

## RETROSPECTIVE

# Can Growth Hormone Prevent Aging?

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Does growth hormone prevent aging? An article by Rudman et al. that appeared in the *Journal* in 1990<sup>1</sup> reported the effect on body composition of administering human growth hormone for six months to 12 older men. This article incited a proliferation of “antiaging” clinics and lay publications, such as “Grow Young with HGH,” extolling the benefits of growth hormone in reversing or preventing aging. There are several Web sites that attempt to sell various oral and inhaled formulations of growth hormone; none of these formulations have been shown to be efficacious. In fact, since growth hormone is a peptide subject to degradation by gastric acid, oral preparations would not be expected to be effective. Other Web sites are selling oral formulations (branched-chain amino acids) that are claimed to release growth hormone. These oral formulations are based on studies of intravenous arginine. Intravenous arginine increases serum concentrations of growth hormone transiently (for less than one hour). The effect of oral branched-chain amino acids is akin to that of eating a steak. Clinical medicine is practiced on the basis of established evidence regarding outcomes. What is the evidence supporting the use of growth hormone to prevent aging?

First, it is necessary to recall exactly what the study by Rudman et al. demonstrated. Twelve healthy men, 61 to 81 years of age, who had serum concentrations of insulin-like growth factor I below those found in normal young men received growth hormone for six months. (Insulin-like growth factor I mediates the action of growth hormone, and its concentration reflects the circulating concentration of growth hormone.) The weekly dose of growth hormone was approximately twice as high as the dose used in adult men with a growth hormone deficiency.

The administration of growth hormone in older men resulted in a 4.7-kg increase in lean body mass, a 3.5-kg decrease in adipose mass, and an increase of 0.02 g per square centimeter in lumbar-spine density; systolic blood pressure and the fasting glucose concentration increased significantly. The study was not double-blind (there was a control group

consisting of nine men who received no treatment); there were no assessments of muscle strength, exercise endurance, or quality of life. This study is the basis for claims that growth hormone reverses aging. My editorial accompanying the article by Rudman et al.<sup>2</sup> concluded that such studies in older adults “should be viewed as an important beginning,” with the implication that subsequent studies would determine the benefits and risks of growth hormone treatment in older adults.

A recent double-blind, placebo-controlled study involving 27 women and 34 men, 68 to 88 years of age, who were given growth hormone or placebo for 6.5 months confirmed the effects of growth hormone on body composition; there was no change in muscle strength or maximal oxygen uptake during exercise in either group.<sup>3</sup> This study corroborated the findings of a study by Papadakis et al. involving 52 healthy men, 70 to 85 years of age, who were given placebo or growth hormone for six months.<sup>4</sup> Not mentioned on the “antiaging” Web sites is a study of 18 healthy men, 65 to 82 years of age, who underwent progressive strength training for 14 weeks, followed by an additional 10 weeks of strength training plus either growth hormone or placebo.<sup>5</sup> In that study, resistance exercise training increased muscle strength significantly; the addition of growth hormone did not result in any further improvement. Going to the gym is beneficial and certainly cheaper than growth hormone.

The second consideration is the effect of long-term administration of growth hormone. It is not known whether long-term administration of growth hormone in the elderly is potentially harmful — particularly with regard to the risk of cancer, given that older age is associated with an increased incidence of cancer. In 152 healthy men, the relative risk of the subsequent development of prostate cancer was increased by a factor of 4.3 among men who had serum concentrations of insulin-like growth factor I in the highest quartile, as compared with those whose concentrations were in the lowest quartile.<sup>6</sup> This finding does not demonstrate causality by growth hormone or insulin-like growth

factor I, but it does raise concern about giving older men growth hormone, which increases serum concentrations of insulin-like growth factor I.

The third matter of concern is the potential misuse of health care resources. Growth hormone replacement in growth hormone-deficient adults with pituitary disease is expensive, costing between \$7,500 and \$10,000 yearly. It is not known precisely how much growth hormone is prescribed for “off label” uses, but estimates suggest that one third of prescriptions for growth hormone in the United States are for indications for which it is not approved by the Food and Drug Administration. How many of these prescriptions are reimbursed inappropriately by third-party payers? It is often difficult to obtain third-party payment for growth hormone replacement for adults with documented hypopituitarism and growth hormone deficiency — hence the concern about the inappropriate allocation of resources and denial of reimbursement for appropriate patients in whom growth hormone replacement is beneficial.

Studies that have followed the 1990 report by Rudman et al. confirm the effects of growth hormone on body composition but do not show improvement in function. In contrast, resistance

training improves muscle strength and function, indicating that real effort is beneficial. There is no current “magic-bullet” medication that retards or reverses aging. It remains to be determined whether growth hormone secretagogues that consistently increase endogenous production of growth hormone are beneficial in the elderly. Antiaging therapy with growth hormone has not yet been proved effective according to objective outcome criteria.

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