Title: Human Growth Hormone Suplementation and Stimulation Therapy for Anti- Aging - Risks and Benefits

Subtitle: Quantum Electro Dynamic Trivector Stimulation as a viable safe, inexpensive, and effective process.

When information from research of human growth hormone (hGH) replacement treatment (GHRT) in elderly men showed that treatment increased muscle mass and decreased abdominal fat, immediate public interest was provoked Since body composition of hGH-treated old men tended to resemble that of younger persons, the data was over-interpreted to suggest that the hormone could restore youth . The press even went as far as to suggest that the hormone could be a "fountain of youth" . Especially important for entrepreneurs was the fact that large numbers of the affluent "baby boom" generation were passing beyond middle age, becoming acutely aware of their mortality and were prepared to purchase the "rejuvenating" hormone, no matter the cost. Making this business opportunity even more tangible was the fact that an unlimited supply of virus free hGH had become available through recombinant gene technology several years earlier. Unfortunately, this link with commercialism and the persisting, exaggerated and unfounded claims of efficacy blunted enthusiasm for continued, legitimate investigation of hGH's true value in opposing the maladaptive effects of aging.

Sylvester Stalone’s arrest and conviction in Australia last year has brought further attention to the issue of hGH. The lack of true research should not be overlooked to satisfy greed or vanity. There are risks to using any hormone therapy. Most importantly is dependency. You own production of hormone goes down when you supplement the hormone externally. The amount of hormone needed is actually quite small. The body makes what it needs and this is a very small amount. The supplement of external hormone uses vast amounts that can overwhelm the body and disturb regulating consequences. There is a extremely complex fractal

environment in the body and upsetting the balance takes a careful consideration.

Using the field of Nelson Bio-Quantum Electro Dynamics can stimulate the production of natural hormone through electro-Dynamic means. By stimulating the trivector signature of the hormone into the body it stimulates a balancing of the hormone production. That stimulates the deficient, while attenuating the excess. The regulatory process of the body is a process of electrical cybernetics. There are sensitive regulating processes that are completely electrical and as such can be accessible to an feedback cybernetic stimulus.

Since growth hormone neuroendocrine function declines during aging, and since there is documented evidence showing that poor health and lost vitality can be reversed by GHRT in young adults with pathogenic growth hormone deficiency (GHD), considerable debate over its value in aging continues even today. At the heart of this debate is the question of whether it is reasonable to extrapolate positive data on GHRT from GHD to the aging condition. Research has proven that electrical stimulus can also be successful in stabilizing hGH and preventing aging.

A Historical Outlook on GHRT

Prior to development of recombinant gene technology, GHRT was restricted almost entirely to children with short stature. Once they reached a height that was considered to be within normal range, therapy was discontinued even though it was known that as adults, GHD children became symptomatic with metabolic "insufficiency." The reason for rigid rationing was limited availability since the only source of hGH at the time was pituitaries from human cadavers. Therefore, children were given first consideration for treatment. However, even the limited supply of hGH was lost in 1983 when Creutzfeldt-Jakob virus was found to be transmitted by the cadaver-derived hormone. Because pooling of pituitary extracts was required, it was not possible to adequately reduce the risk for viral contamination and so the FDA withdrew cadaver derived hGH from the market. However, since GHRT provided an important therapeutic treatment for short stature, alternatives to cadaver-derived hGH were immediately sought. To

facilitate discovery, the FDA provided orphan drug status for hGH, which made it significantly easier for companies to register their product(s) for sale. An additional economic incentive for discovery and development of a synthetic hGH was its high cost, which was based at least in part from the precedent established by its original production process, i.e. isolation and purification from large numbers of human cadavers. Furthermore, with an increased supply of hGH, the hormone could be used for more clinical indications such as treatment of adult GHD, thereby creating an even more lucrative market. The basis for this expanded market was that short-stature children who stopped receiving hGH or adults who suffered pituitary dysfunction displayed a higher than normal incidence of cardiovascular disease, diabetes, high blood pressure, bone loss, reduced muscle mass, increased adiposity, reduced immune function, etc. Thus, it seemed that hGH was necessary for more than growth, hGH was in fact, a somatotrophin that contributed to total body health and well being throughout life. This concept was supported by the fact that GHRT resolved many of the problems associated with adult GHD. Accordingly, these economic and scientific incentives resulted in the first major success of the biotechnology sector. Genentech marketed Protropin¨ in 1985, driving its stock value to unprecedented heights and stimulating immediate competition from other companies. Recognizing that Protropin¨ contained an additional methionyl group as a result of its production process, the Lilly Pharmaceutical Company successfully entered the GH market with its own product, Humatrope¨, which had the exact structure of the human hormone. Currently, all commercially available hGH products- except Protropin¨ have exactly the same structure as the naturally occurring hormone.

Clinical Effects of GHRT in GHD

1. Increased Morbidity and Mortality in GHD

Adults whose pituitary glands produce insufficient hormones of all types suffer increased overall mortality compared to healthy individuals. In many cases the cause of their premature mortality is cardiovascular disease (5,6). Reports of an association between growth hormone deficiency and cardiovascular disorders

showed that when hormone replacement therapy did not include hGH, hypopituitary patients suffered death in greater numbers due to heart disease than expected. This risk is not seen in the Electro Dynamic stimulation.

In addition to increased mortality due to cardiovascular disease, other maladaptive changes associated with GHD were found to include premature atherosclerosis , altered lipoprotein metabolism , abnormal body composition characterized by increased weight with reduced muscle and increased central adiposity , impaired glucose homeostasis , fibrinolysis and cardiac function , decreased exercise capacity and quality of life. Thus, individuals that lack hGH have higher than normal risks for developing intrinsic diseases that contribute to their premature deaths. Conversely, GHRT reduced mortality rate in GHD patients to the expected number for the general population . This risk is not seen in the Quantum Electro Dynamic stimulation.

2. Cardiovascular Effects

Cardiac output and oxygen consumption decline in adults who undergo surgical removal of their pituitary glands. Furthermore, the structure of their hearts becomes altered, exercise capacity is reduced and pumping action or diastolic/systolic function becomes impaired. On the other hand, GHRT in GHD patients has an anabolic effect on cardiac structures thereby providing beneficial effects on diastolic and systolic functions. Direct effects on the heart include stimulation of the velocity of circumferential fiber contraction as well as increasing the degree to which they shorten. It was also reported that the maximum tension of cardiomyocyte fibers from hearts of rats with GH secreting tumors was increased as was the sensitivity of myofiliments to calcium exposure. These observations suggest that GH has a beneficial effect on cardiac muscle fiber contractility. Another dramatic demonstration GH cardiovascular efficacy was reported as the ability of GHRT to reverse atherosclerotic lesions and other sequellae of heart disease. This effect and benefit is also demonstrated in the Quantum Electro Dynamic stimulation.

3. Renal Effects and Body Hydration

GH administration causes the body to retain sodium which in turn causes an acute increase in extracellular water content and a slower increase in plasma volume. Increased extracellular volume which results from GH therapy could contribute to improved cardiac function by the Starling effect- which states that increased filling of the heart leads to greater output. Thus, the effect on hydration in concert with those positive effects on the cardiovascular system cited above could contribute to the improved exercise capacity seen in GHD patients receiving GHRT.

4. Hypertension

Although reports on blood pressure in GHD adults are somewhat conflicting, the hormone deficient patients seem to be predisposed to develop hypertension. The main cause for this effect may be central arousal of the sympathetic nervous system, which has been documented in GHD adults using direct recordings from inside neurons. GH administration was reported to improve left ventricular function without changing mass or thickness of the wall in this part of the heart. This finding suggested that GHRT could also directly increase the strength of heart muscle contraction. Furthermore, GHD is associated with reduced concentrations of vascular system nitric oxide. Since nitric oxide is a locally acting or paracrine vasodilator, multiple factors may contribute to hypertension in GHD. In any event, growth hormone reduces total peripheral resistance, lowers blood pressure and increases nitric oxide production, thereby correcting GHD associated hypertension. In addition to relieving hypertension, GHRT was also shown to actually reverse early signs of atherosclerosis in major blood vessels. This effect and benefit is also demonstrated in the Quantum Electro Dynamic stimulation.

5. Effects on Body Composition

In addition to reversing the negative effects of GHD on cardiovascular structure and function, GH replacement opposed maladaptive changes in body composition associated with the disorder. The most striking effects of GHD on body composition involve the adipose tissue, bone and muscle. Numerous well

controlled clinical studies demonstrate that fat especially within the abdomen is increased, while lean body mass or muscle is reduced in association with low hGH. These changes as well as demineralization of bone, which is also marked, are reversed by hGH administration. This effect and benefit is also demonstrated in the Quantum Electro Dynamic stimulation.

a. Lean Body, Fat Mass & Distribution

Numerous well controlled clinical studies demonstrated that growth hormone deficiency is associated with increased body fat, particularly in the abdomen, as well as reduced lean body mass. When growth hormone is administered to patients suffering these symptoms, they are incontrovertibly reversed. As early as 1959, hGH was shown to cause lipolysis or fat breakdown in man. This effect results from hydrolysis of triglycerides, stimulation of fatty acid transport from adipose tissue to the liver and by inhibition of free fatty acid re-esterification into triglycerides by adipocytes.

GHD adults have increased waist/hip ratios consistent with elevated visceral fat volume. Evidence that this dynamic pattern of fat distribution is due to GHD comes from the fact that visceral fat mass increases in patients suffering from acromegaly, a disease in which excessive hGH is produced by the body, after they receive treatment to reduce GH hypersecretion. Conversely, when adults with GHD receive GH treatment, visceral mass and subcutaneous fat is reduced and this effect is preserved or even increased after prolonged therapy.

Besides reducing fat mass, growth hormone replacement therapy initially stimulates whole-body protein synthesis which after a few months returns toward baseline with establishment of a new steady state. This anabolic action of GH is manifested as increased lean body cell mass associated with increased volume of visceral organs and muscle. The changes resulting from GH exposure are potentially significant to GHD patients as well as to the frail elderly because of their reduced muscle mass and strength relative to age-matched or younger controls. Muscle endurance as well as isokinetic muscle strength is also reduced in GHD. In contrast, GHRT increases muscle volume and maximum voluntary

isometric and isokinetic muscle strength.

b. Bone Mineralization

The anabolic action of GH on bone is demonstrated by delayed bone maturation and short stature in children with GHD. Adults with GHD experience reduced bone mass and density. Histomorphometric bone data from these patients suggest a prolonged reversal phase, delayed coupling or a delay in the mineralization process indicative of low bone turnover. On the other hand GHRT increases bone mass in animals and humans. For example, data from a two year clinical trial with patients suffering adult-onset GHD, bone mineral density (BMD) increased in lumbar spine and proximal femur after GHRT However, it required a treatment period of 18 months to produce the increase in BMD, explaining why trials of shorter duration were unable to demonstrate similar efficacy of hGH on bone. These findings are consistent with the fact that a single bone-remodeling cycle takes approximately 3 to 4 months to complete and underscores the importance of an adequate period of GH replacement to effectively increase BMD. Cortical bone may respond more slowly to GH than trabecular bone as indicated by the fact that treatment for 18 months with GH increased BMD in the lumbar spine and femoral neck but not in the proximal radius.

Increases in BMD following GH treatment may result from direct and indirect actions of GH and insulin-like growth factor -1 (IGF-1) on bone. Indirect actions might include GH enhancement of enzyme activity that increases vitamin D3 concentrations and availability, as well as changes in body weight, fat and mean body mass, and the accompanying sense of well being and exercise performance in response to treatment. Also muscle strength which demonstrates a similar pattern as changes in BMD may be positively associated with the bone changes. A major value of GH on BMD is its potential to reduce fracture risk, especially in the hip and lumbar spine since adults with untreated GHD have increased prevalence of vertebral fractures compared to normal controls. Thus, when GH treatment is administered to GHD patients for two years and BMD increases by approximately 2 - 5%, their fracture rates decrease significantly. This efficiency

and utility is also substantiated in the Quantum Electro Dynamic stimulation on the fracture risk.

6. CNS Effects and Quality of Life

GH receptors are distributed throughout the brain suggesting that this organ may be a site of the hormone's action. While the binding sites in the hypothalamus undoubtedly involve regulation of pituitary GH secretion, those in the other areas such as the hippocampus could modify psychological and other functions. Exogenous hGH can access the brain as indicated by the fact that concentrations of the hormone increase in a dose-related fashion within the cerebrospinal fluid of adults with GHD after GHRT. Receptors that transduce IGF-1 signals are also found in all regions of the human brain and contribute to brain maturation, neural differentiation, neuroprotection and energy metabolism. Human GH that accesses the brain from the periphery may affect local IGF-1 synthesis since its concentrations in cerebrospinal fluid (CSF) increased nearly 50% during GH administration.

Data from animal studies suggest that GH treatment alters monoamine metabolism in the brain including region-dependent changes in dopamine, noradrenaline, serotonin and 5-hydroxyindoleacetic acid concentrations. Similar changes may occur in humans as indicated by the fact that in GHD patients, GH administration was associated with decreased CSF concentrations of homovanillic acid, a dopamine metabolite and increased -endorphin. Perhaps these changes in brain neurochemistry play an important role in improving psychological well being that has been observed during GH treatment of GHD patients.

That growth hormone deficiency erodes quality of life is suggested by the fact that people who acquired GHD as adults have higher levels of perceived health problems, are less energetic, less physically mobile, more socially isolated, sleep less well, have impaired cognitive function and mood disturbances compared with normal individuals. In general, these individuals complain of being tired, having low energy, lack of initiative and concentration, memory difficulties and irritability. However, when hGH is administered, they report increased vigor, ambition and

sense of well being. The beneficial effects of hGH on quality of life have been confirmed in several studies which reported improvement of cognitive functions including memory, less perceived illness and significant psychological improvements in energy levels and mood. Similar results were derived from clinical trials involving over a hundred patients. Again, energy, emotional reaction and social isolation were improved to the extent that they approached levels similar to those in healthy populations and quality of life improved as early as six months after starting hGH treatment.

Basis for GHRT as an "Intervention in Aging"

Important to the topic of using GHRT as an intervention in aging is the resemblance of GHD clinical characteristics and phenotypes to those that accompany aging, as well as the ability of hGH replacement to reverse or normalize at least in part, the maladaptive changes associated with GHD. Relevant to these relationships is the fact that spontaneous secretion of hGH decreases with advancing age. The incremental decrease in hGH is greatest between the ages of 20 to 40 years, with variable reductions ranging from 15% to as much as 70% at middle age and beyond. The temporal characteristics of endogenous GH secretion were also evaluated by many laboratories using analyses of frequently collected blood samples. These showed that GH secretion occurs in episodes that vary in amplitude throughout the day with the greatest amounts occurring during sleep. Although spontaneous secretion of GH continues during aging, the frequency and amplitude of the episodes progressively decrease and thus, a decline in mean GH concentrations can be measured across the life span. Notably, a profound decline occurs during the third decade of life preceding the onset of maladaptive changes in body composition and the increased risk for intrinsic diseases that are associated with middle age and beyond. Thus it would seem that reduced hGH in aging, as in pathogenic GHD, is causally associated with physiological and psychological decline.

Concerns About GHRT in the Elderly

There are at least 3 areas of concern about using GHRT in the elderly:

1. It may be unsafe and have toxic direct effects.
2. It may cause physiological perturbtions that accelerate rather than delay the onset of intrinsic disease and aging itself.
3. It may be ineffective, causing risk and undue expense without offering any tangible benefit.

These risks are not demonstrated in the Quantum Electro Dynamic stimulation.

1. General Safety Concerns

Extensive study of GH replacement in children with GHD resulted in the accumulation of 15-years data showing that recombinant GH has an excellent safety profile. Because the history of treating GHD adults is shorter, there are fewer studies documenting adverse drug reactions in this population. The most common effect noted during early clinical trials was fluid retention which is now recognized as being the result of using too high doses of GH. Because hGH is not yet approved by the FDA for treating age-related decline in body structure and function, correspondingly less information is available on adverse events in normal elderly populations. Furthermore in many studies of GHRT in the elderly, the subjects suffered from diseases such as osteoporosis, or were malnourished or experienced significant weight loss of unknown etiology. Nonetheless, in these small number of studies using dosages of hGH ranging from 0.010 to 0.3 mg./kg. at intervals of a few days to several months, adverse events including hyperglycemia, hypertension, carpal tunnel syndrome, edema, glucose intolerance and hyperinsulinemia were occasionally observed. However, it should be noted that these doses are quite high and not those usually associated with routine GHRT for aging, i.e. 0.002 - 0.005 mg./kg./day.

2. Possible Acceleration of Aging

A few investigators have expressed concern that increased concentrations of GH and IGF-1 associated with GHRT may accelerate the maladaptive changes associated with aging. This view derives mostly from animal studies, which may

have little or no relevance to the human condition. However in one clinical study, men with the highest levels of plasma IGF-1 had a 4.3-fold greater risk for prostate cancer than those with the lowest IGF-1 concentrations. In another study, high concentrations of IGF-1 were associated with increased breast cancer. In contrast IGF binding protein-3 (IGFBP-3) which reduces tissue exposure to free IGF-1 was inversely correlated to risk such that when the relationship between the two was considered, the predictive value of IGF-1 for cancer was greatly increased, especially for colon malignancies. Whether these relationships are causal or simply correlative must still be determined.

These dangers are not displayed in the Quantum Electro Dynamic stimulation.

3. Cost of Treatment and Risk: Benefit

Declining health, increased illness and dependency is a growing social burden of aging. The value of these aging parameters in terms of direct, indirect and intangible costs, including pain or suffering can be significant, so it is reasonable to explore the possibility that GHRT has the potential to reduce such cost by compressing morbidity into the later and perhaps final stages of life. As a result, GHRT has captured the imagination of the general public and of entrepreneurs alike because it has been promoted, especially in the lay literature as being effective in aging, even though actual proof of efficacy has not been forthcoming. Instead, support for GHRT in aging has been extrapolated from dissimilar models, such as adult GHD and from animal studies. The concerned practitioner should recognize that the effects of GHRT in GHD and aging are not the same. The basic difference is that in GHD, GH is therapeutic, i.e., it is administered to relieve changes in specific symptoms that in turn can be objectively measured and evaluated. On the other hand, GH administration to healthy people for the purpose of preventing maladaptive changes and diseases of aging requires negative data to prove efficacy, i.e., the absence of change is the proof. Without formal studies of the outcomes of hGH administration over periods of years, the proof will not be forthcoming.

Conclusion

The purpose of this article was to provide some explanation for employing GHRT as an intervention in aging. A review of both chemical and electrical utility has shown the greater prospect for safety and efficacy with Quantum Electro Dynamic stimulation.

Although the basis for its use for that purpose is extrapolated from GHD, there is a continuing craze for hGH administration to healthy people during aging to minimize the ravages of senescence and thereby promote good quality of life until death. The aging population is definitely increasing and without intervention to minimize the social impact of senescence, the phenomenon could be overwhelming to the health care systems and economies of nations. Perhaps partial relief can be realized by hormone replacement, and specifically by the use of hGH which seems to have potentially positive, global influence over bodily structure and function. Although not as significant as in GHD, GHRT in aging has already been shown to have beneficial effects, at least in the short term. Future studies should evaluate the minimal dosages required to sustain health and vitality without causing side effects or perturbations in bodily function that in the long term might produce the opposite effects from those desired.