

Hormone Replacement

The Fountain of Youth?



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KEYWORDS

- Older adults • Hormone replacement therapy • Antiaging • Menopause
- Andropause • Sexual function

KEY POINTS

- Hormones and hormone precursors have been investigated as antiaging treatments to delay the onset or progression of age-associated changes in body composition, strength, and physical and cognitive function.
- Dehydroepiandrosterone and growth hormone have been investigated. Most studies have included small sample sizes and have been of short duration. Results have generally been mixed, at best.
- Menopausal hormone therapy (MHT) is effective in treating vasomotor and genitourinary symptoms of menopause in women. However, due to safety considerations, patients require individualized treatment and need to evaluate the risks and benefits before MHT use.
- Testosterone has been shown to be effective in older men with hypogonadism who have demonstrated declines in physiologic function. Clinical practice guidelines for appropriate diagnosis and treatment have been published.
- The lack of clinical studies evaluating the long-term effects and risks of hormone replacement for antiaging indications limit its use.

INTRODUCTION

One need only to look at advertising in mass media to recognize that aging is frequently viewed as a health condition that can be remedied by any number of products, from pills to injections to creams and lotions. It often seems that a major goal in life is to age while remaining young (Dorian Gray, anyone?). Toward that end, medical science has brought us hormones, hormone precursors, hormone analogs, and several other products to help people achieve that goal. For some, aging and

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appearance are equated with health status.¹ Antiaging is viewed by many as successful aging.² Supplements and other products are heavily advertised, promising to restore youthful function. These include growth hormone (<https://www.youtube.com/watch?v=CGevQwAYnJo>), dehydroepiandrosterone (DHEA) (<https://www.youtube.com/watch?v=fqBMXqg8XYM>), testosterone supplements (https://www.youtube.com/watch?v=SBx1Cn_GmK4), and female hormone replacement products (<https://www.youtube.com/watch?v=OBW-C31uTyM>).

Natural aging is accompanied by reduced production of growth hormone and sex hormones. The reductions begin in middle age, with noticeable physiologic changes becoming evident by the sixth or seventh decade of life. The changes are responsible for lost muscle mass, reduced energy, exercise capacity, and alterations in sexual function. Several factors are responsible for these changes.

Although some form of hormone replacement therapy (HRT) for women has been prescribed for nearly a century, the use of DHEA, growth hormone, and testosterone for men, has been much more recent.³ There remains much controversy regarding the benefits and risks associated with these treatments. This article reviews the available evidence of therapeutic efficacy and the adverse effects of the more commonly used agents.

Dehydroepiandrosterone

DHEA, a precursor of steroidogenesis, is secreted by the adrenal glands. It is metabolized to androstenedione, which in turn is metabolized to estrone and estradiol in women, and to testosterone in men. DHEA production peaks in early adulthood and declines over time.

The use of DHEA to affect the physical aging process was sparked by results of animal studies, which demonstrated prevention of cancer, heart disease, diabetes, and obesity, as well as positive effects on the immune system. It also has been shown in animal models to improve survival of central neurons and glial cells, and improve learning and memory.⁴ Because it is metabolized to testosterone and estradiol, DHEA has also generated interest as a potential therapy to reverse age-associated declines in sex hormones.

Several studies have been conducted in humans to evaluate the effect of DHEA on several aspects of physical and cognitive aging. Results have been mixed, at best, with few studies identifying any major positive effect (**Table 1**). Most studies have included small samples and have been of short duration. In addition, several other methodological reasons have been identified as constraints to obtaining consistent results in humans, including differences between animal and human models, doses used in studies, effects of aging and comorbidities, and variability in what is considered a normal DHEA serum value.⁵ In general, although relatively free of significant adverse effects in doses of 100 mg/d or less, DHEA has not been found to produce notable benefit to reverse the effect of aging.^{4,6,7} Additionally, the Beers Criteria for Potentially Inappropriate Medications (PIMs) Use in Older Adults recommends avoiding the use of growth hormone, except as hormone replacement after pituitary gland removal.⁸

Growth Hormone

Growth hormone and insulin-like growth factor-1 decline with advancing age, leading to metabolic disorders, including insulin resistance, cardiovascular changes, and increased frailty.²¹ The decline in growth hormone secretion is accompanied by an alteration in release pattern, resulting in altered effects. From peak levels, growth hormone secretion may decline by as much as 70% by the eighth decade of life.²¹

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