

REPORT

Enhancing Growth Hormone Naturally

During our youth, abundant levels of **growth hormone** (GH) promote an energetic physiology essential for healthy metabolism and an optimal ratio of lean muscle tissue to body fat.

By the time we reach middle age, however, levels of essential hormones such as testosterone and DHEA decline, while age-associated decreases in muscle mass and increases in body fat become noticeable.

Furthermore, research shows that in aging men, the amplitude of pulsatile GH release (the magnitude of the GH pulse) declines by 50% every seven years after 18-25 years of age.¹

Exogenous subcutaneous injection of human recombinant growth hormone is expensive and still controversial. Fortunately, studies have shown that there are strategies that may naturally boost the endogenous production of growth hormone and thus provide a viable alternative to expensive injections. In particular, exciting research suggests that the growth hormone-blocker somatostatin can itself be inhibited with a nutrient called **CDP-choline**, thus slowing the rate at which growth hormone declines.

Naturally supporting the body's own endogenous growth hormone production using targeted lifestyle and nutritional strategies may provide a safe method of harnessing the vigor and vitality associated with youthful growth hormone levels.

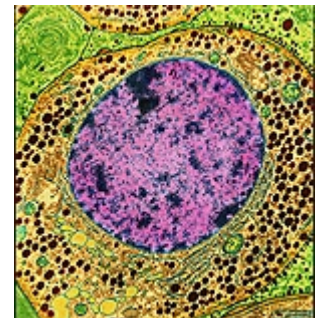
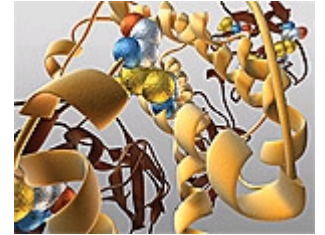
GROWTH HORMONE BASICS

Growth hormone (GH), also known as somatotropin, is a peptide hormone produced by the anterior lobe of the pituitary gland. Growth hormone secretion occurs in a pulsatile fashion following a circadian (daily) rhythm, which is controlled by a central area of the brain known as the hypothalamus. The hypothalamus regulates serum GH levels through the release of two functionally opposing hormones: *growth hormone-releasing hormone* stimulates GH release, while *somatotropin release-inhibiting hormone* reduces it.

Endogenous (made within the body) GH exerts its actions by binding directly to specific receptors on target tissues including muscle, connective tissue (tendons, ligaments, bone, and fat), as well as every major organ. Growth hormone also works indirectly by stimulating liver cells to produce and secrete polypeptide molecules known as somatomedins, the best studied of which is insulin-like growth factor-1 (IGF-1). Like GH, IGF-1 boasts receptors throughout the body and serves many functions. Together, GH and IGF-1 play influential roles in virtually every system—from muscle, bone, and connective tissue growth and repair, to the selective regulation of various aspects of metabolism, as well as helping maintain normal brain function and cardiac health.

However, GH secretion falls precipitously with advancing age. Furthermore, research shows that in aging men, the amplitude of pulsatile GH release (the magnitude of the GH pulse) declines by 50% every seven years after 18-25 years of age.¹

This decline is also mirrored by diminishing IGF-1 levels. The decrease in the secretory activity of the GH/IGF-1 axis, commonly referred to as somatopause, correlates with a number of undesirable symptoms generally associated with aging. Most notably, diminishing GH/IGF-1 has been shown to reflect disordered sleeping patterns, bone frailty, increases in central adiposity (fat accumulation around the middle of the body including the abdomen), as well as decreases in cognition and muscle mass, strength, and conditioning.²⁻⁹



Hormone-producing cell.
Colored transmission electron micrograph of a growth hormone-producing cell from the pituitary gland.

IS SYNTHETIC GH REPLACEMENT THERAPY BENEFICIAL?

Since the decline of GH correlates with the onset of aging-related symptoms, scientists have investigated whether synthetic GH replacement may prove beneficial.

Some of the most compelling evidence that somatopause may respond favorably to synthetic GH replacement therapy comes from investigations involving patients suffering from total or near total absence of GH secretion as a result of pituitary disease. Without treatment, adults suffering from pituitary disease are both physically and psychologically less healthy than their age-matched peers, demonstrating significantly reduced muscle mass, bone density, exercise performance, thyroid function, and collagen production, with a concurrent escalation of central fat mass (especially fat accumulation in the abdominal organs) and insulin resistance, as well as an increased risk for cerebrovascular accidents (strokes) and cardiac events.¹⁰ Psychologically, they tend to experience more emotional lability (abrupt changes in mood in response to everyday events), depression, and social isolation,¹¹⁻¹⁴ and their average life expectancy is measurably reduced.^{15,16}

In the late 1980s and early 1990s, GH replacement studies in adults with poor pituitary function were designed with the goal of restoring normal GH levels. However, the doses used in these chronically GH-deficient individuals produced IGF-1 concentrations that greatly exceeded the expected range, resulting in unacceptably high rates of adverse reactions. In subsequent work, with GH doses adjusted to produce age-appropriate IGF-1 concentrations, negative side effects were largely eliminated or reduced to tolerable levels. Study subjects demonstrated significant and sustained improvements in body composition, physical performance, bone density, and psychological well-being, as well as substantial reductions in biomarkers for cardiac disease.¹⁷⁻²⁴



Computer artwork depicting the location of the pituitary gland.

In light of these results, researchers felt cautiously optimistic that men and women with partial GH deficiency secondary to advancing age might also reap the benefits of GH replacement therapy. However, following a landmark study by Rudman and colleagues in 1990, which provided the first evidence that GH supplementation in the elderly could diminish—and potentially reverse—some of the physical symptoms associated with somatopause,²⁵ exogenous GH therapy has been controversial^{10,26-37} and associated with high costs.

Fortunately, scientists are discovering that the benefits of youthful GH levels can also be harnessed safely by naturally increasing the body's own hormone levels with the right nutrients and lifestyle practices.

NUTRITIONAL STRATEGIES FOR OPTIMIZING GH

Nutritional strategies can offer targeted support for individuals seeking to enhance their endogenous production of GH. Such nutrients may work either by directly enhancing GH release from the pituitary gland or by enhancing the efficacy of sleep or exercise, the two activities that best support GH secretion.

CDP-CHOLINE BOOSTS GH, SUPPORTS BRAIN HEALTH

A growing body of research suggests that the compound *cytidine-5'-diphosphate choline* (CDP-choline) may boost GH secretion while conferring an array of brain health benefits for aging adults.

As adults grow older, GH secretion from the anterior pituitary gland declines precipitously. Exciting scientific research suggests that decreased GH release results in part from increasing levels of somatostatin with aging. Somatostatin produced by the hypothalamus inhibits the release of GH from the anterior pituitary.

This innovative idea has led researchers to search for agents that inhibit somatostatin and thus potentially increase the release of GH. Experimental research shows that treatment with cholinergic agonists increases GH release by inhibiting somatostatin release from the hypothalamus.³⁸

These findings were soon supported by a human study. This compelling investigation showed that administration of CDP-choline to healthy elderly adults resulted in a dramatic **four-fold increase** in serum GH levels, compared with baseline values.³⁹ These findings build upon evidence from an earlier study showing that CDP-choline administration in healthy men increased serum GH levels.⁴⁰



In addition to its effects on GH release, CDP-choline acts through other mechanisms to promote brain cell integrity and health. CDP choline acts as an intermediate in the synthesis of neuronal membranes, promoting healthy brain cell membrane structure and function. CDP-choline counteracts the deposition of amyloid-beta, a pathological protein found in the brains of patients with Alzheimer's disease. Human research suggests that CDP-choline supports release of the essential neurotransmitter norepinephrine, while animal studies show that CDP-choline increases brain levels of key neurotransmitters including dopamine and serotonin.⁴¹

In clinical trials, CDP-choline has shown promise in improving age-associated memory impairment, boosting cognitive performance in the early stages of Alzheimer's disease, and supporting recovery from both ischemic and hemorrhagic stroke.⁴¹

These findings combine to suggest a powerful role for CDP-choline in supporting healthy GH levels and in optimizing brain health with aging.

PROTEIN, AMINO ACIDS ENHANCE GH RELEASE, LEAN BODY MASS

Protein (especially protein derived from animal sources) provides important essential and conditionally essential amino acids known to assist endogenous GH secretion.⁴²⁻⁴⁴ An added bonus: these same essential amino acids are vital for supporting muscle growth and recovery in active men and women.

The most abundant amino acid in the body is glutamine. Consuming even a relatively small amount of glutamine (2,000 mg) has been shown to increase plasma GH levels.⁴⁵ Glutamine has also been shown to help preserve muscle mass in individuals vulnerable to losing lean body mass due to inactivity following surgery.⁴⁶ This suggests that glutamine may provide important benefits in maintaining lean body tissue.

Like glutamine, oral intake of the amino acid arginine increases the release of GH at rest. The combination of arginine intake with exercise produces even greater increases in GH levels.⁴⁷ In addition to its anabolic (tissue-building) effects,⁴⁸ ornithine alpha-ketoglutarate has also been reported to increase GH secretion.⁴⁹

Compelling evidence demonstrates that the combination of arginine and ornithine augments the results of resistance training by helping to increase lean body mass and strength. The investigation also indicated that oral doses as relatively small as 1 gram of ornithine and arginine were effective in enhancing strength and lean tissue mass.⁵⁰

WHAT YOU NEED TO KNOW: ENHANCING GROWTH HORMONE NATURALLY

- Growth hormone (GH) is a peptide hormone that is intimately involved in tissue growth and repair. Together with insulin-like growth factor 1 (IGF-1), GH helps regulate metabolism and maintain normal brain and cardiac function.
- Secretion of GH falls dramatically with aging, correlating with age-related symptoms such as disordered sleep patterns, fragile bones, cognitive decline, and decreased muscle mass and strength.
- Studies examining exogenous GH therapy in elderly adults with declining GH levels have yielded mixed results.
- Given the mixed results and the high cost of subcutaneous injection of human recombinant GH therapy, a more natural approach to maintaining youthful health and vigor is to employ lifestyle choices that optimize the endogenous production of GH.
- Safe methods for enhancing endogenous GH production include: losing excess body fat, particularly abdominal fat; avoiding high-glycemic load carbohydrates; optimizing sleep habits; eating a high-protein, low-carbohydrate snack before bedtime; and exercising regularly to your lactate threshold. Targeted nutrients including CDP-choline, arginine, ornithine, glycine, glutamine, and niacin (vitamin B3) can help support endogenous GH secretion, assist muscle growth and recovery from exercise, and promote healthy sleep.

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GLYCINE SUPPORTS HEALTHY SLEEP, GH RELEASE

Since GH secretion occurs primarily at night, ensuring good sleeping habits is essential for individuals seeking to optimize their natural levels of GH. Unfortunately, one-third of adults report at least occasional bouts of insomnia, and about one-third of them suffer from sleeplessness or disturbed sleep on a more chronic basis, to the point that it regularly impairs daytime functioning. For the millions of sleepless among us, there may be good news—in the form of an inexpensive, naturally occurring amino acid known as glycine.

Within the central nervous system, glycine functions as an inhibitory neurotransmitter, playing a well-documented and critical role in initiating normal patterns of REM sleep.⁵¹ Now, a new study of chronic insomniacs demonstrates that glycine administered orally just prior to bedtime significantly improves sleep quality, shortening the latency between sleep onset and initiation of slow-wave (deep) sleep as measured by polysomnography. Volunteers also reported less daytime sleepiness, a subjective finding that was objectively corroborated by improved performance on cognitive tasks testing memory recognition.⁵²



DECLINING GH LEVELS AND POOR HEALTH

There are a number of lifestyle factors that lead to decreased GH and IGF-1 secretion. For example, multiple studies indicate that central adiposity (the accumulation of central body fat) accurately predicts GH decline.⁶⁵⁻⁶⁸ In addition, it is well established that poor nutritional status, inadequate sleep, and lack of physical fitness can all contribute to decreases in circulating GH and IGF-1, regardless of age.⁶⁰

Individually or in combination, poor nutritional status, inadequate sleep, and lack of physical fitness negatively impact body composition, bone strength, athletic conditioning, and cognition—independent of their effects on serum GH levels.⁴²

It seems clear that an unhealthy lifestyle contributes to somatopause both directly, by causing profound reductions in GH secretion, as well as indirectly, by promoting the physical and psychological symptoms of accelerated aging.

These findings build on previous work showing that a supplement cocktail containing glycine, glutamine, and niacin (vitamin B3) significantly increases endogenous GH secretion in healthy, middle-aged men and women. Individual test subjects in the study who demonstrated a concomitant increase in IGF-1 also exhibited improved memory and vigor.⁵³

LIFESTYLE TECHNIQUES TO NATURALLY BOOST ENDOGENOUS GH SECRETION

Healthy lifestyle practices are an essential component of a program to enhance endogenous GH production. The most important techniques for optimizing GH levels include:

1. Deflate the spare tire. If you happen to suffer from fat stores concentrated centrally around the organs of the abdominal region, GH secretion will be even more impaired. Fortunately, research indicates that declining GH due to body fat gain is partially reversible with weight loss.⁵⁴ Unfortunately, visceral adiposity is often an indicator of both insulin and leptin resistance and, as a result, can be very difficult to shed permanently. Fortunately recent work has led to the discovery of effective, natural methods for combating leptin resistance.⁵⁵⁻⁵⁸ For more information, see: “Deflating your spare tire for a longer, leaner life... Understanding the risks of leptin resistance” *Life Extension*, February 2009,⁵⁸ and “Vindication” (How correcting a testosterone deficit can reduce abdominal adiposity), *Life Extension*, December 2008.⁵⁹

2. Avoid high-glycemic-load carbohydrates. Insulin is a powerful, direct inhibitor of GH secretion.^{42,60} To prevent the unhealthy surges of insulin or “insulin spikes” that decrease endogenous GH levels and increase your risk for type 2 diabetes, avoid highly processed carbohydrates like refined white bread and sugary cereal, as well as high-glycemic-load foods such as white rice, potato chips, cookies, soda, and commercially processed fruit juices (high in fructose and devoid of fiber). Instead, emphasize nutrient and fiber-rich whole fruits, vegetables, nuts, and legumes (beans).⁶¹

3. **Insist on a good night's sleep.** The majority of GH secretion occurs at night during slow-wave (deep) sleep. Along with high-intensity exercise, another natural stimulus of endogenous GH secretion is sleep itself. It is well documented that inadequate sleep, irregular sleeping patterns, and poor quality sleep can substantially inhibit GH secretion.^{1,42} To optimize sleep, maintain good sleep hygiene habits: keep to a regular bedtime and wake up time; do not consume alcohol or caffeine 4-6 hours before bedtime; and keep excess light and noise out of the bedroom.

4. **Plan your last meal of the day carefully.** Your last meal of the day is the most important for maintaining a robust GH/IGF-1 axis. A high-protein, low-carbohydrate snack before bedtime serves a dual purpose. First, it helps minimize insulin release and allows for maximum endogenous GH secretion. Second, important essential and conditionally essential amino acids found in protein assist endogenous GH secretion.⁴²⁻⁴⁴

HARNESSING YOUR LACTATE THRESHOLD

At some point, depending on exercise duration and intensity, the rate of lactic acid formation in your muscles becomes greater than the rate of dispersion. This is known as the lactate threshold, and can usually be elicited at activity levels that demand between 80% and 90% of a trained athlete's maximum heart rate.

One of the easiest ways to surpass your lactate threshold is through resistance training, but you do not have to lift heavy weights to take advantage of increased endogenous GH. Several studies have shown that circuit training, which utilizes relatively light resistances, can be just as effective at driving GH release as a more strenuous workout.^{64,69,70} Intuitively, circuit training might seem less intense than power training. However, circuit training calls for an increased number of repetitions per set and the rest periods between consecutive sets are often considerably shorter, typically on the order of zero to 30 seconds, versus a minute or two for heavier lifting.

If longer-duration, lower-intensity "cardio"-type activities such as running, cycling, or swimming are more your cup of tea, you may need to enhance your workouts to generate optimal GH secretion during exercise. Punctuating your usual, lower-intensity cardio routine with brief, all-out sprints every three to five minutes will rapidly push you to your lactate threshold.

5. **Stay active!** Exercise is a significant, natural optimizer of GH secretion.⁶² The type of exercise you do, as well the intensity and duration of your workouts, all play an important role in determining to what degree your training regimen contributes to GH secretion. A number of studies have suggested that the intensity necessary to trigger exercise-induced GH release corresponds to the lactate threshold—the exercise intensity at which lactic acid accumulates in the blood.⁶³ Exercise training above the lactate threshold appears to amplify the pulsatile release of endogenous GH at rest, increasing total secretion for at least 24 hours.⁶⁴

CONCLUSION

The plentiful growth hormone levels of youth are associated with strength, good health, and vitality. However, given the high cost and mixed study results associated with recombinant GH injections, optimizing lifestyle choices to enhance endogenous GH production may represent the most intelligent way to benefit from this youthful hormone. Through weight management, exercise, healthy sleep habits, minimizing intake of high-glycemic-load carbohydrates, and consuming targeted nutrients such as CDP-choline, niacin, glycine, glutamine, arginine, and ornithine, you may safely and cost-effectively capture the many benefits of naturally high GH levels.

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

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