes.[23]
6. One's production of DHEA can be reliably determined by mea- suring DHEA sulfate in serum or by measuring DHEA metabolites in a urine sample (the Anabolic/Catabolic Index, or ACI). This test has been awarded a US patent, the methodology paper was pub- lished in the Journal of Chromatography, and the age correlation study was published in the international journal Spectroscopy.[159-161] The ACI test provides a snapshot view of anabolic drive and is a valid aging biomarker.
7. As opposed to what is "normal" in the aging population, leading endocrinologists believe that optimal restoration of anabolic drive (true anti-aging) will be achieved by maintaining DHEA at the level of a healthy 30-year-old.[124]
8. DHEA is readily absorbed from an oral dose.
9. Most human studies have used a 50 mg/day dose (the high end of the physiologic dose range), although clinically significant benefits can be achieved with doses as low as 10 mg per day.
10. There is no evidence—clinical or experimental—that associates physiologic dose DHEA supplementation with any untoward effects, save the well- known production of oily skin and acne in a small percentage of women.

My final comment relates to your assumption that declining levels of DHEA are a natural and necessary part of the aging process. This is pure speculation. Far more compelling is research showing that declining DHEA production results from progressive atherosclerosis, which reduces oxygen and glucose delivery to the area of the adrenals e zona reticularis) where DHEA is synthesized.[37] We certainly derstand the consequences of decreased blood supply to the heart brain (heart attacks and stroke). Since the blood vessels leading to se organs are a great deal larger (and less convoluted) than those

leading to the adrenals, it is not hard to see how age-related arterial blockage and stiffening can affect the production of DHEA. Thus, far from being a “natural” part of the aging process, declining DHEA synthesis appears to be an unrecognized aspect of cardiovascular pathology.

For information about Stephen Cherniske's book, The Metabolic Plan, refer to the inside back cover of this magazine. Stephen Cherniske can be reached at stephenC@oasisnetwork.com (mailto:stephenC@oasisnetwork.com).



Page	1 (/Magazine/2004/3/cover_dhea/Page-01)
2 (/Magazine/2004/3/cover_dhea/Page-02)	3 (/Magazine/2004/3/cover_dhea/Page-03)
4 (/Magazine/2004/3/cover_dhea/Page-04)	5 (/Magazine/2004/3/cover_dhea/Page-05)