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On The COVER

The Growing Impact of Growth Hormone

By Carol Kahn

Studies and real-life stories from everyday people show that growth hormone replacement therapy can have a dramatic effect on regaining youthful vitality, increasing muscle mass, improving immune function, bettering learning and memory, and lowering blood pressure.



On July 5, 1990, the New England Journal of Medicine published a clinical study on a drug that sent shock waves throughout the world. The drug-human growth hormone, HGH for short, or simply GH, a substance produced naturally by the pituitary gland-was hailed as a fountain of youth. Injections of synthetic human growth hormone had turned 12 men, ages 61 to 81, and with flabby, frail, fat-bulging bodies, into sleeker, stronger, younger selves.

After just six months of treatment, the men gained an average of 8.8 percent in lean body mass, and lost an average of 14.4 percent in fat mass. In addition, their skin thickened by 7.1 percent, the bone density of their lumbar spines increased by 1.6 percent, their livers grew by 19 percent, and their spleens by 17 percent. In language rarely used in conservative medical journals, Daniel Rudman, M.D., and his colleagues at the Medical College of Wisconsin, wrote, "The effects of six months of human growth hormone on lean body mass and adipose-tissue mass were equivalent in magnitude to the changes incurred during 10 to 20 years of aging."

Rudman's study opened the floodgates to thousands of subsequent studies documenting the benefits of growth hormone therapy in GH-deficient adults. The National Institute on Aging is funding a five-year, multimillion-dollar study in nine medical centers to test whether human growth hormone and nutrition-related factors can retard or reverse aging. However, thousands of persons worldwide are not waiting for these results, but are injecting themselves with GH in the hopes of preventing or reversing the downward course of aging.

In addition, growth hormone received the Food and Drug Administration's imprimatur in 1996 for use in adults with GH deficiency due to pituitary or hypothalamic disease, injury, surgery or radiation therapy. This now allows doctors to prescribe growth hormone as an anti-aging treatment for adults with low levels of IGF-1, which indicates a failure of the pituitary gland to produce adequate amounts of growth hormone.

The most abundant hormone made by the pituitary gland is growth hormone. Pituitary cells, called somatotrophs, make growth hormone, which also is known as somatotrophin (from the Greek, turning towards the body). Fully 50 percent of the cells of the pituitary are somatotrophs.

SECRETION IN BRIEF BURSTS

Growth hormone hits its peak when the body grows rapidly during adolescence; hence, the hormone's name. Most growth-hormone secretion occurs in brief bursts, or pulses, that take place during the early hours of the deepest sleep. Indeed, the old adage that you grow during your sleep appears to have a basis in fact.

The hormone lingers in the bloodstream for only a few minutes, but that is long enough to stimulate its uptake into the liver, where it is converted into growth factors. The most important of these is insulin-like growth factor 1 (IGF-1), also known as somatomedin C. IGF-1 is directly responsible for most of the positive benefits of growth hormone, although GH does exert some action on a local tissue level.

Growth hormone declines with age in every animal species tested to date. In humans, the amount of growth hormone after age 21 to 31 falls about 14 percent per decade, so that total 24-hour growth hormone production is cut in half by the age of 60. In

numerical values, we produce on a daily basis about 500 micrograms of GH at 20 years of age, 200 micrograms at 40 years, and 25 micrograms at 80. The fall in IGF-1 with age mirrors that of growth hormone.

Rudman considered a plasma IGF-1 level under 350 international units (IU) as evidence of deficiency. Between 20 and 40 years of age, less than 5 percent of healthy men have GH readings lower than 350 IU. But after age 60, 30 percent of apparently healthy men have this low amount of GH. And after age 65, about half the population is partially or wholly deficient in growth hormone.

We do not yet have the answer to why this happens. Studies have shown that the aging pituitary somatotroph cell can still release as much growth hormone as the young cell if it is adequately stimulated. This means that the fault must lie in the factors that regulate its release.

Some researchers believe the problem lies with somatostatin, the natural inhibitor of growth hormone. Somatostatin has been found to increase with age and may act to block the secretion of growth hormone. When researchers knocked out somatostatin action in old rats, they found GH pulses as large as those in young rats. Other researchers believe the precursor hormone, growth hormone-releasing hormone (GH-RH), which stimulates GH release, becomes less sensitive to feedback signals. The latest thinking is that, not only does the growth hormone that is available to tissues decline with age, but that our tissues become more resistant to the action of the growth hormone that is there. In this view, aging can be considered a disease of growth hormone resistance in the same way that Type II diabetes is a disease of insulin resistance.

The most recent research shows that whatever causes the decline of growth hormone, it is neither irreparable nor permanent. William Sonntag, professor of physiology, and his colleagues at Bowman Gray School of Medicine in Winston-Salem, NC, has just completed an experiment showing that the decline in growth hormone secretion with age is reversible. Old rats (like old people) have a decline in the bursts of growth hormone secreted. But when Sonntag took old rats (26 months) and restricted their caloric intake, growth hormone secretion came back after two months.

THE TAKE-HOME MESSAGE

The take-home message is that the decline of growth hormone with age can be reversed. Even if growth-hormone releasing hormone activity declines, or somatostatin increases, or receptors become less responsive to growth hormone, it can all be overcome by the administration of growth hormone or growth-hormone releasers. Clinical trials now are being funded by major drug companies, such as Merck & Co. and Wyeth-Ayerst Laboratories, on oral drugs that stimulate the pituitary to release normal youthful levels of growth hormone.

Those who produce little or no growth hormone because they have pituitary tumors, other diseases, or have had their pituitary gland removed often seem like doddering old people. They consistently show mental and physical changes that are characteristics of aging, including a reduced sense of well-being, plus lower energy, vitality and capacity for work. In addition, they also exhibit mood swings, anxiety, depression and increased social isolation. Important physical signs are an increase in body fat, especially around the waist (apple-shaped rather than pear-shaped), a decrease in muscle mass, and thin, wrinkled, or prematurely damaged skin.

Bengt-Ake Bengtsson, M.D., and his colleagues at Salgrenska Hospital in Gothenburg, Sweden, studied 333 patients between 1956 and 1987 who were diagnosed with pituitary insufficiency. The patients were given pituitary-hormone replacement, including cortisone, thyroid hormones and sex hormones. The one hormone not replaced was GH. The GH-deficient patients died at twice the expected rate-107 deaths compared to 57 in the overall population, matched for age and sex. The primary cause of death was cardiovascular disease, which showed an almost two-fold increase (60 deaths vs. 31) over the general population.

Three pioneering studies in Sweden, Denmark and England found that four to six months of growth hormone replacement in adults who had low GH levels that was due to pituitary insufficiency had beneficial effects on body composition, cardiac function, exercise capacity, renal function and quality of life. Bengtsson went on to show that 12 to 18 months of GH therapy increased bone mineral density.

Some of the most striking effects were in quality of life. Before treatment, many of the patients said they were struggling with low self-esteem, anxiety, and depression. But after a short time on GH therapy, the difference was like night and day.

"We called it the Lazarus effect," he says. "We woke them up. With some patients, it was like giving them a kick in the back. Their lives changed within a few weeks." The treatment went on to change the lives of everyone who participated in the program, according to Dr. Lena Wiren, a psychologist who evaluated the patients. "Nobody wants to stop treatment," she says. "Sometimes it is not even the patient who notices the difference it is making. Rather it is their wives or children or friends at work."

DRAMATIC IMPROVEMENT SEEN

L. Cass Terry, M.D., Ph.D., has completed a preliminary study of patients treated with what he calls the high-frequency, low-dose (HF-LD) method. This is about one-quarter to one-half the weekly dosage used by Rudman, whose patients experienced side effects such as carpal tunnel syndrome and gynecomastia. The HF-LD regimen uses about 0.3 to 0.7 IU of GH twice daily.

According to the authors, it is well tolerated and there have been no adverse side effects. At the same time, the average somatomedin C (IGF-1) levels increased by 61 percent, from a mean of 238.8 to 384.5 after treatment. On self-assessment questionnaires from 202 patients, more than 75 percent of the respondents reported body-fat loss, muscle-mass gain, greater strength, exercise-tolerance and energy levels, and improved quality of life. A large majority also reported better skin texture, and greater skin thickness and elasticity.

Growth-hormone therapy may be effective in preventing or treating many common diseases and conditions of aging. In fact, it appears that hormone replacement, which includes growth hormone, may be one of the most effective methods of maintaining health and vigor for people in their 80s, 90s and beyond. Here are some of the areas in which growth hormone has already shown considerable benefit:

- **Immune function.** In 1985, Keith Kelley, M.D., a research immunologist at the University of Illinois at Urbana-Champaign, showed that injections of cells that secrete high amounts of growth hormone could regrow the shriveled thymus gland in old rats until it was as large and robust as in young rats. Kelley's work was confirmed by Israeli scientists who used bovine growth hormone to reverse thymus shrinkage in mice, and similar results have been demonstrated in dogs. Immune activities that growth hormone improves are the manufacture of new antibodies; increased production of T-cells and interleukin 2; greater proliferation and activity of lymphocytes; higher activity of natural killer cells; stimulation of macrophages; increased maturation of neutrophils; and increased production of red blood cells.
- **Cardiac function.** GH therapy improves cardiac function and protects against cardiovascular disease in a number of ways. It reduces body fat, particularly in the abdominal region, which has been shown to be highly correlated with increased risk of heart attack. Growth hormone also improves blood cholesterol profiles, raising high-density lipoproteins (HDL) and lowering low-density lipoproteins (LDL), and reduces diastolic blood pressure by about 10 percent, without affecting systolic pressure.
- **Treatment with growth hormone has reversed heart failure.** In a 1996 study in the *New England Journal of Medicine*, growth hormone given to seven patients-five men and two women with moderate-to-severe heart failure-increased the thickness of the left ventricular wall, enhanced the ability of the heart to contract and pump blood, reduced the oxygen requirement of the heart, improved exercise capacity and enhanced quality of life.
- **Lung function.** Human growth hormone injections have improved heart-lung function by increasing the ability of patients to exercise, raising their maximum oxygen uptake, and increasing their stroke volume and cardiac output. David Clemmons, chief of endocrinology at the University of North Carolina School of Medicine in Chapel Hill, found that three weeks of GH injections in patients in the latter stages of chronic obstructive pulmonary disease raised maximum inspiratory force by 10 to 12 mm on average, and increased maximum expiratory force. "If you were as impaired as these patients, going from 25 mm to 38 mm would be quite a help," says Clemmons, who believes that growth hormone is a promising treatment for emphysema and other forms of chronic obstructive pulmonary diseases.
- **Osteoporosis.** While GH therapy is used to grow the skeletal bones of children who are deficient in the hormone, results in adults have been inconsistent. Rudman found that six months of GH treatment increased the density of the lumbar vertebrae by 1.6 percent in men over 65, but there was no increase in the bone density of the radius bone in the arm or the femur of the leg. Several groups have reported an increase in bone mineral content.
- **Improved Bone Density** Recently, Swedish scientists led by Gudmundur Johannsson, M.D., studied 44 men and women between 23 and 66 who were severely deficient in growth hormone. Two years of growth hormone therapy caused significant increases in the density of the bones that form the hip joint and the vertebrae of the lower spine. The studies also showed an increase in calcium, a calcium-binding bone protein called osteocalcin, as well as two types of collagen, which are markers of bone formation. The researchers estimate that they have reduced the possibility of fracture so that it now equals that of normal healthy controls.
- **Brain function.** Growth hormone raises energy levels, improves slow-wave sleep, and elevates mood. In a startling report, Johannsson's team found that growth hormone actually changed the levels of certain neurotransmitters in the human brain, raising the level of B-endorphin, which has been called the brain's own opiate, and lowering the level of dopamine, which is associated with feelings of agitation. This is similar to the concentrations of these neurotransmitters one sees in antidepressants, says Bengtsson, who was part of the research team.

In other reports, GH appears to reduce stress, improve focus and concentration, and build self-esteem and self-confidence. Growth hormone can reverse decline in memory and cognitive performance. In a study of adult male patients deficient in GH, Dutch researchers headed by Jan Berend Deijem, M.D., found that GH deficiency is associated with impairments in iconic memory (the ability to process flashes of information), short-term memory, long-term memory, and perceptual-motor skills such as hand-eye coordination. Interestingly, the lower the levels of IGF-1, the lower the patient's IQ and education level.

Growth hormone, IGF-1, and nerve-growth factors in the brain show promise in the treatment of neurodegenerative disease and injury. IGF-1, which is also available in recombinant drug form, has been shown to repair and reconnect severed nerve endings of up to 6 mm, a feat previously unheard of, and has increased motor neuron activity in spinal cord cultures. Some of the diseases for which IGF-1 may be useful are amyotrophic lateral sclerosis (Lou Gehrig's disease), and peripheral neuropathies and muscle-atrophy problems such as Charcot-Marie-Tooth disease. It also may allow more aggressive chemotherapy for certain cancers, since drugs like vincristine and cisplatin can cause peripheral neuropathies at high doses.

Growth hormone normalizes the impaired motor activity of dwarfed mice, suggesting that it may be of value in treating Parkinson's patients. It also helps motor activity by stimulating the growth of the myelin sheath on neurons, making it a potential treatment for multiple sclerosis. In Alzheimer's disease, there is a loss in a number of neurotransmitters, especially acetylcholine and noradrenaline, which stimulate growth hormone. Belgian physician Thierry Hertoghe is treating several Alzheimer's patients with multihormone replacement, including growth hormone. Other benefits of GH therapy for the brain include restoration of slow wave sleep, a particular problem among the elderly. There also have been anecdotal reports of improved vision, both near and far, in daytime as well as nighttime.

- **Sexual function.** The decline of male potency parallels the decline of growth hormone release in the body, with GH levels and sexual potency at their peak during puberty and already decreasing in young manhood, until, by age of 80, 75 percent of men are incapable of getting or sustaining erections.

Although there have been no clinical studies looking at the effects of growth hormone on sexual function, people who are growth-hormone deficient due to pituitary disease have decreased libido and sexual function. After treatment with GH replacement, they experience increased sexual drive and function, according to their responses on the Nottingham Health Profile.

Terry, in a study of 202 aging adults, found that 75 percent of the men reported improvement in sexual potency and frequency, and 62 percent had longer-lasting erections. In fact, in interviews with people who have used GH for anti-aging purposes, almost everyone, male and female, reports improvements in libido and sexual function. A typical case is that of a 63-year-old divorced doctor who hadn't had sexual relations with a woman in five years and was no longer interested in sex. After four weeks on GH, he felt a surge of sexual energy. He started dating again and now has sex an average of twice a week.

- **Obesity and body composition.** Growth hormone does something no other weight-loss regimen does: It recontours the body, melting away fat and building muscle. In many cases, people look like they've shed years away along with the fat they've lost. Even better, the greatest loss occurs in deep belly fat-the area associated with increased risk of heart attack. In every study of growth hormone's effects on "normal" people who are aging, GH reduced body fat and increased lean body mass. In a six-month placebo-controlled trial at Thomas Hospital in London of 24 adults with GH deficiency, the hormone-treated group had no net change in weight, but lost an average of 12.5 pounds of fat and gained an average of 12.1 pounds of lean body mass.

Growth hormone may be the most effective fat-loss regimen ever discovered. In a double-blind, placebo-controlled, crossover study on overweight women, GH caused an average loss of more than 4.6 pounds of body fat, mostly in the abdomen. Most diets cause loss of muscle along with fat, but in this study, the women's lean body mass increased by 6.6 pounds. In two double-blind, placebo-controlled studies by David Clemmons, M.D., at the University of North Carolina in Chapel Hill, growth hormone and dieting caused a 25-percent acceleration in the rate of fat loss, above and beyond the effect of dieting alone. In the 11-week treatment period, the GH-treated subjects lost 30 to 32 pounds, compared with 20 to 25 pounds in the controls. And, while the controls lost muscle along with their fat, the treated group maintained their body tone.

Loss of abdominal fat also has implications for Type II diabetes, since there is a close association between central obesity and insulin resistance. While some early studies showed increased blood sugar and insulin resistance in GH-treated subjects, later studies showed that after six months of treatment, insulin sensitivity returned to baseline. While proof is still lacking, it is reasonable to assume that, over the long run, stimulation of growth hormone could help to prevent Type II diabetes or even reverse the disease process.

A QUESTION REMAINS: CAN HUMAN GROWTH HORMONE EXTEND LIFE SPAN?

In 1990, two scientists at North Dakota State University, David Khansari and Thomas Gustad, attempted to answer this question. They gave growth hormone injections to 26 mice that were more than three-quarters through their life span, while another 26 mice received placebo injections of saline solution. After 13 weeks, 16 animals, or 61 percent of the controls, had died, while all but two, or 97 percent, of the growth-hormone treated animals were still alive. In other words, the vast majority of the treated animals had already lived longer than the average lifespan for that species. The results, said the researchers, "suggest that long-term GH

therapy prolongs the average life expectancy of the hormone-treated mice significantly."

Unfortunately, the researchers did not have enough growth hormone to determine what the maximum life span of the treated animals would have been. There are indications that the animals might have lived far longer. The most consistent extension of life span comes from experiments in which animals have their food intake restricted. In well-conducted experiments, animals on calorie-restricted diets have lived to ages that would be comparable to 150 in humans!

DETERMINING MAXIMUM LIFESPAN

Could growth hormone be a significant factor in these animals' ability to defy death? The Bowman Gray School of Medicine's Dr. Sonntag has examined what happens to growth hormone and IGF-1 secretion in animals that are diet-restricted. Normally when we age, the amount of growth hormone and IGF-1 decreases along with protein synthesis in cells and tissues. But Sonntag and his associates found just the opposite in the diet-restricted animals. Young rats on a moderate food-restricted diet actually had their growth-hormone secretion go down, but by the time they reached 26 months-old age for a rat-their growth hormone pulses were the same as that of a young control rat.

"What we have tried to relate that to is that the calorically restricted animals at that age have a higher capacity to synthesize protein in their tissues," say Sonntag. While the rates of protein synthesis went down in old control rats, the aged restricted rats had a 70-percent increase of new protein in the heart and a 30-percent increase in the diaphragm, compared with unrestricted animals. Interestingly, the level of IGF-1 did not rise, but the number of receptors in the cells for IGF-1 increased by 60 to 100 percent.

SYNERGISTIC EFFECTS

Many nutrients have been shown to increase growth hormone in both young and old subjects. The amino acids Arginine and ornithine have been used for a number of years to enhance production of growth hormone since they were first popularized by Durk Pearson and Sandy Shaw in their book, "Life Extension: A Practical Scientific Approach."

A synergistic effect also has been shown between Arginine and another amino acid, lysine. According to a 1981 study by Italian researcher A. Isidori, M.D., and his associates at the University of Rome, the combination of 1,200 mg of lysine and 1,200 mg of Arginine in 15 male volunteers between 15 and 20 was 10 times more effective than taking Arginine alone.

Glutamine is the latest amino acid to generate excitement as a GH releaser, thanks to a 1995 study by Tomas C. Welbourne of Louisiana State University College of Medicine in Shreveport. Welbourne showed that a surprising small oral dose-two grams of glutamine-raised growth hormone levels more than four times, compared with subjects given a placebo. Even more exciting, age did not diminish the response, at least in this study of volunteers ranging from 32 to 64 years of age.

Niacin-commonly referring to the two forms of vitamin B-3, nicotinic acid and nicotinamide-is also a highly effective stimulator of GH. Two scientific studies show that 200 mg of niacin given intravenously increased GH levels eight-fold, with the GH peak occurring two hours after the administration of the niacin.

The Holy Grail of growth hormone replacement is a small, cheap, safe pill that one could take every day to raise GH levels-a kind of anti-aging aspirin. This is the ultimate secretagogue, a fancy word for a growth-hormone releasing compound. And it would work in the body the same way that GH-RH does, by telling the pituitary to release more of the growth hormone stores that are still there, even in old people. Large pharmaceutical companies have joined the hunt for the perfect, oral, growth-hormone secretagogue.

Two secretagogues are now well into clinical trials in this country. The first one developed, GHRP 6, is a growth hormone-releasing peptide being tested by Wyeth-Ayerst. It has now been tested and is remarkably free of side effects, according to its developer, Cyril Bowers, Ph.D., of Tulane Medical School in New Orleans.

The second compound, MK0577, developed by scientists at Merck, does not have a typical peptide structure and is more easily absorbable by the body than growth hormone-releasing peptides such as GHRP 6. The latest clinical trials in men and women aged 64 to 81 showed that as little as 25 mg of the drug taken once a day for two weeks raised the levels of IGF-1 from an average of 141 to 219, with the highest levels reaching a youthful 251. And it appears to be well-tolerated by elderly people. If any of these compounds are approved by the FDA, and considering the impact that growth hormone has been shown to have on almost every system of the body, aging as we know it may soon be a thing of the past.

For more info on Growth Hormone see *Growth Hormone Abstracts*

FOR FURTHER READING:

Ascoli, M., and Segaloff, D.L.,
Adenohypophyseal hormones and their hypothalamic releasing factors, in Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9th Edition, McGraw Hill, New York, 1996.

Bengtsson,
An Introduction to Growth Hormone Deficiency in Adults,
Oxford Clinical Communications, Oxford, UK, 1993.

Beshyah, S.A.,
The effects of short and long term growth hormone replacement therapy in hypopituitary adults on lipid metabolism and carbohydrate tolerance, *Journal of Endocrinology and Metabolism* 1995; 80:356-363.

Bengtsson, BA; et al.,
Cardiovascular Risk Factors in Adults with Growth Hormone Deficiency,
Endocrinology and Metabolism, 1995; 2 (Suppl B):29-35.

Bowers, C.Y.,
Overview: Historical Perspective, Xenobiotic Growth Hormone Secretagogues: *Growth Hormone Releasing Peptides*, Dec 7, 1994.

Bucci, Luke R.;
Anabolic hormone induction by nutrients,
IAACN '95 Nutrition for Hormonal Health Symposium

Chapman, I., et al.
Stimulation of the growth hormone (GH)/IGF axis by daily oral administration of a GH secretagogue in healthy elderly subjects. *Journal of Clinical Endocrinology and Metab.* 81:4249-4257 (1966). Christiansen, J.S. et al.
Effects of growth hormone on body composition in adults.
Hormone Research 1990;33(suppl 4):61-4.

Clemmons, D.R., Underwood, L. E.,
Growth hormone as a potential adjunctive therapy for weight loss.
In: Underwood, L.E. (ed) Human Growth Hormone: Progresses and Challenges. Marcel Dekker, Inc., New York., 1986.

Deijen, J.B., et al.
Cognitive impairments and mood disturbances in growth hormone deficient men.
In Press.

Fazio, S;
Preliminary study of growth hormone in the treatment of dilated cardiomyopathy,
New England Journal of Medicine March 28, 1996; 334:809-814; comment:856-7.

Harvey S,
Growth hormone action: neural function, in Harvey, S., Scanes, C.G., Daughaday, W.H., eds., *Growth Hormone*, CRC Press, Boca Raton, 1995. Isidori, A., et al.
A study of growth hormone release in man after oral administration of amino acids, *Current Medical Research and Opinion* 1981;7 (7):475-81. Johannsson J.O.L., et al.
Treatment of Growth Hormone-Deficient Adults with Recombinant Human Growth hormone Increases the Concentration of Growth Hormone in the Cerebrospinal Fluids and Affects Neurotransmitters,
Neuroendocrinology, 1995; 61:57-66.

Jorgensen, J.O.L., et al.
"Three Years of Growth Hormone Treatment in Growth Hormone Deficient Adults: Near Normalization of Body Composition and Physical Performance."
European Journal of Endocrinology 130 (1994): 224-8.

Kelley, K.W. et al.
GH3 pituitary adenoma implants can reverse thymic aging,
Proceedings of the National Academy of Sciences, USA 1986;83:5663-7.

Khansari, D.N. and Gustad, T.
Effects of long-term, low-dose growth hormone therapy on immune function and life expectancy of mice,

Mechanisms of Ageing and Development 1991;57:87-100.

Pearson, D., and Shaw, S.,
Life Extension: A Practical Scientific Approach,
Warner Books, New York, 1982.

Rosen, T. and Bengtsson.
Premature mortality due to cardiovascular disease in hypopituitarism, *Lancet* 1990;336:285-8.

Rosen, T. et al.
Decreased psychological well-being in adult patients with growth hormone deficiency, *Clinical Endocrinology* 1994;40:111-6.

Rudman, D., et al.
Effects of human growth hormone in men over 60 years old,
New England Journal of Medicine 1990;323:1-6.

Rudman, D.,
Growth hormone, body composition, and aging, *Journal of the American Geriatrics Society*. 1985;33:800-7.

Salomon, F.,
Cuneo, R.C., Hesp, R., and Sonksen, P.H.,
The effects of treatment with recombinant human growth hormone on body composition and metabolism in adults with growth hormone deficiency;
New England Journal of Medicine 1989; 321:1797-803.

Sonksen, P.H.,
Replacement therapy in hypothalamo-pituitary insufficiency after childhood: Management in the adult.
Hormone Research 1990;33(suppl 4):45-51.

Sonntag WE;
Moderate Caloric Restriction Alters the Subcellular Distribution of Somatostatin mRNA and Increases Growth Hormone Pulse Amplitude in Aged Animals, *Neuroendocrinology* 1995; 61: 601-608.

Snyder, D., Underwood, L.D. and Clemons, D.R.
Persistent lipolytic effect of exogenous growth hormone during caloric restriction, *American Journal of Medicine* 1995; 98:129-34.

Takahara, Jiro; Yonuki, Sho; Yakushiji, Wataru; et al.,
Stimulatory effects of gamma-hydroxybutyric acid on growth hormone and prolactin release in humans,
Journal of Clinical Endocrinology and Metabolism 1977;44:1014-17.

Welbourne, T.,
Increased plasma bicarbonate and growth hormone after oral glutamine load,
American Journal of Clinical Nutrition 1995;61:1058-61.

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