Article Title	"HORMONE TREATMENT" A POPULAR ANTI-AGEING THERAPY
Article Summary	Anti-ageing research refers to slowing, preventing, or reversing the aging process. Many researches have been carried out on hormone replacement to delay ageing process. Human growth hormone is the most effective with other hormones which also responsible for anti-ageing, like **IGF-1**, **DHEA,** and Testosterone.
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INTRODUCTION

The discovery of hormone replacement therapies for patients with diabetes, hypothyroidism or Addison's disease has been among the great successes of medicine in the early 20th century. Hence, it is understandable that hormone replacement has also been explored for persons with mild (sub clinical) deficiencies, or for the elderly with a physiological age-related decline in estrogen, testosterone, DHEA and GH. Since the use of hormone prescription for these non-classical indications has expanded over the past decade, US as well as Swiss agencies have issued statements regarding the potential adverse effects of such therapies, including their financial consequences, in the ageing population. The aim of this statement is to summarize the position of the Swiss Society for Endocrinology and Diabetology with regard to the most frequently considered anti-ageing therapies.

AGEING

Ageing is the process of growing old or maturing or an artificial process for imparting the characteristics and properties of age or to become old is to show the effects or the characteristics of increasing age or to acquire a desirable quality (as mellowness or ripeness) by standing undisturbed for some time transitive senses.

The definition of ageing varies. One view, held by biologists, medical doctors and some psychologists is that ageing is associated with decline of most elements (Birren, 1964). Ageing is the point at which development has ceased and subsequent changes are seen as an aggregate of biological change beyond the point of optimal maturity (Buhler, 1968). On the other hand, life-span developmental psychology considers ageing in more positive terms: "the psychology of ageing, geropsychology, focuses on the behaviour of individuals involved in the processes of post-maturity development." (Kermis, 1984). In this perspective, ageing is seen as a continuous development in old age as opposed to an irreversible decline.

In medicine, ageing is generally characterized by the declining ability to respond to stress, increasing homeostatic imbalance, and an increased risk of disease.

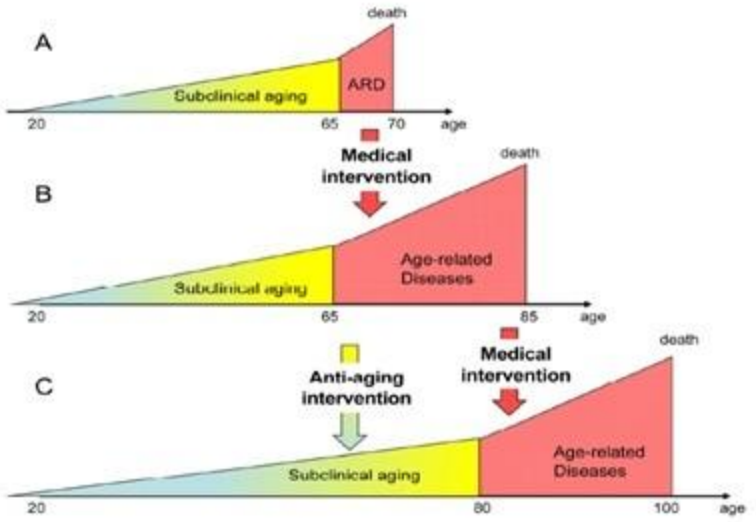


Figure 1. From longer life span to longer health span (and life span). From A to B: Standard medicine increases lifespan by preventing death from age-related diseases. It simultaneously increases a number of old people suffering from age-related diseases. A ratio health span to lifespan is decreased. From B to C: Anti-aging intervention will slow down aging and delay the onset of age-related diseases. This in theory will restore a ratio of health span to lifespan.

Because of this, death is the inevitable consequence of ageing. Differences in maximum life span between species correspond to different 'rates of ageing'. For example, inherited differences in the rate of ageing affect a mouse elderly at 3 years and a human elderly at 90 years. These genetic differences affect a variety of physiological processes.

The Future of Ageing: Ageing is not a Disease

"The failure to distinguish between ageing research (bio gerontology) and research on age-associated diseases (geriatric medicine) has been, and still is, a source of misunderstanding.

There is little evidence that this failure, with its important scientific, political and societal consequences, will soon be rectified. Thus, the present imbalance will continue, in which resources available for research on the diseases of old age far exceed those available to address the core question: why are old cells more vulnerable to disease than are young cells?

Policy-makers, properly impressed with the future demographics of the graying of all economically developed countries, are basing important policies and decisions on a flawed understanding of what constitutes ageing research and what they believe might be accomplished."[1]

Biological Theories of Ageing

The fact that bio gerontology, a relatively recent field of science, is still in need of a comprehensive database has led to speculations, contradictions and to a plethora of biological theories on ageing. An additional cause of the many theories on ageing is that manifestations of biological changes over time affect virtually all components of living systems from the molecular level to the whole organism (i.e. molecule, organelle, cell, tissue, organ, and organism). The hierarchical cause-effect of change over time

thus leads to very different theories and research methods to test those theories. One of the methodological problems underlined by many theorists is that change that is more fundamental than the one observed may induce the effect that was chosen for study. On the other hand, the AAM protagonists have harnessed the complexity of correlated factors' influence over time to question the universality of theories on ageing and argue for an 'open upper limit' to human life span.

ANTI-AGEING

Anti-ageing research [2] refers to slowing, preventing, or reversing the aging process. Many researches have been carried out on skin treatment, hormone replacement, food supplement, herbal therapy etc. to delay ageing process.

Experimental gerontology, and **biomedical gerontology**, is the study of slowing down or reversing the processes of aging to extend both the maximum and average lifespan. Some researchers in this area, and "life extensionists" or "longevity" (those who wish to achieve longer lives themselves), believe that future breakthroughs in tissue rejuvenation with stem cells, molecular repair, and organ replacement (such as with artificial organs or xenotransplantation) will eventually enable humans to have indefinite lifespans through complete rejuvenation to a healthy youthful condition. The sale of putative anti-aging products such as nutrition, physical fitness, skin care, hormone replacements, vitamins, supplements and herbs is a lucrative global industry.

Different Anti-ageing Treatment

- Diets and supplements
- Hormone treatment
- Insulin like growth factor restriction
- Nano technology
- Cloning and body part replacement
- Cryonics
- Genetic Modifications
- Fooling gene replacement
- Reversal of informational entropy
- Ethics and politics of life extension
- Strategies of Engineered negligible Senescence

Here we take a look on the base of treatment of Hormone therapy. Hormone like Growth Hormone (STH) has significance in ageing so by inhibiting the Growth hormone releasing factor we can resist the action of GH. There are various process to do this which we discussing below:--

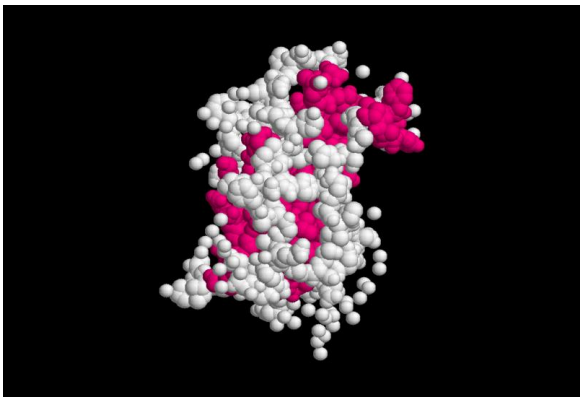
Hormone treatment

Aging adults, even those receiving hormone replacement therapy with DHEA, thyroid, estrogen and/or testosterone, still frequently report fatigue, lethargy, and decreased strength and exercise tolerance. Plus, several recent large population studies show the risk of cardiovascular disease and death is significantly increased in adults whose circulating levels of GH are very low.

Over the last 15 years, a large body of clinical research has shown that Adult Growth Hormone Deficiency (AGHD) is quite common, plays a key role in virtually all age-associated health complaints, and that treatment that restores circulating GH to mid-normal youthful ranges successfully and safely reverses all of these symptoms of unhealthy aging, dramatically improving health and quality of life.

Human growth hormone

The major isoform of the human growth hormone is a protein of 191 amino acids and a molecular weight of 22,124 Daltons. The structure includes four helices necessary for functional interaction with the GH receptor. It appears that, in structure, GH is evolutionarily homologous to prolactin and chorionic somatomammotropin. Despite marked structural similarities between growth hormone from different species, only human and Old World monkey growth hormones have significant effects on the human growth hormone receptor.



Several molecular isoforms of GH exist in the pituitary gland [3] and are released to blood. In particular, a variant of approximately 20 kDa originated by an alternative splicing is present in a rather constant 1:9 ratio[4], while recently an additional variant of ~ 23-24 kDa has also been reported in post-exercise states at higher proportions. This variant has not been identified, but it has been suggested to coincide with a 22 kDa glycosylated variant of 23 kDa identified in the pituitary gland. Furthermore, these variants circulate partially bound to a protein (growth hormone-binding protein, GHBP), which is the truncated part of the growth hormone receptor, and an acid-labile subunit (ALS).

Growth hormone and anti-ageing

The human growth hormone (HGH) is a hormone that is made by your body in the pituitary gland and many claim has anti-aging properties. It is often marketed as an anti-aging hormone. In children, it is important for normal growth. In adults, HGH helps regulate and maintain your tissues and organs. Children sometime receive HGH injections because a lack of HGH in their body is impacting their growth rate. Like many hormones, HGH levels decrease as a person gets older. This is a normal part of aging. HGH is becoming a popular anti-aging supplement. Because HGH is only available in injection form (other forms of HGH have not been proven effective) HGH must be given by a doctor.

There are at least 3 substances which control HGH secretion

- **Growth hormone releasing hormone** (GHRH) [5], a substance which declines with age. Increasing levels of GHRH causes the pituitary to increase its output of HGH.
- **Growth hormone releasing peptide** (GHRP) [5] is another substance that declines with age. Increasing levels of GHRP also causes the pituitary to increase its output of HGH.
- **Somatostatin** is a hormone that blocks the release of HGH by the pituitary gland. The natural production of somatostatin increases with age, and causes a corresponding decrease in HGH production by the pituitary gland.

The production of HGH is controlled by GHRH, GHRP, somatostatin, and other substances in the body. The degree to which changes in the levels of each of these substances is responsible for the decline in human growth hormone varies from individual to individual, and is somewhat gender-dependent. The only naturally-occurring growth hormone releasing peptide appears to be ghrelin. Ghrelin is a hormone with many other effects.

PHARMACOLOGY OF HGH FOR ANTI-AGEING Growth Hormone Secretion and Regulation

The secretion of GH is controlled by two factors viz.

1. Growth hormone releasing factor (GHRH)

2. Growth hormone releasing inhibiting hormone (GHRIH) or Somatostatin.

The mechanism works by negative feedback mechanism Due to disruption in the endogenous rhythms the neurotransmitter stimulates the pituitary gland .This causes the release of either of the factors depending upon the need of GH. In case there is need of GH in body then, the pituitary gland causes a decrease in secretion of GHRIH and increase in secretion of GHRH because of which secretion of GH increases. The GH then gets transported to the liver and then it is supplied to the effector organ or cell. The high levels of GH is later are brought back to normal by increase in secretion of GHRIH.

The Growth Hormone Receptor

The HGH receptor is a single chain 620- amino acid trans-membrane polypeptide. It is a member of haemopoietic receptor superfamily.

Mechanism of action takes place by binding of GH molecule in between the receptor molecules. This binding occurs in the extracellular region and due to this there is receptor dimerization. Due to this there is phosphorylation of the JAK2 protein which causes the desired action. [41]

The use of GH as an anti-ageing therapy has been reported as the most popular health-related internet search (Tsouvalas, 2006). Although the exact number of people who use GH as an anti-ageing therapy is unknown, Perls and his colleagues (2005) reported that 20,000 to 30,000 people used GH in the United States as an anti-ageing therapy in 2004 (Kaufman, 2002), more than 10-fold increase since the mid-1990s (Perls and Olshansky, 2006). In thorough scientific review, Van der Lely (2004) demonstrates the difference between justified and unjustified use of GH. GH has become an accepted therapy for children and adults with GH deficiency due to pituitary disorder.

Growth Hormone Secretagogue Supplements: A Safer, Natural Alternative

Studies over the past number of years have revealed that a combination of certain amino acids, ingested orally as a supplement at specific dosages, can stimulate the pituitary gland to release greater quantities of growth hormone after the age of 40, elevating our IGF-1 blood levels to match those we experienced up to our mid-thirties. Studies show that supplementation with these amino acid combinations, collectively known as growth hormone secretagogues, can raise IGF-1 blood levels up to 275ng/ml, which may be a safer level than 350-400ng/ml, which results from GH injections.

In a three month study, which used a proven growth hormone secretagogue supplement, blood levels of IGF-1 increased by 30% on average by the end of the twelfth week and patient self-assessment scores indicated that, of the thirty-six participants, 58% noted improvement in muscular strength, 42% reported an increase in muscle size, 68% reported body fat reduction, 74% noted an increase in energy, 47% reported improvements in skin texture, 32% reported improved skin thickness, 37% reported reduction in wrinkles (disappearance or reversal), 21% reported improvement in general healing capacity, 37% reported improvement in joint and back flexibility, 47% felt their immune system was stronger, 32% reported improved sexual potency, 44% of men reported better sexual stamina (penile erection), 66% of men reported less frequent nighttime urination, 53% reported improved mental energy and clarity, 37% reported improved attitude and mood elevation and 47% reported improvement in memory. In male subjects there was a reduction in their PSA blood levels (prostate-specific antigen), which signifies that this intervention did not trigger prostate malignancy or enlargement. As well, blood sugar levels in

diabetic subjects were shown to improve, and there was also an improvement in both cardiac (heart) and pulmonary (lungs) tests during the course of the three-month trial. The author of the study (DM. Ladley, M.D.) also noted that blood pressure was better controlled and an improvement in menopausal symptoms among affected women in this age group.

Ladley, an authority on the use of growth hormone secretagogues, elaborates that improved energy, endurance, muscle mass and strength, and reduced body fat, were among the most frequently reported benefits in the first four weeks of supplementation. New hair growth, restoration of hair color, thickening of the skin, and disappearance of skin discoloration generally occurred between the eighth and the twelfth weeks, with continued improvement beyond the twelve-week term. There were no side effects reported from the use of the growth hormone secretagogue by any of the participants in this study. Growth hormone secretagogues are generally well tolerated and no consistent reports of adverse side effects have been reported.

In the study by Ladley initial blood levels of IGF-1 ranged from 21-276ng/ml. Those with lower values appeared to have experienced the largest increases in IGF-1 blood levels with secretagogue supplementation. As a rule, growth hormone secretagogue supplementation cannot elevate blood levels of IGF-1 beyond 275ng/ml. Thus, before beginning a supplementation program with a growth hormone secretagogue, you should first have your blood levels of IGF-1 evaluated.

Supplements

Unfortunately, the growth hormone secretagogue industry is filled with unproven, ineffective and/or scam products that are not worth spending your money on. The well-known and most highly esteemed anti-aging medical doctors in this field often recommend a growth hormone secretagogue supplement [37] to their patients known as Meditropin.

As an alternative to Meditropin, individuals can assemble their own growth hormone secretagogue by stacking several amino acids together and taking them at once, one hour before bedtime.

Growth hormone and anti-aging specialist Vincent Giampapa M.D. suggests a starter amino acid stack program consisting of:

Arginine – 2 gram

Ornithine – 2 grams

Lysine – 1 gram

Glutamine – 1 gram

After an initial course of one month, increase all the amino acids in the stack by 2 grams each.

Growth hormone secretagogue supplements are usually taken for five consecutive days, followed by two days with no supplementation, and then five days on again, repeating this sequence.

It is advisable to have your IGF-1 levels checked after three months of growth hormone secretagogue supplementation in order to see how much of an increase has occurred in this hormone, which demonstrates, anabolic and other anti-aging effects.

Other synthesized HGH Drugs which are available in the market

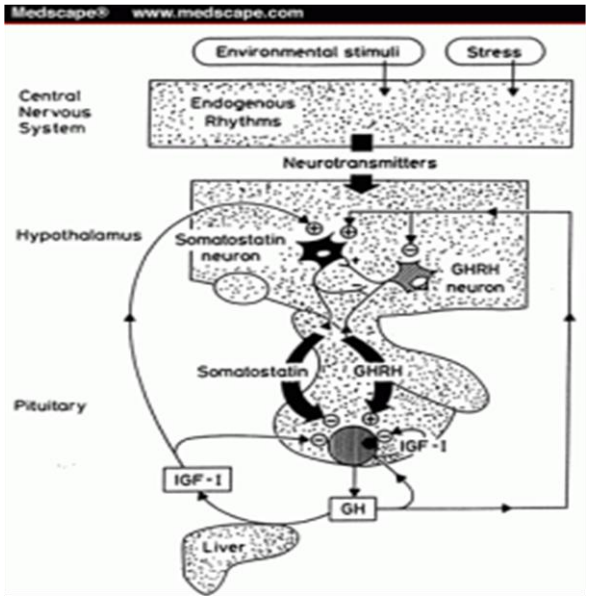
- **Somatropin:** Somatotropin or somatropin is a polypeptide hormone of rDNA origin. It is used to stimulate linear growth in pediatric patients who lack adequate normal human growth hormone. Synthesized in a strain of E. coli modified by the addition of a gene for HGH.

- **Saizen:** Saizen is a commercial preparation of synthetic somatropin that was modified by the addition of the human GH gene.
- **Serostim :** It is an injectable medicine used for treatment of anti-ageing and beside that it helps to increase lean body mass and body weight and improve physical endurance. It is also a useful medicament for AIDS.
- **Zorbtive**: It is a form of human growth hormone. Zorbtive produces effects that are identical to the body's naturally occurring growth hormone. Human growth hormone is important in the body for the growth of bones and muscles. Zorbtive apparently use as anti-ageing drug.

ACTION OF IGF-1 ON ANTI-AGEING

Insulin-like growth factor 1 (**IGF-1**), also called **somatomedin C**, is a protein that in humans is encoded by the *IGF1* gene. IGF-1 has also been referred to as a "sulfation factor" and its effects were termed "non suppressible insulin-like activity" (NSILA) in the 1970s.

IGF-1 is a hormone similar in molecular structure to insulin. It plays an important role in childhood growth and continues to have anabolic effects in adults. A synthetic analog of IGF-1, mecasermin is used for the treatment of growth failure. IGF-1 consists of 70 amino acids in a single chain with three intra molecular disulfide bridges. IGF-1 has a molecular weight of 17,066 Daltons.



Mechanism of action

Its primary action is mediated by binding to its specific receptor, the Insulin-like growth factor 1 receptor, abbreviated as ""IGF1R"", present on many cell types in many tissues. Binding to the IGF1R, a receptor tyrosine kinase, initiates intracellular signaling; IGF-1 is one of the most potent natural activators of the AKT signaling pathway, a stimulator of cell growth and proliferation, and a potent inhibitor of programmed cell death.

IGF-1 is a primary mediator of the effects of (GH). GH is made in the anterior pituitary gland, is released into the blood stream, and then stimulates the liver to produce IGF-1. IGF-1 then stimulates systemic body growth, and has growth-promoting effects on almost every cell in the body, Especiallskeletal muscle, cartilage, bone, liver, kidney, nerves, s kin, hematopoietic cell, and lungs. In addition to the insulin-like effects, IGF-1 can also regulate cell growth and development, especially in nerve cells, as well as cellular DNA synthesis.

Deficiency of either growth hormone or IGF-1 therefore results in diminished stature. GH-deficient children are given recombinant GH to increase their size. IGF-1 deficient humans, who are categorized as having Laron syndrome, or Laron's dwarfism, are treated with recombinant IGF-1. In beef cattle, circulating IGF-I concentrations are related to reproductive performance.[6]

Effect of IGF-1 on Ageing

One of the spectacularly exciting uses of growth hormone and IGF-1 may be to prevent and treat the effects of brain aging. In an experiment that has momentous implications for brain injury, stroke, aging, and neurodegenerative disease, a team of scientists in New Zealand showed that IGF-1 can stop the death of cells in the brain. Barbara Johnston, Peter Gluckman, and their colleagues at the University of

Auckland found that injections of IGF-1 given 2 hours after brain injury in fetal lambs rescued the damaged neurons and salvaged cells that would otherwise have died during apoptosis, which is the programmed cell death that is believed to cause the loss of brain cells for up to 3 days after the original injury. The treatment was effective in stopping the cell death throughout the brain, including the hippocampus, the cortex, the areas associated with thinking and memory. The treatment was also effective in the striatum, the part of the brain that plays a role in Parkinson's disease in humans. IGF-1 replacement was also found to reduce seizures in animals with brain damage.

These researchers also suggest that IGF-1 might be used to inhibit the effects of neonatal hypoxia during birth (lack of oxygen to the brain) which can leave a baby with permanent brain damage. If IGF-1 can stop the programmed death of cells, then this opens up a world of undreamed-of-possibilities. For instance, the programmed death of cardiac cells after a heart attack leaves the victim with a heart full of dead tissue that before could not be repaired. Brain tissue is destroyed due to a stroke (CVA), and this cell death many times leaves the victim unable to walk, talk, or think clearly. It may also play a role in other neurodegenerative diseases such as Alzheimer's disease, muscular dystrophy, and multiple sclerosis. For the first time we may have a weapon against death at the cellular level.

The decline in IGF-1 blood levels as we age has been shown to contribute to many aspects of aging, which include, thinning of our skin, more rapid wrinkling, brittle hair, and nails, grayed or dulled hair color, reduced energy, loss of muscle and bone mass, decreased libido and sexual performance ability, increased body fat and other common signs and symptoms of aging. Conversely the use of growth hormone injections and/or supplementation with natural agents that stimulate the release of growth hormone, have been shown to boost IGF-1 blood levels back to more youthful levels and reverse many age-related changes in the body. Studies show that by boosting IGF-1 blood levels back to more youthful levels, subjects have experienced a multitude of anti-aging benefits including:

- **improved immune function**
- **increased sexual potency and function**
- **increased muscle strength, muscle mass and energy**
- **decreased body fat**
- **elevated mood**
- **improved sleep patterns**
- **improved memory**
- **improved skin thickness, texture, and reduced wrinkle lines**
- **restoration of hair color**
- **improved vision**

The most pronounced anti-aging effects have been seen in patients where IGF-1 blood levels have been returned to a level at or greater than 350ng/ml, which certain anti-aging doctors claim can single-handedly reverse aging by up to 20 years in older subjects. To achieve blood levels in this range, regular injections of growth hormone are required by a physician who is trained in anti-aging medicine.

However, growth hormone injections have been shown to cause side effects, especially in subjects where IGF-1 returned to levels approaching 400ng/ml. The most common side effects include swelling of the feet, fluid retention, joint pains, carpal tunnel syndrome and more rarely, allergic responses.

A number of research papers have correlated higher IGF-1 levels (290-300ng/ml) with and increased risk for breast and prostate cancer. This doesn't necessarily mean that IGF-1 causes cancer, but it does imply that more research is required before we can state with certainty that growth hormone injections are a completely safe anti-aging intervention.

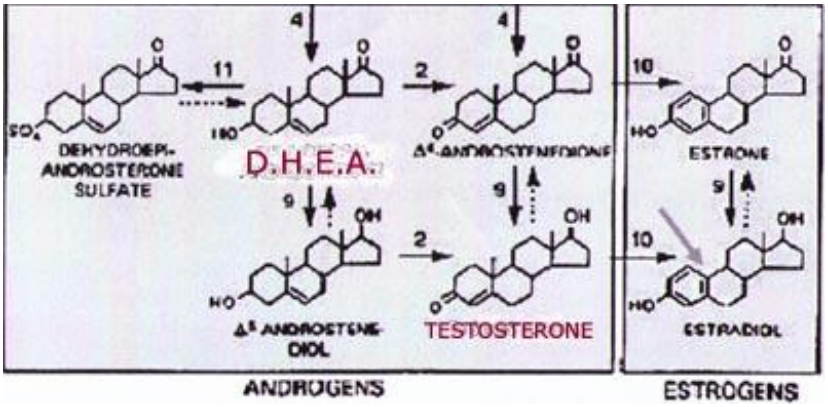
OTHER HORMONES responsible for ANTI-AGEING

DHEA and anti-ageing

DHEA (Dehydrate epiandrosteron) is a hormone made by the body that has become popular for anti-ageing purpose. DHEA is a raw ingredient that the body can convert into the sex hormones an Estrogen Testosterone. As a person ages, his or her DHEA level naturally drops. DHEA advocates claim that talking the supplement will slow ageing by increasing muscles mass, increasing bone mass burning fat amongst other thing.

TESTOSTERON AND ANTI-AGEING

Testosterone levels in men drop as age increases. This has led to a recent increase in doctors prescribing "testosterone therapy" to counter the effects of aging. Well finally, research has been done to determine if these effects are true or just another hyped-up (and expensive) anti-aging "cure."[7]



Testosterone and Aging Research

The study, published in the prestigious medical journal JAMA, enrolled 237 healthy men aged 60 to 80. All men had a testosterone level below 13.7 nmol/L. The men were randomly assigned to be either in a group that received a twice daily oral 80 mg testosterone supplement or a placebo. The researchers measured hand strength, time to stand/sit, cognitive functioning (how well your brain is working), bone density, body composition, cholesterol, insulin, quality of life and other factors.

The results showed that the group who took the testosterone did not improve (compared to the placebo group) in mobility, strength or quality of life. This group also tended to have a higher rate of metabolic syndrome after 6 months. The group taking the supplement did have increased lean body mass and reduced fat in the body after 6 months taking the supplement.

Conclusion

These studies show that once-daily evening subcutaneous injections of GHRH are generally well tolerated and can increase 24 hrs.

GH secretion, boost circulating levels of IGF-I, and improve body composition in older patients.

Preliminary analyses also suggest beneficial effects on cognitive performance. Effects on physical function are equivocal; and with the formulation and dosing schedule used there appears to be no significant benefit on sleep. While they encourage further study, these results are far short of those needed to support regulatory approval for formal drug registration. As aging is not a disease, drug therapy cannot be broadly encouraged until meaningful functional benefits. Thus, one can anticipate research proceeding on two tracks: better definition of the clinical benefits of increasing GH, and development of new GHRH and its agonists to make these benefits accessible to seniors who currently represent the fastest growing segment of the population.

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