

Human Growth Hormone: Endogenous Production and Lifelong Health Benefits

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Abstract

Objective: To present a clear explanation of the purpose of Human Growth Hormone (hgH). Inform the reader of ways to naturally increase hgH. Increase awareness as to what benefits this hormone holds. Decrease the negative connotation surrounding hgH.

Methods: Published literature on the topic of Human Growth Hormone (hgH) was collected and reviewed. Search subjects included, but were not limited to, endogenous production of hgH, nutritional considerations, and the effects of exercise on production of hgH.

Results: An increase in endogenous secretion elicits a greater capacity for cell regeneration. Deep sleep is one of the highest yielding states for our bodies to be in for the production of the hormone. Some studies have shown that modifications of diet and exercise can push hgH production to it's limits. Unfortunately, it is almost impossible to detect exogenous sources with current drug testing methods.

Conclusions: In light of the medicinal use of human growth hormone (hgH) there are many other ways we can utilize the benefits surrounding this substance. Short wave sleep patterns, as well as good nutrition is an important diurnal approach to exogenous production of the hormone. The amino acid leucine holds a very important secondary role in the longevity of hgH in the blood by decreasing oxidation of the hormone. Lastly, intense exercise that requires forced and negative repetition training also invokes an enormous response of acute stress which in turn requires the central nervous system to boost production.

Keywords: *human growth hormone, hgH, Leucine, exercise, stress, sleep, nutrition*

Introduction

Over the past several decades the term hgH (human growth hormone) has only been recognized with performance enhancement as well as illegal use by some of our favorite professional athletes. This kind of stigma has made giant waves of controversy throughout the sports and medical community alike. We are now facing a new dilemma amongst the young old as it's use as an anti-aging supplement. The objective of this review is to eliminate the misnomers placed upon this very important and crucial hormone our body naturally produces. Subjects covered will include the benefits of hgH and how exercise, proper sleeping habits, and diet will increase the efficacy and utilization without an exogenous supply.

The lack of exercise, improper diet, and poor sleeping habits deplete the ability for hgH to be produced. Human growth hormone is an important hormone for regeneration of mainly muscle and bone but many other connective tissues as well. Before hgH can be used, several requirements mediating its production must be met. Somatotrophs in the anterior pituitary release bursts of human growth hormone every few hours, especially during sleep. Their secretory activity is controlled mainly by two hypothalamic hormones; growth hormone releasing hormone (GHRH) promotes secretion of human growth hormone, and growth hormone inhibiting hormone (GHIH) suppresses it. A major regulator of GHIH and GHRH secretion is the blood glucose level. Low glucose concentration, stimulates the hypothalamus to secrete GHRH, which flows toward the anterior pituitary in the hypophyseal portal veins. Upon reaching the anterior pituitary, GHRH stimulates the somatotrophs to release hgH (1). Human growth hormone stimulates secretion on insulin like growth factors, which speed up breakdown

of liver glycogen into glucose, causing glucose to enter the blood more rapidly. As a result, blood glucose rises to the normal level, this will inhibit the release of GHRH. To maintain balance an opposing process has to occur. High blood glucose concentration stimulates the hypothalamus to secrete GHIH while simultaneously inhibiting the secretion of GHRH. Upon reaching the anterior pituitary in portal blood, GHIH inhibits secretion of human growth hormone by somatotrophs. A low level of human growth hormone and IGF's slows breakdown of glycogen in the liver, and glucose is released into the blood more slowly. Thus glucose falls to normal levels (2).

Other stimuli that promote secretion of human growth hormone include decreased fatty acids and increased amino acids in the blood, deep sleep (non-rapid eye movement), and increased activity of the sympathetic division of the autonomic nervous system (i.e. stress and vigorous physical activity). Factors that inhibit human growth hormone secretion are increased levels of fatty acids and decreased levels of amino acids in the blood, rapid eye movement sleep, emotional deprivation, obesity, low levels of thyroid hormones, and the exogenous hgH itself.

In order to quantify the information used to determine the usefulness of hgH we must evaluate effects of low production in comparison to normal levels. The three specific measures will include endogenous production/secretion from increased exercise, improved diet, and optimal sleep patterns. These scenarios will be investigated in order to support the hypothesis that if practiced; ones very own endocrine system can become their very own anti-aging clinic.

Discussion

Human growth hormone (hgH) is composed of 191 amino acids. Secretion of the hormone depends on the stimulation of cells within the hypothalamus from specific messengers. As we age hormonal states change due to decreased sensitivity to negative feedback mechanisms. The consequences related to these deprived levels are osteoporosis, slower healing times for connective tissue, a decrease in lean body mass, and a weakened immune system. In other words, “old age” (3).

In the 1920's the New England Journal of Medicine published an article regarding hgH. This study revealed conclusive evidence that this hormone held many anti-aging properties. Subjects tested showed a decrease in body fat, increase in skin thickness, bone density, as well as improved function of the spleen and liver. Since then the medical field has approved it's use as treatment for patients suffering from hgH deficiency. In all respects hgH is the major hormone which is directly in charge of the secretion and production of several other hormones produced in the body.

The benefits of hgH are well documented. The literature over the past fifty years have opened our eyes to the positive effects on multiple organs throughout our biological systems. One of the better known and well studied modulators of GH is simply our circadian rhythms. Within a 24 hour pattern of time GH is released in all young adults. Surges of hormone will oscillate every ninety minutes during stage three or slow-wave-sleep (SWS) (4). Just before REM (stage 4) the SWS signals neuropeptides to generate a response in the suprachiasmatic nucleus which is located in the hypothalamus. This endogenous reaction is a crucial negative feedback mechanism. If this sequence is disrupted in any way the amount of GH is diminished and the supply will not meet its demand. A multitude of variables impact the half-life of

serum somatotropin. Cortisol, the stress hormone, will in essence burn up more of the GH peptides. The quality of the said hormone is also of questionable integrity when the amino acids are in short supply. However, free form IGF-1 levels can couple to GH and prolong the efficacy it has with target cells.

There is a substantial difference between the sexes and secretory patterns of GH. Men have the highest spike within the first phase of SWS; up to seventy percent per twenty four hour cycle. Women on the other hand have a longer distribution throughout the day leaving considerably less of percentage to be accounted for during sleep cycle. Of course any disruption of sleep will cause a dramatic decline in production of GH. In accordance to these observations, shift workers and trans-meridian travelers are greatly effected (5).

The secretory patterns between growth hormone and cortisol have a tremendous physiological interrelationship. Stress, be it environmental, chemical, or physiological increases cortisol levels. If in the case of acute stress hgH is secreted. Long standing stress will in fact decrease hgH by increasing corticotropin releasing hormone from the elevated levels of somatostatins. Sleep deprivation is a perfect example of chronic stress (6). Amazingly, what is seen after a subject has suffered from lack of SWS, the hypothalamic-pituitary-adrenal axis(HPA) will stimulate extra amounts of hgH to make up for the previously lowered levels once sleep is regained (7). It is however, unpredictable the amount of time it takes for the homeostatic balance of hgH and cortisol to return to normal. With this being said an obvious result was recorded (8). By simply reducing the amount of chronic stress, increased hgH was noted thus supporting the thesis.

Exercise and its affect on hormone production has been an area of increasing research over the past several decades. Scientists and doctors have partnered with trainers around the world in order to develop the most efficient and effective way to maximize production of these highly anabolic endocrine peptides. In this time many approaches have been made to design a strategy of resistance training that has optimal results. Here are the most dynamic regimens that demonstrate such a response.

One specific form of acute stress that is a potent stimulator for increasing hgH is heavy resistance exercises. These spikes in hgH are entirely dependent on maximum physical output. Variables include; amount of sets, repetitions, rest periods, and muscle mass recruited for the exercise (9). Few techniques have been documented as having a greater impact on muscle growth and strength. These methods are designed to increase mechanical tension on the muscle cells to maximize damage and metabolic stress. This will result in the stimulation for circulating more hgH as well as other anabolic hormones.

A particular training technique called “negative forced reps,” was investigated by Ahtiainen et. al. Two individuals are required for this exercise protocol. The individual will perform a maximum rep range of six without assistance. Next, the spotter will assist almost entirely with two to four additional concentric contractions, while the lifter slowly, and with strict form, executes the eccentric phase. This puts a tremendous amount of metabolic stress on muscles utilized for the exercise and results in an exponential increase in hgH (10).

A slight variation to the previous technique is referred to as “heavy negatives.” These strictly focus on the eccentric portion of the lifting movement while using a much

greater amount than the subjects one rep max. Given that the average lifter is twenty to fifty percent stronger during the eccentric phase of the movement, heavy negatives typically produce greater muscle tension and muscle damage (11).

This shock to the central nervous system again impacts the neuromuscular responses to muscle damage markers such as creatine kinase. "Further explanation might also be an increased acidity in the muscle caused by anaerobic muscle work, which stimulates metaboreceptors and sends afferent feedback to the central nervous system and hypothalamus leading to an increased secretion of hgH (10)."

The "drop sets," technique requires the subject to perform a set to failure with a given load, then immediately reduce the load and continue to failure. This again promotes growth by increasing stress within muscle cells due to the extra time the muscle is under tension from more reps, thus producing more hgH to accommodate for the acute physical stress (12).

The anabolic effects of GH is caused by the increased ability for cells to transport amino acids and increased protein synthesis. This heavy resistance exercises is crucial for this process of training induced muscle hypertrophy to occur. The physiological process is easily explained by the sympathetic nervous systems response to hypoglycemia and the stimulatory effect from the motor cortex through the hypothalamus(13). Like most things in life, more is not always better. Creutzfeldt-Jacobs disease, Acromegaly, Gigantism, and diabetes are a few examples of growth hormone gone awry. Fortunately, our bodies are constantly regulating these plasma levels.

The concentration of free form hgH is dependent upon a multitude of variables. In order for researchers to measure these levels, significant blood testing was required

over a large area of volunteer test subjects. Here they were able to determine a normal value and base set points for men as well as woman. Through these studies information was gathered in order to find a half-life for hgH (14). The purpose was intended for treating diseases but of course unpredictable findings were discovered. One of the largest differences in clearance was simply changing the subjects position from vertical to decubitus, another significant factor was the correlation with cortisol as we discussed earlier. These outcomes were measured by coupling hgH with Iodine 125, and collecting plasma over a twenty four hour period (15). Unfortunately, this new found data was dubbed to be less than practical since the control group did not have to face any environmental variables a patient would normally endure. The list of factors is virtually infinitesimal in regards to circulating plasma hgH. However, as unexpected of an outcome this seemed to be researchers opened several doors to which hgH needed to be investigated.

Besides sleep, the consumption of food is one more random action humans take part in diurnally. Some more regularly than others and some make much better choices. That being said one of the objectives of this review is to uncover dietary components that have an effect on circulating growth hormone. Since the constituents of hgH are amino acids it comes as no surprise that a high protein diet is of great importance in regards to its production. The majority of the amino acids are synthesized within our bodies however, nine of which are obtained from food (16). Most of these are abundant through the guidelines suggested by the United States Department of Agriculture. Out of these nine essential amino acids three of them are known as branched chain amino acids (BCAA's) leucine, isoleucine, and valine. Together they slow catabolism during

exercise, which results in a faster rate of recovery (17). Out of these three; leucine shows to have the greatest influence with the anabolic activation potential. The overall effect is due to leucine becoming oxidized twice as fast as any other amino acid especially during exercise (18). This increase in protein turnover signals both GH and IGF-1 to exert direct anabolic effects on other endocrine pathways. Insulin possesses powerful antiproteolytic properties; which are observed with the extra-thyroidal conversion of T4 to T3 (19). Recommended dose for optimal results is three to five grams pre and post exercise. This amount at such a specific time allows maximum increase in protein turnover but a reduction in the loss of leucine since it is so readily oxidized with physical activity.

Nutritious, high protein diets, intense exercise, and impeccable sleeping patterns may still not be enough for some individuals. We have all seen them on television and exploited in the media. These are the ones who feel that if a little is good, then more is better. Pushing the limits of maximum human abilities, these are what we refer to as the “super’ elite athletes. Disregarding physiology and the law they insist on continuing to set the bar higher for future competitors. The problem remains in that the human anatomy has not evolved to meet these standards without the use of performance enhancing substances of some kind. At the current time, exogenous forms of GH are not detectable through any testing means unless it is infused with a radioactive isotope. Other hormones can be detected via urine and/or blood samples (20). Given this information, exogenous GH is an ideal way for such unethical athletes to abuse its benefits. In many cases those who are caught abusing GH are due to addictive personalities which become engrossed in the benefits wanting more and more. Often

this leads to utilization of other detectable substances. It is important to educate the public that there is a drastic difference between the exogenous forms of GH which are classified as performance enhancing substances, and the natural form of the hormone which occurs in the human body. Lifestyle changes and improvements may contribute to enhancing the body's natural production of GH, vastly different than injectable synthetic forms of the hormone. Educating the public about the incredible capabilities of the human body and helping them to realize that lifestyle change is the only way to effectively "slow down the clock" and enjoy the life in our years.

Conclusion

In conclusion, the search for the magic pill or fountain of youth remains to be seen. In today's society most people are not as active as they once were. This is where it all begins, lack of movement and fast food diets perpetuates this vicious cycle. The only answer to staying young and full of vigor is the act of implementing a lifestyle of health and wellness. Eating foods rich in anti-oxidants, getting plenty of rest, and staying mobile are the best strategies for maintaining youth. Naturally increasing levels of human growth hormone may be an important piece of this equation. The key is living the healthy lifestyle. There is no easy way out, eat well, move well, live well. Keeping this mantra as the determining factor for health is good place to start.

References

1. Daughaday W, Parker ML. Human pituitary growth hormone. *Ann Rev Med.* 1965; 16:47-66
2. Tortora GJ, Derrickson B. *Principles of anatomy and physiology.* 12th ed. Hoboken (NJ): Wiley & Sons Inc; 2009. 650-4 p.
3. Rudman D, Feller AG, Nagraj HS, Gergans GA, Lalitha PY, Goldberg AF, Schlenker RA, Cohn L, Rudman IW, Mattson DE. Effects of human growth hormone in men over 60 years old. *N Engl J Med.* 1990 July; 323(1): 1-6.
4. Hersch EC, Merriam GR. Growth hormone (GH)-releasing hormone and GH secretagogues in normal aging: fountain of youth or pool of tantalus. *Clin Interv Aging.* 2008 March; 3(1): 121-9.
5. Gan EH, Quinton R. Physiological significance of the rhythmic secretion of hypothalamic and pituitary hormones. *Prog Brain Rsch.* 2010; 181: 111-26.
6. Radomski MW, Hart LEM, Goodman JM, Plyley MJ. Aerobic fitness and hormonal responses to prolonged sleep deprivation and sustained mental work. *Aviat Space Environ Med.* 1992 Feb; 63(2): 101-6.
7. Davidson JR, Moldofsky H, Lue FA. Growth hormone and cortisol secretion in relation to sleep and wakefulness. *J Psychiatr Neurosci.* 1991 June; 16(2): 96-102.
8. Ilias I, Vgontzas AN, Provata A, Mastorakos G. Complexity and non-linear description of diurnal cortisol and growth hormone secretory patterns before and after sleep deprivation. *Endocrinol Regulat* 2002; 36: 63-72.
9. Roth J, Glick SM, Yalow RS, Berson SA. Secretion of human growth hormone: physiologic and experimental modification. *Metab Clin Exper.* 1963; 12: 577.
10. Ahtiainen JP, Pakarinen A, Kraemer WJ, Hakkinen K. Acute hormonal and neuromuscular responses and recovery to forced vs maximum repetitions multiple resistance exercises. *Int J Sports Med.* 2003 Aug; 24(6): 410-8.
11. Eliasson J, Elfegoun T, Nilsson J, Kohnke R, Ekblom B, Blomstrand E. Maximal lengthening contractions increase p70 S6 kinase phosphorylation in human skeletal muscle in the absence of nutritional supply. *Am J Physiol Endocrinol Metab* 2006 July; 291(6): E1197-E1205.
12. Goto K, Sato K, Takamatsu K. A single set of low intensity resistance exercise immediately following high intensity resistance exercise stimulates growth hormone secretion in men. *J Sports Med Phys Fitness* 2003; 43: 243-9.

13. Kraemer WJ, Marchitelli L, Gordon SE, Harman E, Dziados JE, Mello R, Frykman P, McCurry D, Fleck SJ. Hormonal and growth factor responses to heavy resistance exercise protocols. *J Applied Phys.* 1990 Oct; 69(4): 1442-50.
14. Refetoff S, Sonksen PH. Disappearance rate of endogenous and exogenous human growth hormone in man. *J Clin Endocr.* 1970 March; 30: 386-92.
15. Taylor AL, Finster JL, Mintz DH. Metabolic clearance and production rates of human growth hormone. *J Clin Invest.* 1969; 48: 2349-58.
16. Horber FF, Haymond MW. Human growth hormone prevents the protein catabolic side effects of prednisone in humans. *J Clin Invest.* 1990 July; 86: 265-72.
17. Pasiakos SM, McClung JP. Supplemental dietary leucine and the skeletal muscle anabolic response to essential amino acids. *Nutr Rev.* 2011 Sep; 69(9): 550-7.
18. Anthony RC, Reiter AK, Anthony TG, Crozier SJ, Lang CH, MacLean DA, Kimball SR, Jefferson LS. Orally administered leucine enhances protein synthesis in skeletal muscle of diabetic rats in the absence of increases in 4E-BP1 or S6K1 phosphorylation. *Diabetes.* 2002; 51(4): 928-36.
19. Healy ML, Gibney J, Russel-Jones DL, Pentecost C, Croos P, Sonksen PH, Umpleby AM. High dose growth hormone exerts an anabolic effect at rest and during exercise in endurance-trained athletes. *J Clin Endocrin Metabol.* 2003 Nov; 88(11): 5221-6.
20. Bowers LD. Analytical advances in detection of performance-enhancing compounds. *Clin Chem.* 1997; 43: 1299-304