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The DHEA Debate

March 2004

COVER STORY

A critical review of clinical and experimental data

x) **Naysayer:** But DHEA is converted to testosterone and estrogen . . .

Stephen Cherniske: Some DHEA is converted to testosterone and estrogens. But there are enzymes in every tissue of the human body and brain that metabolize DHEA itself. The idea that DHEA is merely a reservoir for sex steroids was debunked decades ago. A recent study in the journal Steroids documents the anticancer effects of DHEA and all of its major metabolites.¹¹⁵ Likewise, the ability of DHEA to reduce risk for cardiovascular disease is independent of its conversion to sex steroids.¹¹⁶ A study with 375 men with a mean age of 60 found that sexual activity and satisfaction was far more closely associated with DHEA levels than testosterone.⁹⁸

Naysayer: But it is converted to testosterone and estrogen . . .

Stephen Cherniske: Yes it is, but are you saying that is inherently unsafe?

Naysayer: Well, look at the disaster that we just saw with hormone replacement therapy (HRT).

Stephen Cherniske: That was caused by conventional HRT

ing large doses of synthetic hormones. Yes, that was a disaster, given more than 80 million women, which actually increased risk for breast cancer, stroke, and pulmonary embolism.¹¹⁷ So, because large amounts of synthetic hormones increased disease risk, you believe that small



amounts of a natural hormone will do the same thing, even though we've been over this already and you've seen that there is no evidence that DHEA promotes abnormal growth of any tissue in the human body. Even though studies with human volunteers show that a 50-mg daily dose of DHEA does not elevate systemic or blood levels of estradiol.¹⁹ Heck, human studies with 200 mg of DHEA per day have shown no systemic elevation of estradiol.¹¹⁸ On the contrary, conversion of DHEA to sex steroids appears to take place on an as-needed basis, through an inherent self-regulating activity.



The dangers of HRT stem not only from the systemic elevation of estradiol. We now know that HRT lowers DHEA levels.¹¹⁹ Importantly, DHEA supplementation does not raise sex steroid levels above normal. Most of the repair and regenerative benefits of DHEA come from local (or peripheral) anabolic activity such as was recently demonstrated in Mechanisms of Ageing and Development. This important study utilizing genomic technology revealed that DHEA improves bone density, not by raising systemic levels of estradiol but through local conversion to estrone by osteoblasts.¹²⁰ In other words, DHEA is converted by repair cells in the bone to estrone, which does not promote cancer, while leaving estradiol levels in the breast and uterus unchanged.

In fact, a growing number of endocrinologists are realizing that the solution to maintaining bone density in postmenopausal women was staring us in the face for more than 40 years, but the pharmaceutical-based health care system ignored this natural, safe, and effective treatment in favor of prescription drugs, even though those drugs have been known to be unsafe for at least the last 15 years.



Research shows conclusively that DHEA deficiency contributes significantly to age-related bone loss in men and women.⁴² And a recent study with postmenopausal women demonstrates the significant anabolic benefits that can be obtained from DHEA supplementation. Women in the treatment group experienced improvements in virtually all anabolic (repair) hormones, including DHEA, estrone, estradiol, androstenedione, and testosterone. Importantly, none of these steroids rose to levels that would be considered unsafe. What's more, increases in osteocalcin and IGF-1 indicate that 50 mg of DHEA might be more effective in maintaining bone density than high doses of synthetic estrogen and progestins (conventional HRT). The researchers conclude:

“Our data support the hypothesis that DHEA treatment acts similarly to estrogen-progestin replacement therapy on the GHRH-GH-IGF-1 axis. This suggests that DHEA is more than a simple ‘antiaging product’; rather it should be considered an effective hormonal replacement treatment.”¹²¹

The final note on women's health is the ability of DHEA supplements to help balance estrogen and progesterone.



Naysayer: How can that be? DHEA is not converted to progesterone.

Stephen Cherniske: Not directly, but DHEA can raise progesterone levels by inhibiting conversion of pregnenolone to cortisol (via 17-hydroxyprogesterone).¹²² Thus, by any measure, DHEA appears to be a valuable and safe hormone supplement for women and men.

Naysayer: Men don't need progesterone.

Stephen Cherniske: Of course they do. And a study just published with men suffering from fatigue and depression suggests that improvements in mood, energy, and libido derived from 25 to 50 mg of DHEA resulted from increased progesterone levels, not testosterone.¹⁸

Naysayer: There's still no proof that DHEA is safe.

Stephen Cherniske: Yes, there is. You've been trying to persuade the public that safety data do not exist, when there are adequate human clinical trials, including year-long studies with as many as 300 volunteers. Listen to the conclusion of one of these studies published in the Journal of Clinical Endo-crinology and Metabolism. This is a human study with a 25-mg/day group and a 50-mg/day group:



“No accumulation of steroids was observed. No worrying transformation to androgen and estrogen was recorded; indeed, the limited increased estradiol in aged women could be predicted to be beneficial. These results suggested that daily oral administration of DHEA (25/50 mg) is safe in elderly subjects. The 50-mg dose was chosen for a 1 yr, double blind, placebo-controlled trial of daily oral administration of DHEA in 60- to 80-yr-old individuals.”¹²³

This was followed by an even larger, year-long evaluation. This landmark project, known as the DHEAge study, was published in the Proceedings of the National Academy of Science. The conclusion:

“No potentially harmful accumulation of DHEAS and active steroids was recorded . . . A number of biological indices confirmed the lack of harmful consequences of this 50 mg/day DHEA administration over one year, also indicating that this kind of replacement therapy normalized some effects of aging.”¹²⁴

Naysayer: Well, what about the well-known side effects that DHEA produces in women?

Stephen Cherniske: Such as?

Naysayer: Oily skin, acne, and growth of facial hair.





Stephen Cherniske: Those are overdose effects, and to produce these effects, a woman would have to take an excessive dose of DHEA for months. Importantly, these effects are obvious and sequential.

In other words, if a woman takes too much DHEA, she may experience side effects from the conversion of DHEA to testosterone. The first sign is oily skin. If she ignores this and does not reduce her dose, she may develop testosterone-related acne. If she ignores the acne and continues to overdose, she may start to see hair growth on her upper lip. Importantly, these side effects are reversible and certainly not life threatening.

Naysayer: Still, such side effects are distressing.

Stephen Cherniske: But you're talking as if side effects are common, when in fact they are rare. At the clinically effective dose of 5 to 25 mg, the incidence of androgen-related side effects is less than 2%.¹²³ Compared to the known benefits, and the ease by which a safe dose can be determined, it is unreasonable and unscientific to harp on side effects that are rare and innocuous. Tremendous health benefits are obtainable from 5 to 25 mg of DHEA. It significantly reduces risk for diabetes and cardiovascular disease at 25 mg per day.³ These two degenerative diseases account for more than 70% of deaths in the US and all you can do is wring your hands about an adverse effect that might occur at four or five times that dose.

Naysayer: Well, DHEA is sold in health food stores. People are naturally going to think that any dose is safe.

Stephen Cherniske: Aspirin is sold in convenience stores and gas stations. Aspirin can cause gastrointestinal bleeding and other side effects.

There is an absurd double standard being used here. You promote the sale and use of high-dose aspirin, which can have serious side effects, because you believe in the principle of informed choice. Yet when it comes to DHEA, you don't think people are capable of making an intelligent decision.

Naysayer: But women do not know how much DHEA they are presently producing.

Stephen Cherniske: Exactly. This is part of the education process that should be in high gear; but the exact opposite is taking place. Instead of encouraging women to measure their DHEA levels, many doctors are telling them that it doesn't matter. Instead of receiving guidance on a critically important aspect of health and wellness, patients are being misled. With what we know about the influence of DHEA on health and disease, this should be a top priority. Women with severe symptoms associated with menopause (known as climacteric syndrome) have DHEA levels that are roughly half those of age-matched controls,¹²⁵ but few physicians know this.



FACT: For 70% of women, the gynecologist is the only doctor they see.

Naysayer: You keep talking about DHEA supplementation, but couldn't people just exercise and get the same benefit? After all, studies show that individuals who exercise regularly have higher levels of DHEA and IGF-1.^{126,127}

Stephen Cherniske: I agree, but let's look carefully at this correlation. In a recent study with elderly women, DHEA and IGF-1 were directly related to daily activity, physical exercise, muscle strength, and respiratory efficiency. The authors conclude that exercise must therefore have a positive effect on anabolic hormones.¹²⁸ I call this the Jack LaLanne effect, but it is important to understand that the converse is also true; that some people have a genetic ability to maintain higher levels of DHEA, which stimulates IGF-1, and this maintenance of anabolic drive is what enables them to remain active and to perform physical exercise. The vast majority of Americans do not have this genetic advantage. If people are on the "catabolic" side of life with poor exercise tolerance, telling them to "just exercise more" is unfair and unscientific. Better to improve anabolic drive via DHEA supplementation, and then go to the gym. They will suffer less and achieve better results.



Naysayer: You don't know that.

Stephen Cherniske: Yes, we do. In a study funded by the National Institutes of Health, Dr. Dennis Villareal and his colleagues conducted a double-blind, placebo-controlled human clinical trial using 50 mg of DHEA per day with a group of elderly men and women. After only six months, those taking DHEA experienced improvements in muscle mass and bone density, and a reduction in body fat.²

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