

Orentreich  
Foundation for the  
Advancement of  
Science, Inc.

# VitalLongevity™

Logo: Life's blood flows through the hourglass; the stopcock represents the alteration of aging and disease as biomedical research progresses.

December 2005

## DHEA and DHEAS

First, some technical basics: Dehydroepiandrosterone sulfate (DHEAS) is the most abundant steroid circulating in the blood. DHEAS and its non-sulfate form, DHEA, are readily interconvertible in the human body. DHEAS is water/blood soluble whereas DHEA is fat-soluble and is used and stored by fat and other tissues.

More than 20 years have passed since OFAS researchers first published the normal human blood levels of this controversial 'aging hormone' (see graph, page 2). But as the American population ages, and as its blood levels of DHEAS produced by the adrenal gland continue to decline, the controversy still rages about the supposed benefits and risks of DHEA supplementation. In this issue of *VitaLongevity*, OFAS weighs in again on this much touted—and much maligned—molecule.

### Natural Adrenal Prohormone

The adrenal glands are central to the body's system for handling stress. They make vital steroid hormones that maintain blood sugar (glucocorticoids, principally cortisol) and blood volume (mineralocorticoids, principally aldosterone). They also make a class of compounds called adrenal androgens, but this is an unfortunate misnomer because the adrenal androgens are inactive metabolic intermediates that can only be turned into active androgens (or estrogens) by other tissues. Adrenal androgens are, therefore, more correctly referred to as prohormones.

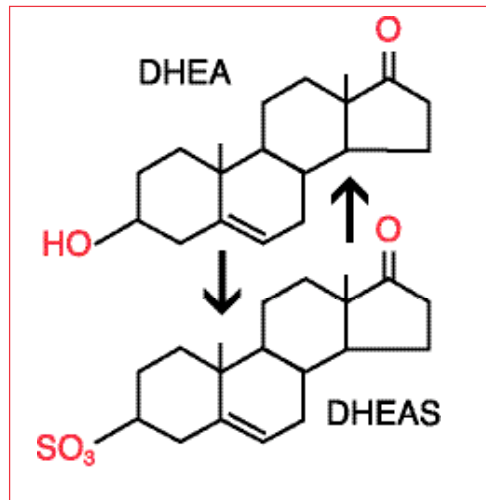
### Changes with Age

The fetal adrenal glands make large amounts of DHEAS. After birth, DHEAS levels in the blood fall to almost zero and remain low until age 7 or 8, when they start to rise (an event called adrenarche) year by year. DHEAS levels peak during the third decade of life and decline steadily thereafter, falling about 80% by age 70. On average, women have about one third lower levels than men, but the pattern of change with age is the same in both genders, as shown on page 2. (The graph, adapted from

the 1984 paper by Orentreich, *et al.*, is one of the most commonly cited, authoritative references for normal blood levels of DHEAS.)

### Natural Roles

In women, DHEA is a major source of prohormone for the synthesis of androgens, such as testosterone, which are needed by certain tissues, *e.g.*, oil (sebaceous) glands in the skin. This is why many women in their thirties begin to feel their skin getting naturally drier, when their DHEAS production has begun to fall. (DHEA penetrates the skin, and DHEA in creams and lotions actually gets to the oil glands to reactivate sebum production.) For young women in whom adrenal DHEAS production is high, it is sometimes clinically beneficial to suppress its production with cortisol for the treatment of acne. Androgens and estrogens made from DHEA also play important roles in maintaining the health of bones and proper functioning of the immune and nervous systems. In addition, DHEAS itself is made in the nervous system (and thus sometimes referred to as a neurosteroid); it can act on some neurons rapidly and directly, *i.e.*, without being converted to an active androgen.



DHEA and DHEAS are interconvertible in the human body.

### Replacement

In 2004, a major 5-year clinical trial of estrogen/progestin hormone replacement therapy (HRT) for postmenopausal women had to be halted after only 3 years. The study was designed to confirm earlier data that HRT is beneficial for cardiovascular health. However, contrary to expectations, HRT was found to increase significantly the risk of stroke and heart attack, as well as breast cancer. This bad news caused a tectonic shift in medical thinking about the benefits of HRT; since then the use of HRT has dropped about 50%, with many women still searching for a safe alternative.

Enter DHEA. While not a cure-all for every postmenopausal ailment, the benefits of DHEA are impressive. Clinical studies have proven that it cures vaginal dryness, being converted to estrogen by vaginal tissue. DHEA has also been shown to restore bone mass lost to postmenopausal osteoporosis. And just this year, an NIH

research team reported their clinical trial results in the American Medical Association's Archives of General Psychiatry, with rare conclusive language: "We find DHEA to be an effective treatment for midlife-onset major and minor depression." Long-term DHEA replacement could help ward off Metabolic Syndrome by improving fat utilization and increasing lean body mass. In one study, for example, men and women taking 50 mg/day of DHEA for six months lost significant amounts of abdominal fat, and their insulin action improved.

## How Safe Is It?

Most readers probably are expecting a list of potential risks as impressive as the list of DHEA's benefits. Happily, that is not the case because, unlike some other steroid hormone precursors such as "andro" (androstenedione), the ability of cells to convert DHEA to active androgens and/or estrogens is very selective. For example, DHEA has consistently been associated with lower—not higher—risk of breast cancer; also, it does not increase the risk of uterine cancer because the uterine lining cannot convert it to estrogen. Further, the skin's ability to turn DHEA into active androgens is essentially restricted to oil glands. Thus, DHEA can increase the skin's natural moisturizing capacity, while neither increasing facial hair growth nor making scalp hair fall out. In fact, the only frequent side-effect is mild acne in susceptible women: a cosmetic, easily reversible condition.

## Bad Press

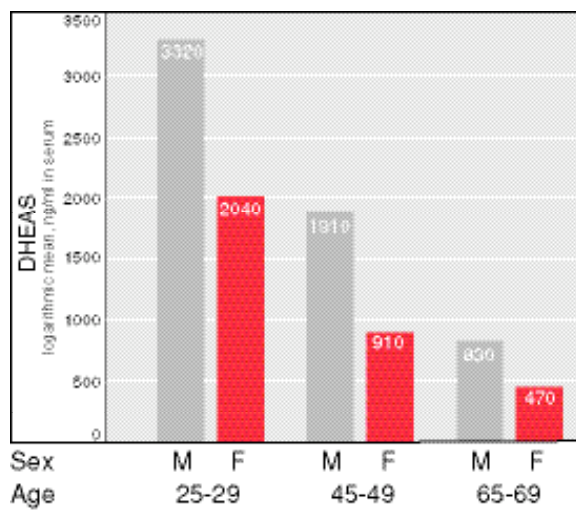
Despite its impressive upside and almost non-existent downside, DHEA—since it is technically a steroid—is often lumped with performance-enhancing drugs. DHEA is even naïvely banned as such by the International Olympic Committee and some professional sports associations. And this is despite the fact that DHEA cannot be converted to active androgens by muscle tissue and thus cannot build muscle (in contrast to advertising claims).

## Catch-22

Without substantiating reports of any serious side-effect(s), those wanting DHEA banned for even prescribed use point to a "catch 22", *i.e.*, the absence of large-scale clinical trials. Such trials typically cost millions of dollars, and DHEA—a benign substance naturally produced in large

quantities by the human body—will never make a large-scale return on corporate investment. This phenomenon almost guarantees that the safety of DHEA will never be proven. Therefore, we maintain a healthy skepticism of published clinical trials that question the safety of DHEA while showing no evidence of risk; potentially more suspect are studies funded by makers of HRT.

If laboratory tests show your DHEAS level to be low for your age and sex, 25-50 mg/day of DHEA taken in the evening restores serum DHEAS to concentrations within the normal range and maintains that level throughout the day.



DHEAS Decreases with Chronologic Age

Adapted from: Orentreich N, Brind JL, Rizer RL, Vogelman JH. *Journal of Clinical Endocrinology and Metabolism* 59:551-5, 1984.

## Bottom Line

As a dietary supplement, DHEA has been around for decades, with no serious side-effects reported, despite use by millions of men and women.

Does it cure everything or live up to all the claims made for it by food supplement sellers? No.

Does it have demonstrable benefits for older people, whose own DHEA production has markedly declined, especially postmenopausal women? Yes.

Is it safe to take without a prescription or medical supervision? Most likely, especially if in 'rational' amounts. One distinct advantage of medical supervision, however, is that blood tests can guide dosage to achieve the desired replacement or physiologic level.

## INFORMATION FOR DONORS

The Orentreich Foundation for the Advancement of Science, Inc., was founded in 1961. OFAS is a non-profit institution dedicated to biomedical research to prevent, halt, or reverse those disorders that decrease the quality or length of life. It is duly registered with the US Internal Revenue Service as an Operating Private Foundation under Section 4942(j)(3).

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