

# DHEA Deficiency and Treatment

## An information sheet for Doctors and Patients

DHEA (dehydroepiandrosterone) is one of the most abundant substances made by the adrenal gland. It is the precursor of the sex steroids oestrogen and testosterone. A small amount of DHEA is also made by the ovaries. Individuals with a deficiency of the pituitary gland, the adrenal gland or ovaries have low circulating concentrations of DHEA. Recent studies have shown that treatment of DHEA deficiency can be beneficial. In earlier years it was thought sufficient for well-being to replace only the major hormones made by the adrenal gland - cortisol is replaced by hydrocortisone and aldosterone by fludrocortisone. DHEA has weak male hormone effects and a lack of DHEA is thought to contribute to fatigue, poor concentration and diminished overall well-being. It is only very recently that good quality scientific studies have shown that replacing DHEA, particularly in women, improved these symptoms.

DHEA has been considered a "peripheral substance" and as yet it does not appear in the British National Formulary. The reason for this omission is probably historic. That is, DHEA has been the focus of research into ageing and many studies have attempted to show that supplements of DHEA in old age might slow the ageing process. These studies have taken place in individuals with normal adrenal and pituitary glands and have unfortunately obscured the benefit to individuals with clear-cut medical conditions of proven DHEA deficiency. DHEA can be measured on a simple blood test as is reported at DHEAS (S for sulphate). The normal range for DHEA at the Middlesex Hospital is female 0.95 - 11.6 umol/L for women and 2.20- 15.2 umol/L for men.

In the United Kingdom DHEA is available through IDIS World Medicines, Millbank House, 171-185 Ewell Road, Surdinton, Surrey, KT6 6AX, Tel: 0208 410 0700. Tablets are available in the dose range 5, 10, 25 and 50 mg. The average replacement dosage for individuals with DHEA deficiency is 25 to 50 mg although some gain benefit with the lower doses of 5 to 10 mg.

The side effects of DHEA relates to its weak male hormone activity. Women might experience greasiness of the skin, unwanted hair growth and acne. These side effects are usually avoidable if sufficiently low doses of replacement are used. DHEA is prescribed in the usual way but pharmacies will usually need to order a supply. Two recent papers are available which show the benefit for individuals with adrenal failure or pituitary disease in randomised controlled trials. These papers show particular benefit in concentration and libido in women.

### Improvement in Mood and Fatigue after Dehydroepiandrosterone Replacement in Addison's Disease in a Randomized, Double Blind Trial

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#### Abstract

Dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS) are adrenal precursors of steroid biosynthesis and centrally acting neurosteroids. Glucocorticoid and mineralocorticoid deficiencies in Addison's disease require life-long hormone replacement, but the associated failure of DHEA synthesis is not corrected. We conducted a randomized, double blind study in which 39 patients with Addison's disease received either 50 mg oral DHEA daily for 12 weeks, followed by a 4-week washout period, then 12 weeks of placebo, or *vice versa*. After DHEA treatment, levels of DHEAS and D 4 -androstenedione rose from subnormal to within the adult physiological range. Total testosterone increased from subnormal to low normal with a fall in serum sex hormone-binding globulin in females, but with no change in either parameter in males. In both sexes, psychological assessment showed significant enhancement of self-esteem with a tendency for improved overall well-being. Mood and fatigue also improved significantly, with benefit being evident in the evenings. No effects on cognitive or sexual function, body composition, lipids, or bone mineral density were observed. Our results indicate that DHEA replacement corrects this steroid deficiency effectively and improves some aspects of psychological function. Beneficial effects in males, independent of circulating testosterone levels, suggest that it may act directly on the central nervous system rather than by augmenting peripheral androgen biosynthesis. These positive effects, in the absence of significant adverse events, suggest a role for DHEA replacement therapy in the treatment of Addison's disease. (*J Clin Endocrinol Metab* 85: 4650-4656, 2000)

### Low Dose Dehydroepiandrosterone Affects Behavior in Hypopituitary Androgen-Deficient Women: A Placebo-Controlled Trial

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#### Abstract

Thirty-eight women, aged 25-65 yr, with androgen deficiency due to hypopituitarism were treated with oral dehydroepiandrosterone (DHEA; 30 mg/d if <45 yr of age and 20 mg if >45 yr of age) for 6 months in a randomized, placebo-controlled, double blind study, followed by a 6-month open treatment period. The administration of DHEA raised the serum levels of DHEAS to normal age-related reference ranges and increased androstenedione and T to subnormal levels. Androgen effects on skin and/or pubic and/or axillary hair were observed in 84% (32 of 38) of the women after all received 6 months of DHEA treatment. No such effects were observed after the placebo treatment. These effects after 6 months were correlated with the serum levels of DHEAS ( $r = 0.37$ ;  $P = 0.03$ ), androstenedione ( $r = 0.42$ ;  $P = 0.01$ ), and T ( $r = 0.37$ ;  $P = 0.03$ ). The percentages of partners who reported improved alertness, stamina, and initiative by their spouses were 70%, 64%, and 55%, respectively, in the DHEA group and 11%, 6%, and 11%, respectively, in the placebo group ( $P < 0.05$ ). According to the partners, sexual relations tended to improve compared with placebo ( $P = 0.06$ ). After 6 months of treatment, increased sexual interest or activity was reported by 50% of the women taking 30 mg DHEA, by none taking 20 mg DHEA, and by two women taking placebo ( $P = NS$ ). Compared with levels after placebo administration, high density lipoprotein cholesterol and apolipoprotein A-1 levels decreased after DHEA. Serum concentrations of IGF-I, serum markers of bone metabolism, and bone density did not change. In conclusion, oral administration of a low dose of DHEA to adult hypopituitary women induced androgen effects on skin and axillary and pubic hair as well as changes in behavior, with only minor effects on metabolism. (*J Clin Endocrinol Metab* 87: 2046-2052, 2002)