Homeopathic Human Growth Hormone for Physiologic and Psychologic Health

Alternative and Complementary Therapies
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Three Double-Blind Placebo-Controlled Studies

Barbara Brewitt, Ph.D., James Hughes, M.D.,
Elizabeth A. Welsh, Ph.D., Robert Jackson, D.C.

Human growth hormone (hGH) receives a good deal of public attention for the ability to build lean body mass, increase physical performance, enhance immune function, and improve body composition and shape.[1-7] Lean body mass includes muscle, bone, and organ density, i.e., the body's fat-free mass. Maintenance of lean body mass extends life, because muscle weakness, organ failure, and death are direct results of lost lean body mass.[8, 9]In one study, men, ages 61-80 years old, who injected pharmacologic concentrations of 50 mg of recombinant hGH 3 times per week for 6 months improved in health achieving a state that is more similar to a youthful state by raising lean body mass by 8 percent, decreasing fat by 14 percent, increasing spleen and liver sizes by 18 percent, and increasing bone density.[10]Other clinical studies on adults with growth-hormone deficiency (GHD) found that hGH replacement therapy improved subjects' body composition and quality of life.[3-5, 11, 12]

Problems Associated with Too Much or Too Little hGH

The American Association of Clinical Endocrinology defines GHD as a cluster of self-perceived symptoms as listed in **Table 1.** Age-related declines in hGH and insulin-like growth factor (IGF)-1 levels are also used to define GHD. Following puberty, hGH declines exponentially.[13]Growth-hormone (GH) secretion peaks at 31 years of age, then declines by 14-50 percent per decade, depending upon gender, activity level, and diet or the onset of chronic disease.14 Women have slower, yet more statistically significant, age-related declines of GH. [15, 16] The prevalence of GHD is not agreed upon and symptoms may occur in a large number of adults.[14] Pharmaceutical company representatives state that GHD is present in approximately 70,000 U.S. adults,[17]while other people say that the incidence is at 40 percent in persons 60-88 years old[18] or others state 1 out of every 4000 people.[19]
Table 2 documents some adverse side effects after 6 months to 1 year use of pharmacologic doses of injectable hGH (0.15 mg per day to 5.0 mg per day) or the associated pathologies of acromegaly. [20, 21]

Gigantism and acromegaly are excellent human models for understanding the dangers of excessive GH. Gigantism is caused by the presence of excess hGH before puberty, with consequences that can include extreme height, abnormal proportion s of the body to the arms and legs, and early death. Acromegaly is caused by the presence of excess hGH after full skeletal growth has occurred. Both of these pathophysiologies are accompanied by a host of abnormal

metabolic changes, such as those that cause glucose intolerance, occasional diabetes mellitus, osteoporosis, respiratory problems, decreased bone mineral density, cardiac arrythmias, and hypertension.

Table 1: Symptoms of Growth Hormone Deficiency

Fatigue is the key symptom and there are clusters of the following symptoms:

- decreased lean body mass
- abdominal obesity and weight gain
- decreased physical strength
- decreased muscle mass
- reduced cardiac performance
- impaired sense of well being
- poor sleep

source : http://www.AACE.com and Ref. 14.

In acromegaly, the most striking problems are enlargement of the heart, lungs, liver, thymus, and spleen. Hyperthyroidism may result in addition to hyperglycemia and glucosuria. Finally, overgrowth of the bones in the face, hands, and feet occur. The jaw protrudes and becomes massive, with thick lips and an overly large tongue, and there is accentuation of the orbital and frontal ridges. The adrenal, thyroid, and parathyroid glands hypertrophy or overgrow. The most notable abnormality caused by excess hGH is early hypersexual drive followed by gonadal atrophy, impotence, and amenorrhea.

Positive and negative effects of hGH highlight the body's complex feedback mechanisms, which respond to various time-dependent and environmental conditions to achieve homeostasis. It may be possible to develop a new, nontoxic, delivery for hGH as an over-the-counter medicine to address the self-diagnosed symptoms of GHD during the aging process. Oral supplementation with homeopathic hGH necessitates systematic evaluation for efficacy. In clinical practice, homeopathic drugs have demonstrated effectiveness repeatedly, [22-24] bringing the body closer to homeostasis. [25]

Our results suggest that HhGH provides a safe, affordable, statistically significant method of improving body composition and shape.

Table 2: Abridged List of Adverse Side Effects From Pharmacologic Concentrations of hGH

• Peripheral edema[a,b]	• SGOT Increase[i]
• Cardiovascular and heart disease[c,d,e]	• SGPT increase [f]
• Increased tissue turgor[f]	• Increased sweating[j]
• Musculoskeletal distress [d]	• Pain[b]

• Loss of lean body mass [g] • joint disorders[b] • Hypertension and sodium retention[h]	• Upper respiratory tract infections[j] • Arthralgia[b,k] • Headaches[k]

[a]Ref. 5; [b] Ref. 21; [c] Ref. 51; [d] Mardh, G., Lundin, K., Borg, Jonsson, B., Lindeberg, Å. Growth hormone replacement therapy in adult hypopituitary patients with growth hormone deficiency: Combined data from 12 European placebo-controlled clinical trials. Endocrinol Metab 1 (suppl A): A43-A49, 1994; [e] Lombardi, G., Colao, A., Ferone, P., Marzullo, P.M., Landi, M.L. Longobardi, S., lervolino, F., Cuocolo, A., Fazio, S., Merola, B., Sacca, L, Cardiovascular aspects in acromegaly: Effects of treatment, Metabolism 45 (suppl I): S57-S60, 1996; [f]Source Serano Laboratories, Norwell, Massachusetts, product insertion for injectable recombinant human growth hormone; [g]Lee P.D.K. Pivarnik, J.M., Bukar, J.G., Muurahainen, N., Berry, P.S., Skolnik, P.R., Nerad, J.L, Kudsk, K.A. Jackson, L., Ellis, K.J., Gesundheit, N,A randomized, placebo-controlled trail of combined insulin-like growth factor 1 and low dose growht hormone therapy for wasting associated with human immunodeficiency virus infection. J Clin Endocrino Metab 81 :2968-2975, 1996;[h]Ho, K,Y., Weissberger, A.J. The antinatriuretic action of biosynthetic human growth hormone in man involves activation of the renin-angiotensin system. Metabolism 39: 133-137, 1990; Genentech Inc., Apple Valley, Minnesota, product insert for injectable recombinant human growth hormone; Ref. 27; [k] Ref. 20.

Some Homeopathy Basics

Homeopathy uses drugs that have been highly diluted to produce safe, less-expensive, and nontoxic medicines. Injectable recombinant hGH is expensive, often costing $1,000 or more per month. Samuel Hahnemann, M.D., the founder of homeopathy, developed the well-known Law of Similars after years of observing the interactions between drugs and the body.[26]He identified two elements underlying the fundamental principle of pharmacology, i.e., a drug has a physiologic effect on the body and the body reacts positively and negatively to a drug, producing symptoms. Dr. Hahnemann found that, by serially diluting drugs into homeopathic preparations, he could induce patients to experience key positive attributes of drugs without having their associated negative reactions. The first systematic study of drug action was the homeopathic practice of "proving" potential medicines on healthy volunteers. [27]

Typically, a homeopathic drug proving includes assessment of the drug's action on healthy subjects at concentrations high enough to produce or alleviate symptoms in sensitive individuals. Data collected from self-perceived symptoms on verum (treatment) versus placebo are compared to determine each drug's guiding symptoms and characteristics.

The Three Studies

We evaluated the efficacy of homeopathic recombinant human growth hormone (HhGH) in three different double-blind placebo-controlled studies. First, we evaluated if there was statistical significance between treatment and placebo; second, we evaluated different treatment effects based on the concentration of treatment. Our results suggest that HhGH provides a safe, affordable, statistically significant method of improving body composition and shape, in terms of increasing upper-arm size, decreasing hip size, and increasing chest size. We also demonstrated improved self-perceived quality-of-life parameters over the placebo effect.

Subjects and Methods

Studies, Subjects, and Protocols

A total of 162 healthy people, ages 18-72 years old, were evaluated for serum IGF-1 levels in three differently designed phase I/II, double-blind placebo-controlled trials (DBPCT).

The *first study*, the Seattle Study, was a 30-day study on 15 subjects, 18-57 years old, who exercised 3 to 5 times per week.

The *second study*, the Santa Fe, Proving Study, included 46 subjects, 19-59 years old, who participated in a homeopathic proving in which the identity of the test substance was not revealed. All subjects noted their symptoms daily. All subjects were given placebo and instructed to chew 1 tablet 3 times per day for 7 days

or until symptoms began, at which point they stopped taking the medication, but continued to record their symptoms in journals that were kept during the study. After this time, there was a 14 day-washout period during which no substance was given; however the subjects described symptoms in their journals. Subjects were then given either a single 6X or 6C HhGH or placebo. These tablets were administered for 7 days or until symptoms began. Symptoms produced by placebo were compared to symptoms produced by verum.

The *third study*, the Boulder Study, enrolled 101 individuals who did not exercise regularly, 29-72 years old, in a 42-day, DBPCT with a crossover after 21 days to the opposite test substance, i.e., treatment was crossed to placebo and vice versa. Test subjects were selected to receive one of two formulations of HhGH, a 6X + 12C (higher concentration of hGH) or a 6C + 100C + 200C (lower concentration of hGH) or placebo, in the form of chewable tablets for 21 days. Following this period, subjects crossed over to another set of tablets that contained either placebo (if they had been given HhGH previously) or one of two formulations of HhGH (if they had been given placebo previously) for an additional 21 days. Subjects were instructed to chew 1 tablet 3 times per day, upon rising, in midafternoon, and in the evening. Additionally, one group was given 6C + 100C + 200C HhGH for 42 days. Another group of three subjects, ages 33, 35, and 62, years old exercised regularly, without taking treatment or placebo. Blood analyses were performed by AAL Reference Laboratories (Santa Ana, California).

Subjects in the Seattle and Boulder studies, but not in the Santa Fe study knew the benefits of the test substance. The three studies are summarized in **Table 3.**

Weight loss occured during HhGH treatment but not during pacebo in the same subjects.

Table 3: Summary of Three Studies

Study name	Type	Size (n)	Length	Potency of test substance(s)
Seattle	DBPCT	(15)	30 days	6C+100C+200C animal source GH
Santa Fe	DBP run-on*a*	(46)	21 days	6X recombinant single potency
	Proving			6X recombinant single potency
Boulder	DBPCT	(101)	42 days	6X + 12C recombinant

	with crossover		42 days	6C+100C+200C recombinant *b*

[a] Santa Fe used a washout period of 14 days in between placebo and treatment; [b]One arm of the crossover design tested unbuffered hGH crossing to buffered hGH; thus, these subjects were given the 6C + 100C +200C HhGH for 42 days (n=14).

Preparation of Homeopathic hGH and Subject Pool

In Seattle, HhGH was derived from purified human growth hormone and serially diluted and hand succussed to produce a final tablet of 6C + 100C + 200C HhGH. Hand succussion was withheld during placebo preparation. In Santa Fe, single 6X (10^{-6} molar) and 6C (10^{-12} molar) HhGH and placebo were prepared. In Boulder, 6C + 100C + 200C HhGH, 6X + 12C HhGH, and placebo were prepared as they were in Seattle. Dropouts occurred in the Boulder Study during the first 21 days as follows: 6X + 12C HhGH, 21 percent; unbuffered HhGH, 14 percent; placebo, 9 percent; and 6C + 100C + 200C HhGH, 9 percent. Results on serum IGF-1 are from all three studies, all other results are from Boulder.

Manual Measurements-Boulder Study

Body composition was determined by using bioelectric impedance analysis (Bioanalogics, Beaverton, Oregon) as validated.[28-30] Blood pressure was monitored every 10 days as was body shape via tape measurements around the circumference of each subject's upper arms, upper chest, hips, and waist.

Laboratory Measurements

In Seattle, subjects voluntarily arrived at the laboratory for blood tests at a consistent time of day that was most convenient for them, most generally from 9-11 am or 2-5 pm. None of the subjects on placebo arrived for the final blood draw. In Boulder, serum IGF-1 was determined at 5-7 pm to control for potential diurnal changes.

Statistical Analysis

For statistical comparison, multivariate analyses were used for different outcomes in the four crossover groups of the Boulder study (n=69). There were two types of analyses conducted for each parameter tested. Pearson and Wilcoxson ranking were done, using The GENMOD Procedure software (SAS ® Institute, Inc., Cary, North Carolina). There was no adjustment for multiple testing because there were separate statistical questions; thus, possibilities for statistically significant artifacts are present. Controls were built into all analyses by testing for differences in age, gender, and baseline values.

Statistical questions were addressed by:

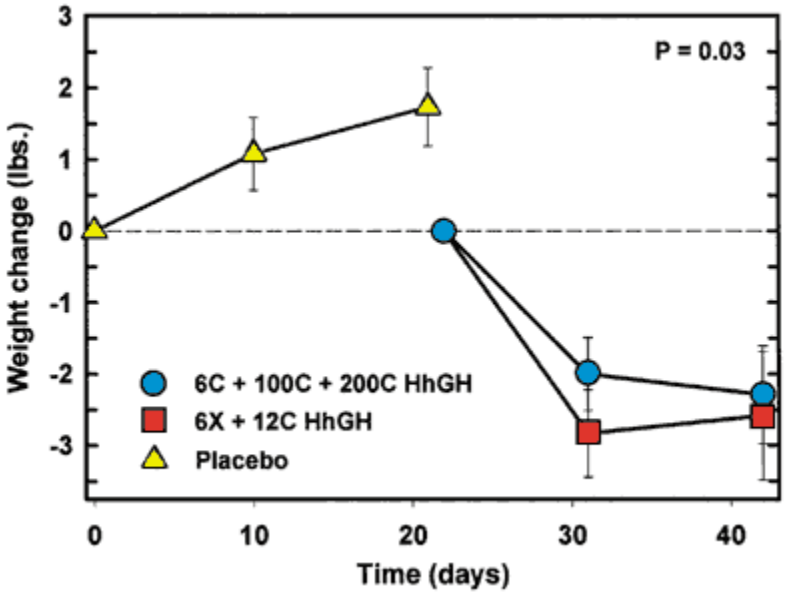
1. comparing HhGH treatment to placebo for each endpoint by:
    - testing mean differences between treatment and placebo.
    - testing time trends
    - testing time and treatment trends

2. testing 6C + 100C + 200C HhGH versus 6X + 12C HhGH.
3. testing 6C + 100C + 200C HhGH versus placebo as in question #1.
4. testing 6X + 12C HhGH versus placebo as in question 1.

Results

Body Composition

Weight changes. Weight loss occurred during HhGH treatment but not during placebo in the same subjects (P=0.03, **Figure 1**).



Individuals on either HhGH treatment maintained -2.07 ± 0.52 lb lower body weight per month versus the weight maintained during the placebo period (P<0.0002). Additionally, subjects on 6X + 12C HhGH tended to lose another -1.2 ± 0.6 lbs per month versus subjects on 6C + 100C + 200C HhGH (P=0.05).

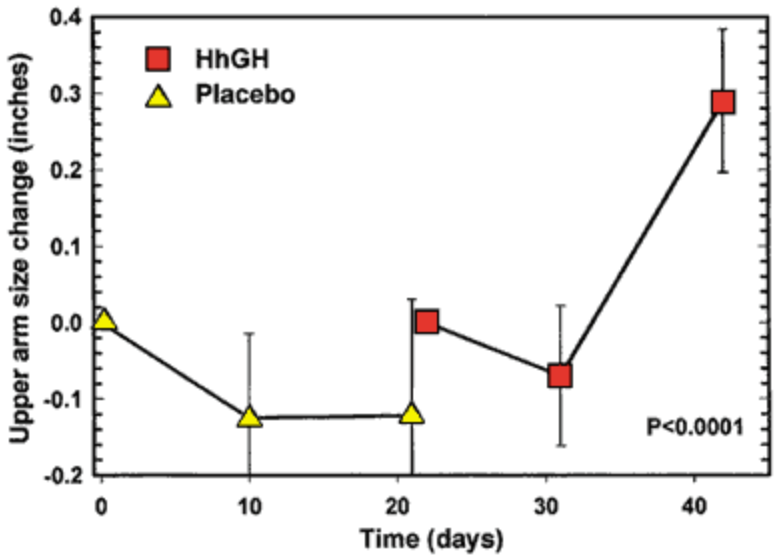


Figure 2. (above) Upper-arm circumference change in subjects on placebo compared to when these crossed over to HhGH. Standard error bars are shown. Body shape. Figure 2 shows an upward trend in upper-arm size (+0.29 ± 0.09 inches) after HhGH compared to a downward trend on placebo (-0.21 ± 0.11 inches; P<0.0001). Trends in upper-arm measurements had statistically divergent time-and-treatment differences between HhGH and placebo (P=0.01). Neither age nor gender affected outcome; only HhGH determined outcome.

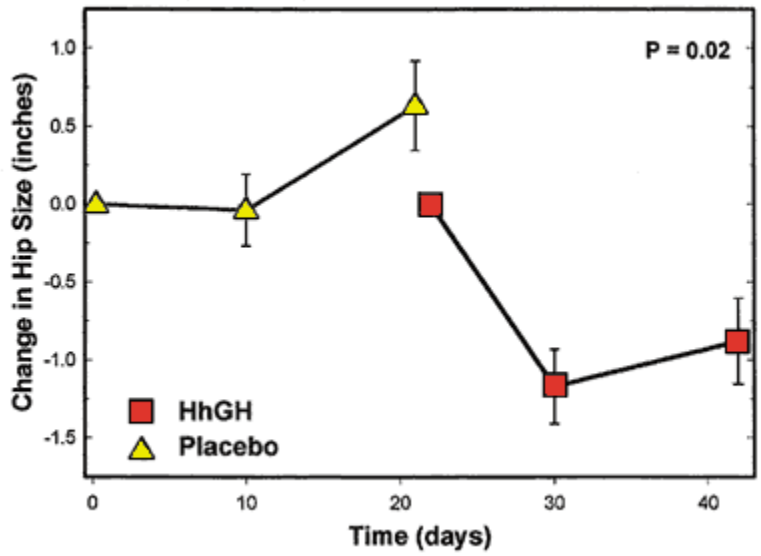


Figure 3. (above) Hip circumference change in subjects on placebo compared to either of the HhGH formulations. Standard error bars are shown. Figure 3 illustrates the decreasing trend in hip size in subjects on HhGH compared to an upward trend for those on placebo (P=0.02). At the end of the study, a time-and-treatment effect correlated to a loss of -2.09 ± 0.50 inches per month versus placebo (P<0.001). Men on 6X+ 12C HhGH lost more hip inches than did women on the same formula (P<0.05). In addition, baseline hip size was a highly significant parameter

for responsiveness to 6X + 12C HhGH (P<0.001). Chest measurement between treatment and placebo did not vary statistically. However, both treatment groups differed from each other statistically (Figure 4). Chest size of subjects on 6X + 12C HhGH averaged +0.4 ± 0.2 inches larger at the end of the study than the chest size of subjects on 6C + 100C + 200C HhGH (P=0.02).

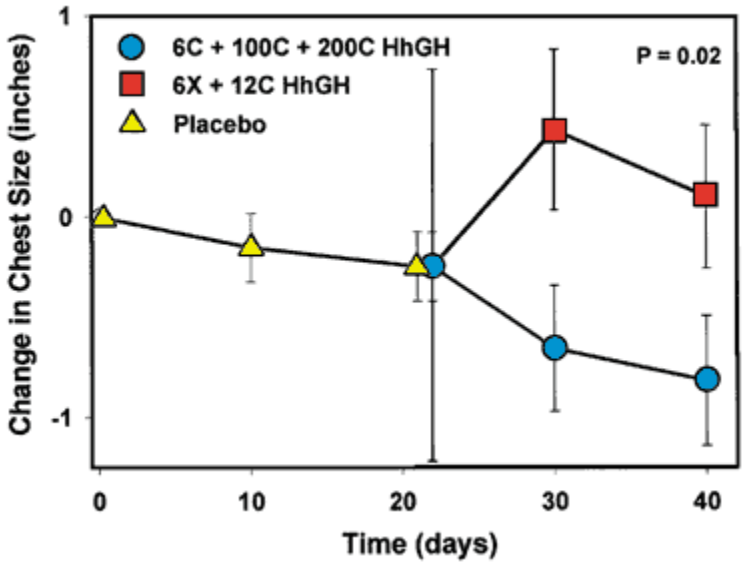


Figure 4. (above) Chest circumference change in subjects on placebo compared to either of the HhGH formulations. Standard error bars are shown. Waist measurements decreased continually by -0.9 ± 0.3 inches over the 42-day period following treatment with 6C + 100C + 200C HhGH (Figure 5). Subjects on placebo decreased waist size minimally (-0.5 ±0.3 inches). Waist size of subjects on 6X + 12C HhGH decreased by -0.3 ± 0.2 inches after 21 days and the subjects continued to lose inches in waist size once treatment stopped with a loss of -0.8 ± 0.4 inches at the end of the study. Three people who only exercised reduced waist size by -2.3 ± 0.9 inches in 42 or fewer days.

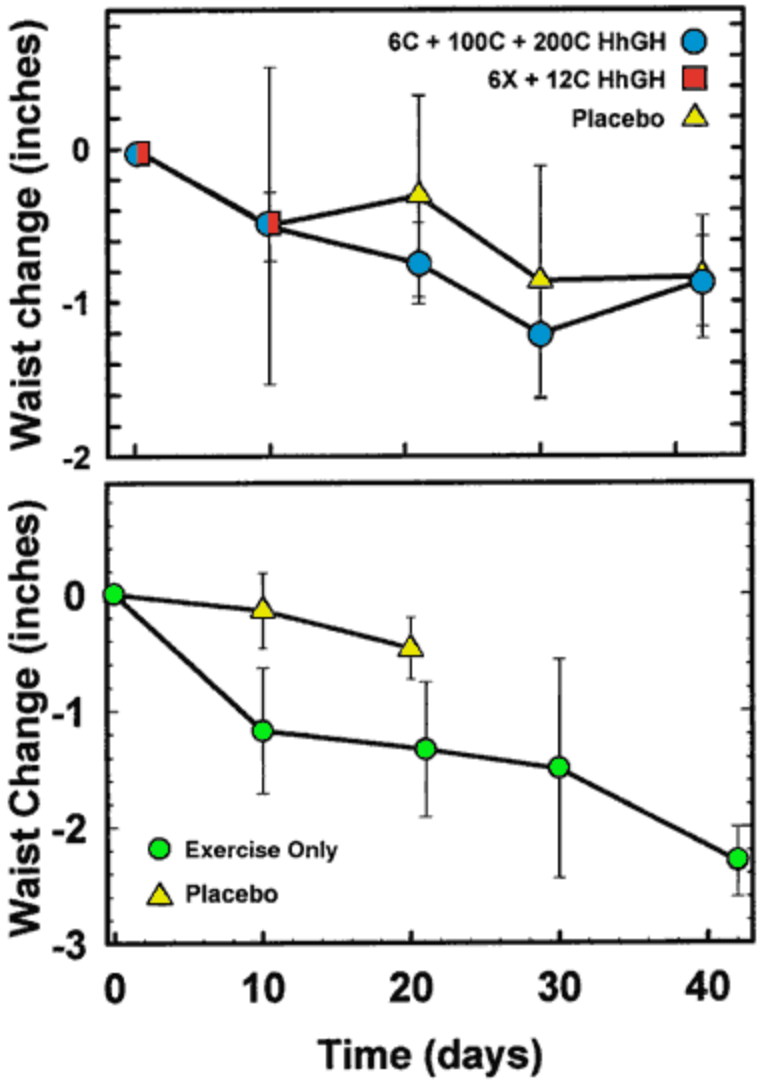


Figure 5. (above) Waist circumference change. Subjects administered 6C+100C+200C throughout the 42-day study (upper graph) or administered 6X+12C for 21 days and then crossed over to placebo for 21 days. Lower graph shows Subjects on placebo for 21 days and subjects who only used regular exercise for throughout the 42-day study.

Insulin Like Growth Factor-1 Measurements-All Three Study Sites

Nearly all baseline measurements of IGF-1 in the Seattle and Santa Fe studies fell below the mean average reference range ($P<0.0001$). In the Boulder study, baseline serum IGF-1 levels were more evenly distributed around the mean average range; 53 percent of individuals in the Boulder study had levels above and 46 percent of subjects had levels below the mean average reference range. All three test sites showed age-related declines in baseline serum IGF-1 levels (Figure 6). There was a statistically significant decline of -1.6 ng/mL/year-of-age in serum IGF-1evel ($P<0.003$); therefore, when entering the study, persons who were 10 years older than other subjects had on average -16 ng/mL lower IGF-1 levels than those subjects at baseline.

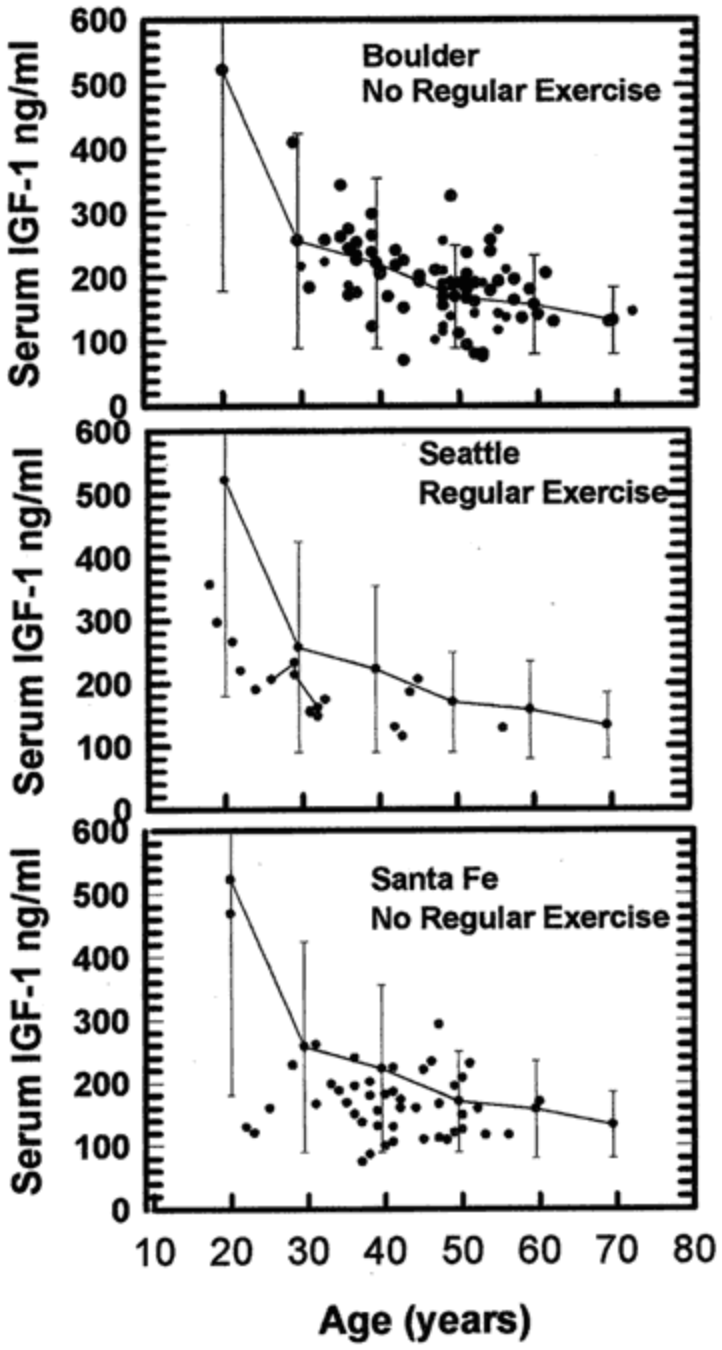


Table 4: Boulder Study

Treatment	(n)	Age	Range	Mean IGF-1	Start range	Finish Range	Trend
6X +12C	17	50 ± 2	29-62 years	198 ± 19	76-410 ng/mL	103-394 ng/mL	Up
6C + 100C + 200C	20	50 ± 2	30-72 years	172 ± 11	102-274 ng/mL	83-381 ng/mL	Up
Placebo	(31)	42 ± 2	31-69 years	194 ± 11	70-343 ng/mL	52-382 ng/mL	Down

Baseline serum IGF-1 levels in subjects of different ages and exercise routines from all three study sites, Boulder, Seattle and Santa Fe.

Oral administration of HhGH stimulated an upward trend in IGF-1 levels by 14 ± 31 ng/mL/month (Table 4). In contrast, placebo demonstrated an average downward trend of -71 ng/mL per month. There was a difference of -81 ± 54.5 ng/mL in IGF-1 between treatment and placebo.

The randomization process in Boulder did not distribute the subjects' IGF-1 levels, ages, or genders evenly into treatment and placebo groups baseline. Because of age differences in Boulder, statistical significance was not measured in serum IGF-1 levels with this small sample size although the trends over time were opposite in direction.

In treated individuals using either HhGH formula, 28 percent increased serum IGF-1 levels above 12 percent and up to 78 percent in 21 days (P=0.058). In contrast, 17 percent of individuals on placebo had increased serum IGF-1 levels above 12 percent and up to 62 percent during the same time frame.

Individuals who were most responsive to treatment produced an age- and time-related bell shaped curve (data not shown). Subjects who were most responsive to early treatment effects on IGF-1 levels were 31-57 years old. Subjects who were more than 32 years old in Seattle increased serum IGF-1 levels by 18 ± 5 percent within the first 15 days of treatment. Boulder subjects who were 35-57 years old had increased serum IGF-1 by a mean of 45 percent (12-78 percent). In contrast, subjects who were between 18-32 years old in Seattle showed no change in IGF-1 during the first 15 days; however these subjects had increased IGF-1 levels by 26 ± 10 percent after 30 days of treatment (data not shown).

Reproducible rises in serum IGF-1 levels occurred in the different cities and in the different study designs

Table 5: Guiding Symptoms for HhGH

Symptom	Boulder	Boulder	Boulder Placebo	Santa Fe Placebo
	6X + 12C	6C		
Constitutional				
Relief from fatigue	**70%**	**69%**	58%	36%
Weight loss	**66%**	50%	33%	50%
Skin and extremities				
Relief from dry scaly skin	**75%**	**58%**	50%	45%
Greater softness/suppleness	25%	**60%**	55%	31%
Eyes				
Visual improvements	50%	**82%**	50%	73%
Relief from floaters	**60%**	**44%**	56%	50%

Oral				
Bleeding gums stopped	**100%**	50%	37%	64%
Respiratory				
Less coughing	56%	**100%**	67%	47%
Less shortness of breath	**75%**	**100%**	50%	40%
Less phlegm buildup	**50%**	**71%**	25%	55%
Gastointestinal/abdominal				
Less pain	0%	**83%**	50%	60%
Less bloating	**67%**	**80%**	25%	25%
Less abdominal obesity	**50%**	**73%**	63%	40%
Urogenital				
Relief from discharges	**100%**	**67%**	75%	0%
Decreased libido *a*	**100%**	57%	80%	71%
Increased libedo *a*	**100%**	**60%**	83%	38%
Musculoskeletal				
Improved physical appearance	50%	**80%**	50%	50%
relief from jaw pain	**100%**	**80%**	67%	75%
Psychologic				
Relief from apathy	**100%**	**80%**	50%	66%
Relief from anxiety	**83%**	**60%**	63%	50%
Relief from anger	-	**83%**	67%	59%
Improved quality of sleep	**57%**	45%	38%	44%
Neurologic				
Relief from headaches	**64%**	**69%**	60%	50%
Relief from weakness in arms and legs	40%	**100%**	60%	66%
Relief from joint swelling	**100%**	**100%**	100%	50%
Relief from knee swelling	**100%**	**100%**	100%	66%

NOTE: Bold numbers indicate that the results were 5 percent greater than those obtained with placebo effects in Santa Fe subjects, who had no knowledge of the substance that was being tested on them. This percentage is accepted as significantly above placebo by the Homeopathic Pharmacopoeia of the United States.

In Boulder, a treatment effect occurred once the placebo group crossed over to treatment (Figure 7A). The 6X + 12C HhGH stimulated serum IGF-1 levels to rise 25 ± 14 percent after 21 days of use. The 6C + 100C + 200C HhGH increased serum IGF-1 levels by 21 ± 13 percent, closely replicating the increase found in Seattle (Figure 7B). Seattle subjects had increased serum IGF-1 levels by 16 ± 8 percent after 30 days. The Santa Fe Proving reproduced the increased serum

IGF-1 measured in Boulder with 6X + 12C HhGH (Figure 7C). Serum IGF-1 increased by 18 ± 10 percent in Santa Fe subjects treated with a single potency of 6X HhGH after only 7 days.

In contrast, there was no significant increase in serum IGF-1 caused by oral administration of a single potency of 6C HhGH or caused by placebo after 7 days in Santa Fe. Placebo groups had no significant change in serum IGF-1 in the three study sites. Subjects in Boulder experienced a transient-rise in serum IGF-1 during the first 10 days of the study and the exercise-only group had decreased serum IGF-1 levels by -28 ± 4 percent after the first 21 days (Figure 7A). After 42 days of exercise only, there was no net change (-3 ± 3 percent) in serum IGF-1.

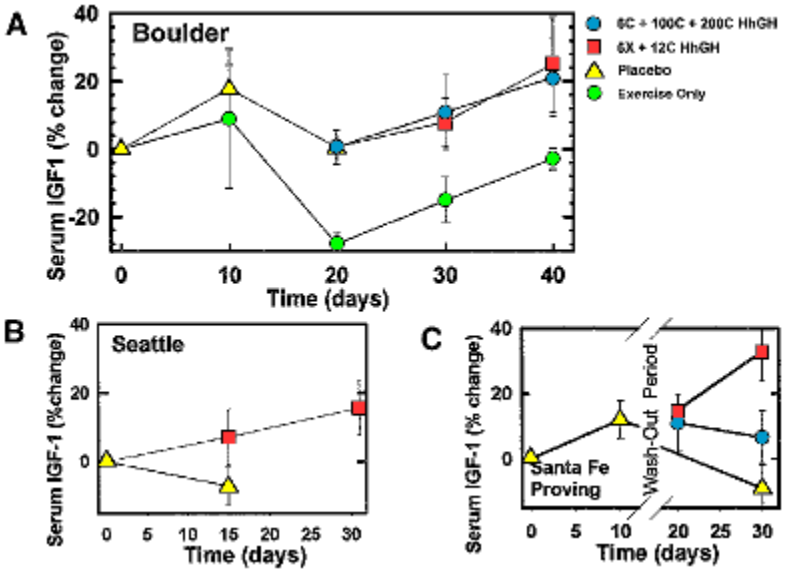


Figure 7. (above) Percent change in serum IGF-1 levels in three different double-blind placebo-controlled sites of: A] Boulder subjects 35-57 years old; B] Seattle subjects who exercised 3-5 times per week; and C] Santa Fe subjects. In Santa Fe, subjects took placebo for 7 days, took nothing for 14 days for the washout period, and then were given either placebo or 6C+100C+200C or 6X+12C for seven day. Standard error bars are shown.

Lean body mass. Lean body mass increased on 6C + 100C + 200C HhGH compared to placebo (Figure 8). The 6C + 100C + 200C HhGH stimulated lean body mass increase by +2.5 ± 1.2 lbs in the first 21 days (Figure 8A.) The placebo group experienced no net gain in lean body mass (1.6 ± 1.9 lbs) after the first 21 days. Once the placebo group was crossed over to 6C + 100C + 200C HhGH, lean body mass increased +2.1 ± 0.98 lbs, reproducing the earlier findings in Boulder (Figures 8A and 8B). In contrast, those people on 6X + 12C HhGH experienced no net gain in lean mass (0.05± 1 lb) after the first 21 days. Overall, the placebo group decreased in lean mass by -0.26 ± 0.09 lbs per month compared to the treatment treatment group (data not shown; P=0.004). The greater the lean body mass at baseline, the greater the ability to gain lean body mass was by the end of the study (P=0.006). The baseline lean body mass was statistically indicative of how well a person could add lean body mass on 6X + 12C HhGH, (P<0.01). Women responded less well because they were -7.3 ± 3.5 lbs lower in lean body mass than men at baseline (P=0.04)

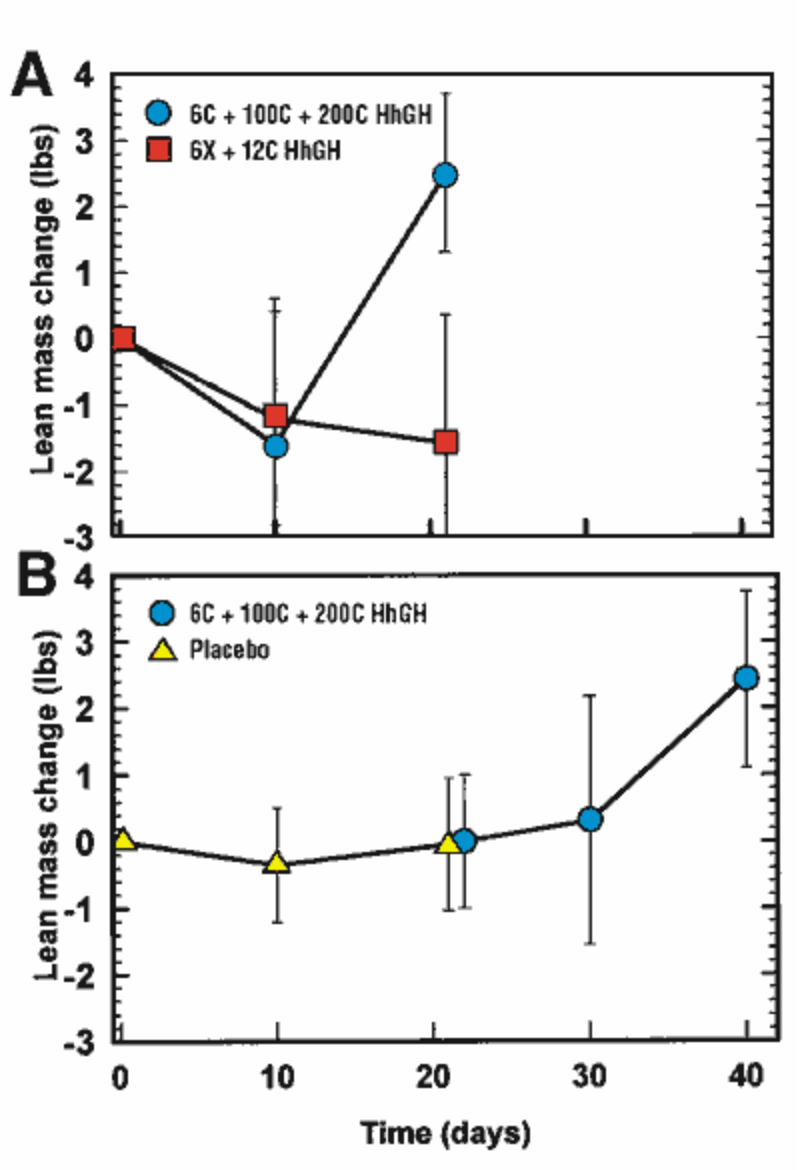


Figure 8. (above) Change in lean mass in subjects who: A] were given 6C+100C+200C or 6X+12C for the first 21 days or B] were given placebo and then crossed over to 6C+100C+200C HhGH. Standard error bars are shown. A treatment effect occurred in terms of gain in lean body mass/total body mass (Figure 9). There were positive gains with both treatments at all time points compared to negative losses in lean body mass with placebo or when using only exercise. A positive ratio indicated greater gain in lean body mass compared to total body mass. Placebo and exercise-only groups experienced negative ratios between lean body mass/total weight, indicating gains in fat rather than in lean body mass.

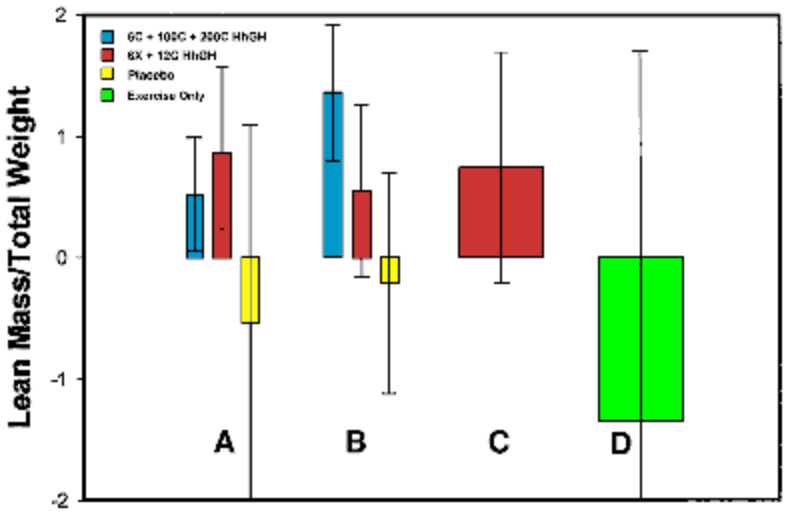


Figure 9. (above) Lean-mass to total-mass ratio in subjects who were given: A] 6C+100C+200C HhGH or 6X+12C HhGH or placebo, respectively, for 10 days; or B] same conditions for 21 days; or C] 6C+100C+200C HhGH for 42 days; or D] exercised only for 42 days. Standard error bars are shown.

Blood Pressure

There was a statistically significant time effect with regard to systolic blood pressure, whereby the treatment group experienced a downward trend compared to an upward trend in subjects on placebo +14.06 ±5.48 mm/Hg per month, P=0.01 (Figure 10). When subjects on placebo crossed over to 6X + 12C HhGH, these same individuals had decreased systolic pressure by -4 ± 3 percent. Prolonged treatment over 42 or fewer days with 6C + 100C + 200C HhGH produced decreased systolic blood pressure in subjects by -8 ± 4 percent.

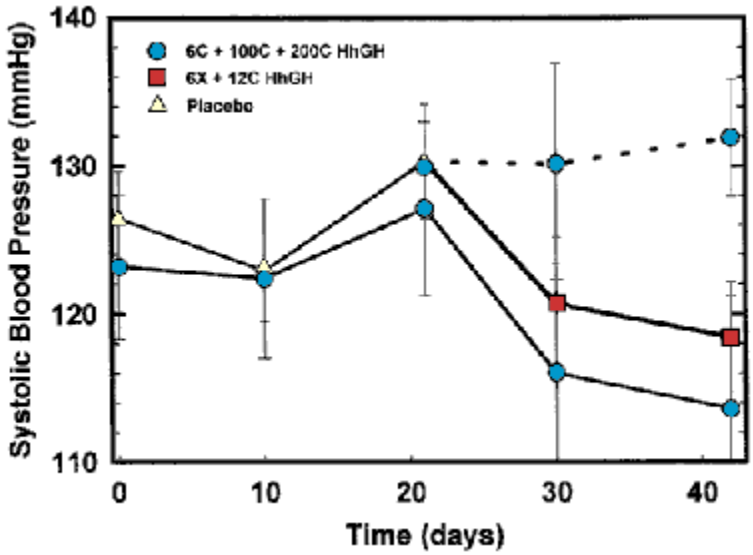


Figure 10. (above) Systolic blood pressure in subjects on placebo who crossed over to 6C+100C+200C HhGH or crossed over to 6X+12C or who were given 6C+100C+200C HhGH for 42 days.

Guiding Symptoms and Characteristics

Self-perceived symptoms of GHD improved with either treatment versus placebo, as noted in Table 5. In Boulder or Santa Fe, respectively, fatigue, reported by 46 percent of enrollees when they entered the study, improved in 69 percent and 70 percent of subjects after either treatment compared to 36 percent and 58 percent on placebo. Other age-related GHD symptoms, such as abdominal obesity, weight gain, decreased physical strength, decreased libido, poor sleep, depression, and mood swings, reported in 21-31 percent of enrollees at study entry were relieved effectively with treatment. Subjects also reported relief from bleeding gums, less buildup of phlegm, relief from coughing, relief from anger, relief from apathy, and relief from urogenital discharges on treatment compared to placebo.

Discussion

Chewable tablets of homeopathic recombinant human growth hormone promoted significant physical, physiologic, and self-perceived quality-of-life benefits compared to placebo in healthy adults, ages 18-72 years old. Statistically significant were weight loss, decreased hip size and increased upper-arm size compared to placebo after 21 days of HhGH. Decreased hip size corresponds directly to less fat storage. Injectable pharmacologic hGH at concentrations of 0.125 international units(IU)/kg per week and 0.250 IU/kg per week reduced hip size statistically after 6 months. [31] The weight loss measured in Boulder was consistent with increased lean body mass. Clinical studies on GHD subjects who had injected pharmacologic concentrations of hGH for 6 months showed no marked changes in body weight.[4, 5 31-33] 6C + 100C + 200C HhGH evoked statistically significant treatment and time effects and 6X + 12C HhGH evoked statistically significant changes that were sensitive to gender, age, and baseline parameters. Specifically, males responded better to 6X + 12C HhGH in increasing upper-arm size, decreasing hip size, decreasing fat, and increasing lean body mass. The greatest weight loss occurred in participants who were using 6X + 12C HhGH. Reproducible increases of more than 2 lbs in lean body mass occurred in subjects using the 6C + 100C + 200C HhGH for 21 days compared to placebo. Chest size in men increased significantly in 21 days on 6X + 12C HhGH versus 6C + 100C + 200C HhGH.

Human GH stimulates lipolysis in adipose tissue directly. The findings in this HhGH study are consistent with hGH's effect on fuel redistribution via the preferential utilization of fat over glucose. [34] A given subject's upper-arm size at the end of the study was influenced by baseline age and arm size, i.e., the younger the person, the greater were the increases in upper-arm size at the end of the study. Clinical studies with injectable GH demonstrated that the dosing schedule for people who are more than 60 years old is considerably less than that required with younger people.[20] It may also be important that different HhGH concentrations be provided to different age groups.

Uneven, random distribution of men and women into the different groups may have affected the statistical significance of treatment compared to placebo. In Boulder, the subjects in placebo group were younger by an average of 2 years than the people in treatment group. There was a statistically significant response effect related to each subject's age, gender, and baseline values with 6X +12 C HhGH. Entry-level lean body mass had a proportionate effect on how much lean body mass could be gained. Thus, the health status of a person upon entering the study was statistically significant on his or her ability to respond to HhGH. Two treatment effects of HhGH that were not significantly influenced by baseline status were body weight and hip size.

Age-related declines in normal serum IGF-1 levels have been reported.[35] We also observed age-related and time-related responsiveness to HhGH in terms of changes in serum IGF-1 levels. Subjects in the Seattle and Boulder studies between 32-57 years old responded rapidly to treatment. Within the first 21 days of HhGH therapy, IGF-1 levels rose 18±5 percent in Seattle and 21±13 percent in Boulder, while younger subjects required longer treatment periods to achieve similar levels. A clinical study on healthy elderly subjects 78 ± 2.5 years old injecting 0.03 mg/kg per week had peak increases in serum IGF-1 levels in the first month of 9 ± 3 percent.[11] Because of the age- and time-related variables, further study with larger sample sizes of subjects clustered into specific age, gender-, and time-matched groups may be necessary to show statistical significance.

Conclusion

There were three major findings from these different double-blind placebo-controlled studies.

Homeopathic hGH Produced Physiologic Effects

The first finding was that oral administration of HhGH produced physiologic effects. Rises in serum IGF-1 levels occurred with both 6C + 100C + 200C HhGH and 6X + 12C HhGH compared to transient rises and final downward trends in subjects who were on placebo. It is important to note that 6X + 12C HhGH stimulated a rapid 18 ± 10 percent physiologic rise in serum IGF-1 level after only 7 days in Santa Fe subjects who were not aware of what substance was being tested. These three studies are the first double-blind placebo-controlled studies to demonstrate differences in the bloodstreams of healthy people in response to HhGH. There have been several double-blind placebo-controlled studies that used a combination of four homeopathic growth factors on people infected with human immunodeficiency virus (HIV) that demonstrated measurable increases in peripheral blood lymphocyte counts and decreases in viral load.[36-39] Although homeopathy's molecular mechanism of action remains to be fully elucidated, HhGH clearly evokes quantifiable physiologic changes in the bloodstream.

Multiple Beneficial Effects of Treatment Were Demonstrated

The second significant finding from these studies is that pharmacological benefits of injectable hormonal replacement were experienced with a homeopathic oral chewable tablet. Injectable growth hormone is well known for its positive effects on lean body mass, producing weight and fat loss, improving pulmonary function, lowering blood pressure, relieving fatigue, improving

vision, producing body shape changes, and improving psychologic well-being, skin quality, sleep quality, and libido among other benefits.

Similar to injectable hGH, chewable tablets of HhGH had positive effects on lean body mass, produced weight and fat loss, relieved fatigue, produced body shape changes, and improved psychologic well-being.

Homeopathic hGH also improved self-perceived measures related to quality of life significantly, such as energy increase, weight loss, improved vision, increased libido, improved sleep quality, improved breathing, and improved skin softness. Thus, an oral formulation that was at least 4000 times lower in concentration than an injectable hGH provided some of the same benefits of the injectable hGH without its side effects.

Oral administration of HhGH lowered systolic blood pressure after 3 and 6 weeks, depending upon the formula that was used. Injectable hGH at 700 µg per day, 3 times per week, for 6 months, corrected systolic heart function that was caused by left-ventricle low-mass index.[40] The degree of change in systolic function induced by HhGH requires further and more extensive clinical study.

It is noteworthy that subjects who enrolled in this study reported unique self-perceived benefits, far above the placebo effect and never-before associated with hGH injections. For example, subjects reported relief from bleeding gums, less phlegm build-up, relief from coughing, relief from anger, relief from apathy, and relief from urogenital discharges. These unique characteristics derived from HhGH underlie the possibility that a different signaling pathway is utilized than the pathway commonly outlined by molecular biologists. [41] In this way, HhGH is a different type of medicine than injectable hGH. It is conceivable that the serial dilution and shaking methods used to prepare homeopathic medicines contribute to significant alterations in the physical and chemical properties of the solvent and evoke bioelectric field signals to users.[42-45] The degree of effectiveness of HhGH compared to injectable hGH requires further study. It is obvious that the number of molecules in a preparation is not equal to the biologic activity evoked at the physiologic level. The transfer of information to cells via nonmolecular mechanisms of action are being investigated by several laboratories.[43, 46, 47]

The current double-blind placebo-controlled study represents a clinical demonstration of Hahnemann's Law of Similars, i.e. positive actions of hGH can be gained with a homeopathic formulation. Conventional clinical practitioners administer pharmacologic concentrations of injectable hGH for 3-4 weeks until optimal physiologic responses are achieved and then they cycle the dose to every 3-4 days at lower concentrations with periods of no treatment.[48] The same dosing schedule of 3-4 weeks with daily HhGH followed with cycling the dose to every 3-4 days may be ideal for achieving optimal quality-of-life benefits without negative effects. Additional and long-term studies are necessary to determine if side effects above placebo effects occur with HhGH. In our studies, no toxic side effects were reported.

Hahnemann's Law of Similars Was Applicable

The third significant implication of these findings relates to the other part of Hahnemann's Law of Similars, which states: "Whatever symptoms and syndromes a substance causes in large or toxic doses, it can heal when given in specifically prepared, exceedingly small homeopathic doses."[49] Subjects who received HhGH in these three differently designed studies reported relief from symptoms that they reported when they entered the studies. Symptoms relieved by HhGH treatment often matched the symptoms known to be caused by toxic doses of injectable hGH. Specifically relieved above placebo were headaches, edema, pain, and anxiety. Reductions in systolic blood pressure from HhGH are consistent with the findings that excessive hGH in patients with acromegaly correlated directly with cardiac abnormalities.

Exercise and Serum Insulin-Like Growth-Factor-1 Levels

Serum IGF 1 has been cited most frequently as a reliable measure of hGH physiologic activity, however serum IGF-1 levels are not good indicators of GHD.[14] We found that a statistically significant number of people enrolled in these studies were below national laboratory reference ranges for serum IGF-1. The potential high frequency of GHD within the general population observed in these studies suggest that stress, exercise, and lifestyle/diet in American society may play a significant role in aging. It is noteworthy that the participants from the Seattle study had a history of exercising at least 3-5 times per week. Yet, these "healthy subjects," who were 18-57 years old were all below the normal reference range for serum IGF-1 levels at baseline. Additionally, 3 people in Boulder that exercised regularly and did not administer treatment or placebo fell below their baseline values of serum IGF-1 throughout much of the study. Thus, exercise without adequate nutrition may contribute to low serum IGF-1 levels.

Homeopathic hGH Works; More Studies Can Bolster Findings

The data collected in the Boulder study on lean body mass raises an interesting question related to the dose-response curve between lean body mass gain and concentration of hGH administered to the body. Lean body mass increased after pharmacologic doses of injectable hGH by approximately 7 percent in patients with hypothalamic-pituitary disease or GHD, and/or in healthy elderly subjects (ranging from 0.03 mg/kg per week to 0.55 mg per week) for 6-12 months. [11, 20, 52]Loss of fat mass did not always accompany the lean body mass increases of 0.88-1.1 lbs per month induced by injectable hGH. In our studies with healthy adults, chewable tablets of the 6C + 100C + 200C HhGH, lean body mass increased by approximately 3.2 ± 1.7 lbs per month during a short-term 3-week treatment period). Further research is warranted with age-matched, gender-matched, and baseline-specific controls on larger sample sizes and for longer-term treatment periods to test if HhGH produces long-term positive results at far lower concentrations than injectable hGH. Overall, HhGH is an effective oral therapy that evokes positive physiologic and psychologic benefits above the placebo effect without toxicity.

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References

1. Wolfe, J. Growth hormone: A physiological fountain of youth? *J Anti-Aging Med* 1:9-25, 1998. :p>
2. Klatz, R., Kahn, C. *Grow Young with hGH.* New York: HarperCollins, 1997.
3. DeBoer, H., Blok, G.J., van der Veen, E.A. Clinical aspects of growth hormone deficiency in adults. *Endocr Rev* 16:63-86, 1995.
4. Bengtsson, B.Å., Eden, S., Lonn, L., et al. Treatment of adults with growth hormone (GH) deficiency with recombinant human GH. *J Clin Endocrinol Metab* 76:309-317, 1993.

5. Jørgensen, J.O., Pedersen, S.A., Thuesen, L.L., et al. Beneficial effects of growth hormone treatment in GH-deficient adults. *Lancet* i:1221-1225, 1989.

6. Kelley, K.W. The role of growth hormone in modulation of the immune response. *Ann NY Acad Sci* 594:95-103, 1990.

7. Crist, D.M., Peake, G.T., Mackinnon, L.T., Sibbitt, W.L., Kraner, J.C. Exogenous growth hormone treatment alters body composition and increases natural killer cell activity in women with impaired endogenous growth hormone secretion. *Metabolism* 36:1115-1117, 1987.

8. Griffin, G.E., Paton, N.I., Cofrancesco, Jr., J., Arastéh, K., Bauer, G., Schwenk, A., Mauss, S., Mulligan, K. Nutrition and quality of life in HIV infection: The role of growth hormone in HIV-associated wasting. *J Clin Res* 1:199-218, 1998.

9. Kotler, D.P., Tierney, A.R., Wang, J., Pierson, Jr., R.N. Magnitude of body-cell-mass depletion and the timing of death from wasting in AIDS. *Am J Clin Nutr* 50:444-447, 1989.

10. Rudman, D. Feller, A.G., Nagraj, H.S., Gergans, G.A., Lalitha, P.Y., Goldberg, A.F., Schlenker, R.A., Cohn, L., Rudman, I.W., Mattson, D.E. Effects of human growth hormone in men over sixty years old. *N Engl J Med* 323:1-6, 1990.

11. Cuttica, C.M., Castoldi, L., Gorrini, G.P., Peluffo, F., Delitala, G., Fillippa, P., Fanciulli, G., Giusti, M. Effects of six-month administration of recombinant human growth hormone to healthy elderly subjects. *Aging Clin Exp Res* 9:193-197, 1997.

12. Cuneo, R.C., Salomon, F., McGauley, G.A., Sönksen, P.H. The growth hormone deficiency syndrome in adults. *Clin Endocrinol* [Oxford] 37:387-397, 1992.

13. Rudman, D. Growth hormone, body composition and aging. *J Am Ger Soc* 33:800-807, 1985.

14. Ho, K.Y., Veldhuis, J.D. Diagnosis of growth hormone deficiency in adults. *Endocrinol Metab* 1(suppl. A):S61-S63, 1994.

15. Gregerman, R.I., Bierman, E.I.L. Aging and hormones. In: Williams, R.H. (ed.) *Textbook of Endocrinology*. (5th ed.) Philadelphia: W.B. Saunders, 1981, p. 1192.

16. Ho, K.Y., Weissberger, A.J. Secretory patterns of growth hormone according to sex and age. *Horm Res* 33 (suppl 4):7-11, 1990.

17. Pramik, M.J. Recombinant human growth hormone. *Genetic Engineering News*, January 1,1999, pp. 15, 27, 31.

18. Gelato, M.C. Aging and immune function: A possible role for growth hormone. *Hormone Res* 45:46-49, 1996.

19. Kiess, W., Kessler, U., Schmitt, S., Funk, B. Growth hormone and insulin-like growth factor-1: Basic aspects. In: Flyvberg A. Ørskov, H., Alberti, G. (eds.) *Growth Hormone and Insulin-Like Growth Factor-1 in Human and Experimental Diabetes*. New York: John Wiley & Sons, 1993, pp. 1-22.

20. Toogood, A.A., Shalet, S.M. Growth hormone replacement therapy in the elderly with hypothalamic-pituitary disease: A dose-finding study. *J Clin Endocrinol Metab* 84:131-136, 1999.

21. Holloway, L., Butterfield, G., Hintz, R.L., Gesundheit, N., Marcus R. Effects of recombinant human growth hormone on metabolic indices, body composition, and bone turnover in healthy elderly women. *J Clin Endocrinol Metab* 79:470-479, 1994.

22. Linde, K., Clausius, N., Ramirez, G., Melchart, D., Eitel, F., Hedges, L.V., Jonas, W.B. Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. *Lancet* 350:834-843, 1997.

23. Reilly, D., Taylor, M.A., Beattie, N.G.M., Campbell, J.H., McSharry, C., Aitchison, T.C., Carter R., Stevenson, R.D. Is evidence for homeopathy reproducible? *Lancet* 344:1601-1606, 1994.

24. Kleijnen, J., Knipschild, P., ter Riet, G. Clinical trials of homeopathy. *Br Med J* 302:316-323, 1991.

25. Van Wijk, R., Wiegant, F.A.C. The similiar principle as a therapeutic strategy: A research program on stimulation of self-defense in disordered mammalian cells. *Altern Ther Health Med* 3:33-38, 1997.

26. O'Reilly, W.B. (ed.) (Decker, S., transl.) *Organon of the Medical Art*, 6th ed. Redmond WA: Birdcage Books, 1996.

27. Endler, P.C., Schulte, J. *Ultra High Dilution: Physiology and Physics*. Boston: Kluwer Academic Publishers, 1994, p. ix.

28. Girandola, R.N., Contarsy, S. The validity of bioelectrical impedance to predict human body composition., Olympic Scientific Congress, September 10, 1988, Seoul, Korea. In: Olympic Scientific Congress. *New Horizons of Human Movement*, Seoul: Olympic Scientific Congress, 1988, p. 9

29. Jodoin, R.R., Trott, S.G., Shizgal, H.M. Determination of whole body composition from whole body electrical impedance. *Surg Forum* 39:50-52, 1988.

30. McDougall, D., Shizgal, H.M. Body composition measurements from whole body resistance and reactance. *Surg Forum* 37:42-44, 1986.

31. Stiegler, C., Leb, G. One year of replacement therapy in adults with growth hormone deficiency. *Endocrinol Metab* 1 (suppl. A):A37-A42, 1994.

32. Whitehead, H.M., Boreham, C., McIlrath, E.M., Sheridan, B., Kennedy, L., Atkinson, A.B., Hadden, D.R. Growth hormone treatment of adults with growth hormone deficiency: Results of a 13-month placebo controlled cross-over study. *Clin Endocrinol Metab* (Oxford) 36:45-52, 1992.

33. Salomon, F., Cuneo, R.C., Hesp, R., Sönksen, P.H. The effects of treatment with recombinant human growth hormone on body composition and metabolism in adults with growth hormone deficiency. *N Eng J Med* 321:1797-1803, 1989.

34. Møller, N. The role of growth hormone in the regulation of human fuel metabolism. In: Flyvberg, A., Ørskov, H., Alberti, G. (eds.) *Growth Hormone and Insulin-Like Growth Factor-1 in Human and Experimental Diabetes.* New York: John Wiley & Sons, 1993, pp. 77-108

35. Prewett, N.A., Bettica, P., Mohan, S., et al. Age-related decreases in insulin-like growth factor-1 and transforming growth factor-b in femoral cortical bone from both men and women: Implications for bone loss with aging. *J Endocrinol Metab* 78:1011-1016, 1994.

36. Brewitt, B., Traub, M., Hangee-Bauer, C. Patrick, L., Standish, L.J. Recovery of homeostasis and functional immune system: Positive short term and long term effects with homeopathic growth factors IGF-1, PDGF-BB, TGF beta 1 and GM-CSF. In: Standish, L.J., Calabrese, C., Galantino, M.L. (eds.) *AIDS and Alternative Medicine: The Current State of the Science.* New York: Harcourt Publishers International, in press.

37. Brewitt, B. Homeopathic growth factors-support for the functional immune system [presentation at Alternative Medicine Symposium at the meeting]. 12th World AIDS Conference, June 28-July 3, 1998, Geneva, Switzerland.

38. Brewitt, B. Homeopathic growth factors support long term survival and maintain low viral loads [poster presentation, abstr. 60495]. 12th World AIDS Conference, June 28-July 3, 1998, Geneva, Switzerland.

39. Brewitt, B., Standish, L.J. High dilution growth factors/cytokines: Positive immunologic, hemotologic and clinical effects in HIV/AIDS patients [abstr. Th.B.4108]. In: *Abstracts of the XIth International Conference on AIDS*, July 7-12, 1996, Vancouver, Canada, vol. 2.

40. Edán, S., Johnston, D.G. Cardiovascular risk factors in growth hormone deficiency and effect of growth hormone replacement therapy. *Endocrinol Metab* 1 (suppl. A):A67-A69, 1994.

41. Spagnoli, A., Rosenfeld, R.G. The mechanisms by which growth hormone brings about growth: The relative contributions of growth hormone and insulin-like growth factors. *Endocrinol Metab. Clin N Am* 1996; 25:615-631.

42. Elia, V., Niccoli, M. Thermodynamics of extremely diluted aqueous solutions. *Ann NY Acad Sci* 879:241-248, 1999.

43. Brewitt, B. Bioelectromagnetic medicine and HIV/AIDS treatment: Clinical data and hypothesis for mechanism of action. In: Standish, L.J., Calabrese, C., Galatino, M.L. (eds.) *AIDS and Alternative Medicine: The Current State of the Science.* New York: Harcourt Publishers International, in press.

44. Lo, S.Y., Lo, A., Chong, L.W. Physical properties of water with I_E structures. *Modern Physics Lett B* 10:921-930, 1996.

45. Brewitt, B. Quantitative analysis of electrical skin conductance in diagnosis: Historical and current views of bioelectric medicine. *J Nat Med* 6:66-75, 1996.

46. Benveniste, J. Transfer of biological activity by electromagnetic fields. *Frontier Perspectives* 3:12-15, 1993.

47. Bourguignon, G.J., Jy, W., Bourguignon, L.Y.W. Electric stimulation of human fibroblasts causes an increase in Ca^{+2} influx and the exposure of additional insulin receptors. *J Cell Physiol* 140:379-385, 1989.

48. Janssen, Y.J.H., Frölich, M., Roelfsema, F. The absorption profile and availability of a physiological subcutaneously administered dose of recombinant human growth hormone (GH) in adults with GH deficiency. *Br J Clin Pharmacol* 47:273-278, 1999.

49. Ullman, D. *The Consumer's Guide to Homeopathy.* New York: Jeremy Tarcher/G. Putnam's Sons, 1995, p. 5.

50. Saccà, L. Cittadini A., Fazio, S. Growth hormone and the heart.*Endocr Rev* 15:555-573, 1994.

51. Maison, P., Balkau, B., Simon, D., Chanson, P., Rosselin, G., Eschwêge, E. Growth hormone as a risk for premature mortality in healthy subjects: Data from the Paris prospective study. *Br Med J* 316:1132-1133, 1998.

52. Bramnert, M., Berntorp, E., Groop, L., Manhem, P. Effects of growth hormone replacement therapy on blood pressure regulation and coagulation factors. *Endocrinol Metab* 1(suppl. A):A57, 1994.

- **Barbara Brewitt, Ph.D.,** is chief scientific officer at Biomed Comm., Inc., Seattle, Washington;
- **James Hughes, M.D.,** is the medical director of Hilton Head Longevity Center, Bluffton, South Carolina;
- **Elizabeth A. Welsh, Ph.D.,** is the head of growth factor research and therapeutics at Biomed Comm., Inc., Seattle, Washington;
  Robert Jackson, D.C., is a chiropractic physician and consultant at Applewood Health Center, Wheat Ridge, Colorado.