

# **Hormonal and nutritional treatments in anti-ageing medicine: A position statement from the Swiss Society for Endocrinology and Diabetes**

## **INTRODUCTION**

The discovery of hormone replacement therapies for patients with diabetes, hypothyroidism or Addison's disease has been among the great successes of medicine in the early 20th century. Hence, it is understandable that hormone replacement has also been explored for persons with mild (sub clinical) deficiencies, or for the elderly with a physiological age-related decline in estrogen, testosterone, DHEA and GH.

Since the use of hormone prescription for these non-classical indications has expanded over the past decade, US as well as Swiss agencies have issued statements regarding the potential adverse effects of such therapies, including their financial consequences, in the ageing population (refs 1, 2). The aim of this statement is to summarize the position of the Swiss Society for Endocrinology and Diabetology with regard to the most frequently considered anti-ageing therapies, while more detailed statements and references can be found on our web site (<http://www.sgedssed.ch>).

## **TESTOSTERONE**

Observational studies suggest that male aging is associated with a gradual decrease in circulating testosterone levels, although the reality and potential clinical significance of so-called 'andropause' remain unclear. Since androgen deficiency in younger men is corrected safely and effectively by testosterone replacement, this created an opportunity to harness the beneficial anabolic and mental effects of testosterone to improve physical functioning in older men: testosterone replacement was expected to prevent the frailty, falls and fractures that affect quality of life and threaten independent living.

Randomized, placebo-controlled trials in elderly men have been characterized by small sample size and inclusion of healthy subjects with low or low-normal testosterone levels who were otherwise asymptomatic. In such trials, testosterone administration has been associated with sustained increases in its own levels accompanied by significant changes in body composition and partial improvement in muscle strength. Effects on bone mineral density, sexual and cognitive functions were at best inconsistent. Importantly, the studies did not have sufficient power to detect meaningful gains in patient-important outcomes such as physical function, fracture risk and quality of life. Finally, the available evidence of long-term prostate and cardiovascular safety remains very limited.

Testosterone supplementation of healthy elderly men is therefore currently not recommended. Noting the absence of convincing evidence of efficacy, a report of the Institute of Medicine has recommended that further research should focus on men older than 65 years who are most likely to benefit from androgen therapy, specifically those with characteristic (albeit non-specific) symptoms and considerably low serum testosterone levels.

## **DHEA**

DHEA is produced by the adrenal gland and other than being a pro-hormone, its physiological relevance is not yet fully elucidated. Nevertheless, a benefit of treatment with small doses of DHEA has been reported in women with complete adrenal failure.

The levels of DHEA may decrease with age, and several trials have aimed at demonstrating benefits of replacement therapies on cognitive and sexual function, or bone health. None of these studies has yielded conclusive results for clinically relevant benefits. On the contrary, DHEA can be metabolized into estrogens or androgens in various tissues (e.g. breast and prostate), raising concerns for long-term adverse effects. DHEA supplementation of healthy elderly subjects is therefore currently not generally recommended. It could however be justified for selected patients with adrenal failure who remain symptomatic despite adequate replacement with hydrocortisone.

## **GROWTH HORMONE**

The function of growth hormone (GH) is to promote growth in children. Physiological growth relies - amongst other influences - on the anabolic effect of GH (increase in muscle mass and bone mass), which also has a potent lipolytic role, thus providing efficient energy for its anabolic action. However, GH induces peripheral insulin resistance that can lead to glucose intolerance and diabetes mellitus in cases of hormonal excess. The rationale for using GH as an antiaging therapy lies in the physiological age-related decline in activity of the hypothalamic GH-insulin-like growth factor-1 (IGF-1) axis as well as in the observation that severe GH-deficiency is associated with increased adiposity and decreased lean body mass, two changes also occurring with aging.

A systematic review of randomized controlled trials of GH therapy vs. no GH or lifestyle changes in elderly patients confirmed that GH decreases fat mass and increases lean body mass, without altering bone density or serum lipid levels. However, the studies examined were of short duration and relatively small size (including a total of 220 subjects). Moreover, elderly subjects receiving GH supplementation were significantly more likely to experience soft tissue edema, arthralgias and carpal tunnel syndrome, in keeping with symptoms of patients with acromegaly. It is therefore, conceivable that long-term GH therapy in healthy elderly subjects will also result in an increased incidence of colon polyposis and cardiomyopathy. GH supplementation in healthy elderly subjects supplementation is therefore currently not generally recommended. Available data suggest that the risks far outweigh potential benefits when it is used as an antiaging treatment in healthy older adults.

## **THYROID HORMONES**

T4 is the treatment of choice for hypothyroidism, with the aim of normalizing serum TSH levels. However, thyroid hormones are also used occasionally as part of certain weight loss programs in patients with normal thyroid function. Although the administration of excess thyroid hormones to such patients may induce weight loss and a decrease in fat mass, this is accompanied by a decrease in muscle mass, as well as accelerated bone loss and adverse cardiovascular outcomes. Hence, the use of T4 must be limited to patients with proven hypothyroidism and excess doses are only indicated in patients with uncured or high-risk differentiated thyroid cancers.

## **NUTRITIONAL SUPPLEMENTS AND ANTI-OXYDANTS**

Free radicals, the reactive products of normal oxidative cellular processes, can accelerate ageing via protein degradation, damage of DNA and RNA and alteration of cell membranes. Administration of antioxidants and/or essential nutrients has been advocated to decrease free radicals and reduce their damaging effects. Five major categories of food supplements have been identified: essential micronutrients, metabolites having vitamin-like roles, natural oils, natural plants and antioxidants (vitamins C-E,  $\beta$ -carotene, selenium and zinc). However, evidence of benefit from the consumption of antioxidant agents and/or micronutrient supplement is sparse. While observational evidence suggests that high intake of these products can protect against chronic diseases and reduce the risk of cancer, several large placebo-controlled trials have shown that supplements are ineffective or even damaging. Even worse, increases in both total and cancer mortality have been reported in smokers treated with  $\beta$ -carotene, and a recent meta-analysis has also suggested that retinol and vitamin E supplements may increase mortality.

The use of nutritional supplements and anti-oxidants is therefore generally not recommended. However, it can be justified for selected patients with clinical or sub clinical nutritional deficiencies.

## **CONCLUSIONS**

Many symptoms associated with aging resemble those of true hormone deficiency in young adults. Since appropriate hormone replacement therapy has proven beneficial for hormone-deficient patients, and given the fact that aging has been associated with decreasing hormonal levels, hormone replacement of healthy elderly subjects has become increasingly popular in anti-aging medicine. However, associations do not imply causality, and there is very little evidence to link symptoms such as decreasing muscle mass, increasing adiposity or a depressed mood with any hormonal deficit in the elderly. Until the evidence comes, we recommend that regardless of the hormone under consideration, replacement therapy at any age should be restricted to symptomatic patients with clearly documented hormonal insufficiency.

## **REFERENCES**

1. DHSS / GAO report on the dangers of anti-ageing medicine
2. SWTR Report

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