The Non-Science Witch Hunt Against Hormone Replacement Therapies for Deficiency Syndromes Must End:
An A4M Position Paper on Physician-Prescribed HRT
Issue Date: 23 September 2013

SUPPLEMENTAL RESOURCES

White Paper "Guidance for Physicians on Hormone Replacement Therapy"; A4M, May 2007; available at: http://www.worldhealth.net/white-papers-official-statements/

"Is consensus in anti-aging medical intervention an elusive expectation or a realistic goal?"; Archives of Gerontology & Geriatrics (Elsevier); 48(3):271-276; (May 2009); available at: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T4H-4VT0GW8-1&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=7c846ae92417c7b587d070eeb4f71149

INTRODUCTION

"Unless we put medical freedom into the Constitution, the time will come when medicine will organize into an undercover dictatorship to restrict the art of healing to one class of Men and deny equal privileges to others; the Constitution of the Republic should make a Special privilege for medical freedoms as well as religious freedom."

-- Benjamin Rush (1745-1813), physician, writer, educator, humanitarian, and Founding Father of the United States

Since the inception of the anti-aging medical movement in 1991, various establishment parties have ruthlessly leveraged their positions of power in academic, political, and regulatory arenas for the purpose of attempting to limit the use of hormone replacement therapies (HRT) in adults with documented clinical deficiencies. For over 15 years, a prolonged and calculated campaign of deceit, fraud, and suppression has threatened physician licensures and liberties to treat and prescribe life-improving therapies, leading potentially to the direct compromise of patients' health and longevity. Dozens of physicians have been sanctioned and punished with loss of license and academic standing. This pernicious abuse of position and power is particularly prevalent with regard to RECENT challenges made against human growth hormone (HGH), testosterone (TRT), and DHEA replacement therapies that are trumpeted by the mainstream media. Biased reporters frequently – and inappropriately – demonize legitimate physicians and clinical compounding pharmacies who are reluctantly positioned on the frontline of a decades' old agenda to limit freedom of choice and information, and the physician's most essential responsibility to select the best course of therapy and medication for their patients.

This conflict is being played out of late in the arena of anti-aging medicine, a clinical specialty that has flourished in its twenty-two year long history, garnering the support of more than 100,000 physicians and scientists worldwide who practice or research life enhancing, life extending interventions today. Prof. Dr. Imre Zs.-Nagy, of the University of Debrecen Medical and Health Science Center (Hungary), and founder of the Archives of Gerontology and Geriatrics (published by Elsevier), observes[1] that: "In my role as a basic and clinical scientist, I have had an opportunity to witness more than four decades of advances and declines in the arena of preventive medical care … there has been little else as dramatic, important, beneficial, and significant as the anti-aging medical movement."

Continual vigilance is necessary to countermand those whose financial and professional successes depend on repeated, calculated attempts to discredit the science and substance of anti-aging medicine.

Remarks[2] Tanjung Subrata, MD, of Udayana University School of Medicine (Indonesia):

> "Anyone who does not believe in evil is not paying attention to the recent affairs of the past twenty years. We are living in a time of unprecedented tribulation and changes at-large – and in healthcare, in particular. All that is necessary for evil to prevail is for men of good will to do nothing. In this modern age of zero tolerance for alternatives to establishment medicine, and the willingness of our governmental officials to resort to police state tactics to suppress innovative schools of thought, progress in medicine halts and dies."

A4M POSITION

The American Academy of Anti-Aging Medicine (A4M), its numerous worldwide affiliated scientific and medical societies, and befriended organizations, supports the judicious application of modern and advanced medical technologies to address the changes in chemical, hormonal, physical, and nutritional needs that occurs with aging. Such repletion includes the restoration of hormones to an optimal physiological state when deficiency is determined by objective assessment.

Hormone replacement therapy (HRT) is an essential and extensively documented protocol for clinical intervention in the disorders of aging. HRT maintains an unblemished safety and efficacy profile that has been documented by 20 years of clinical application. Yet, a perfect storm of misguided media combined with biased parties whose livelihoods hinge on disparaging the anti-aging medical movement has grossly compromised access to HRT, placing the lives of hundreds of thousands of patients worldwide in potential jeopardy.

Experienced anti-aging physicians have been prescribing HRT for more than 20 years. PubMed contains more than 20,000 peer-reviewed studies of HRT, of which a preponderance document the life-enhancing and/or life extending benefits of HRT in aging adults. See Appendix A "Literature Review" which presents a selection of such studies that represent the objective evidence that supports the A4M position.

THE ANTI-AGING MEDICAL MOVEMENT

The goal of anti-aging medicine is not to merely prolong the total years of an individual's life, but to ensure that those years are enjoyed in a productive and vital fashion. As established in 1991 by the physicians of the American Academy of Anti-Aging Medicine (A4M), the field of anti-aging medicine was established as a direct extension to the science of elite sports medicine of the 1980s. Just as sports medicine aims to keep the athlete's body functioning at its optimum level, anti-aging medicine seeks to keep the human physiology performing at its peak. In other words, the similar principle, of extending and maximizing the healthy human lifespan, is at the core of both anti-aging medicine and sports medicine.

The Official Definition of "Anti-Aging Medicine"

The clinical specialty of anti-aging medicine was established in 1991 by the physicians of the A4M, and thus is defined as follows:

> Anti-aging medicine is a clinical specialty is founded on the application of advanced scientific and medical technologies for the early detection, prevention, treatment, and reversal of age-related dysfunction, disorders, and diseases. It is a healthcare model

> promoting innovative science and research to prolong the healthy lifespan in humans. As such, anti-aging medicine is based on principles of sound and responsible medical care that are consistent with those applied in other preventive health specialties. The phrase "anti-aging," as such, relates to the application of advanced biomedical technologies focused on the early detection, prevention, and treatment of aging-related disease.

The clinical specialty of anti-aging medicine utilizes diagnostic protocols that are supported by scientific evidence to arrive at an objective assessment upon which effective treatment is assigned. Physicians who dispense anti-aging medical care are concerned with the restoration of optimal functioning of the human body's systems, organs, tissues, and cells. Attempting to rebrand what it cannot deny, those in positions of power in academic, political, and regulatory arenas are Inventing new catch phrases including "longevity medicine," "successful aging," "healthy aging," and the like, in an effort to dilute and absorb the A4M's original definition of anti-aging medicine. To implement this campaign, we suspect that these individuals have pejoratively solicited major media outlets to denigrate the A4M, its officers, and its members.

Anti-aging medicine is, in essence, a euphemism for early detection and advanced preventative medicine. It is a healthcare model that emphasizes personalized, patient-focused, high-quality metabolic-specific medical care.

Critics with A Dark Agenda (Political Elites)

Scientifically based and well documented in leading medical journals, anti-aging medicine is among the fastest growing medical specialties throughout the world. As an innovative model for advanced preventive healthcare that cannot be denied, individuals with their own political and financial agendas have disparaged anti-aging medicine in attempts to restore monopolistic control over the field of aging intervention. Critics of the science of anti-aging medicine most commonly hail from academia: as such, these naysayers many times have little or no medical training in aging intervention, and may be non-clinicians.

Perhaps the most inconceivable reality is that at the very highest levels of academia, government, and science, truth and objective scientific method are not at all sacred to the political elites. We in clinical medicine via our training, discipline, and conditioning naively believe and act in the public interest, for the good of our patients' health, and by professional standards of medical ethics. The (elite) medical establishment operates contrary to this position, reports investigative reporter Tim Bolen (www.bolenreport.com), who for 30 years has amassed data and evidence exposing a calculated effort to deride innovative medical therapeutics. Mr. Bolen observes[3] that:

> "Without a doubt, a stealthy control group – a cabal, if you will, in status-quo medicine exists. Approved by Big Pharma, parts of academia, and segments of the government, this group exerts its control in many different ways. I have uncovered information showing anonymous, and not-so-anonymous, funding of groups, loosely describing themselves as "Quackbusters or Skeptics" whose only purpose is to attack cutting-edge health care offerings. Those groups, in turn, train, and fund sub-groups. Data suggests that the "Quackbusters or Skeptics" donated over $1 Million US to Wikipedia to purchase control over pages with medical content. More, the Skeptic training camps teach their recruits how to operate together to control that same Wikipedia and Search Engines. Further, these covert groups drive media on issues particularly pertaining to alternative healthcare, in an effort to limit coverage of innovative discoveries and to vilify therapies that are not part of AMA/FDA/Big Pharma establishment medicine healthcare.

There are TWO main "skeptic" organizations - the James Randi Educational Foundation (JREF) and the Center For Inquiry (CFI). Both are well funded from secret sources.

JREF reported, in 2010, a total income of $999,971.00 and a Total Asset claim of $1,736,101.

The Center For Inquiry, Inc (CFI), based in Amherst, New York shows on their Form 990 that they took in $5,242,304 in Total 2009 Income, and they had, that year, Total Assets of $3,017,144. Their Schedule B ANONYMOUS contributions totaled $2,318,652.

More, CFI claimed that they received, in 2009, in addition to their anonymous contributions, a so-called "Management Fee Income" of $2,458,156. What do you suppose they managed? And who paid them to manage it? Maybe they manage Wikipedia health care articles? How about Search Engine Optimization (SEO) bringing skeptic, including Stephen Barrett's (Quackwatch), articles to the first page of Google?

Much more - This cabal minimizes and delays innovative medical advancements by lodging anonymous complaints to state licensing boards against cutting-edge practitioners. Their insidious campaign also controls grant monies and research funding, somewhat silencing the voices of innovative medicine in favor of mainstream views. By leveraging control of the media in direct jeopardy of journalistic integrity, this control group seeks to suppress all in medicine that is not fully controlled by the establishment. To permit this level of manipulation and disinformation is wrong and ethically corrupt. The fate of a valuable avenue of medical innovation for the public interest – anti-aging medicine – stands at-risk."

A JAMA commentary[4] purported to address the legality of Human Growth Hormone (HGH, GH) treatment by physicians for growth hormone deficient (GHD) patients. It is the view of A4M that the commentary contained a number of incorrect, misplaced references and studies, and multiple basic scientific errors, in what A4M views as an apparent attempt to damage the anti-aging medical profession and the physicians practicing solid, evidence-based medical healthcare focused on improving and maintaining patients' quality of life. It is A4M's further opinion that the authors selected self-serving studies, in which they failed to qualify the conclusions in an effort to bolster what A4M believes is a disinformation campaign. It is A4M's opinion, for example, that they incorrectly intermingled internet sales of homeopathic pseudo "GH" sprays, amino acids, and sports nutritional over the counter products in order to inflate their incorrect claims suggesting an illegal diversion of HGH by physicians and pharmacies, implying a black market in FDA approved prescription injectable HGH for hormone replacement treatments by anti-aging physicians where none exists.

Misrepresentation in Competitive Sports

As an unfortunate consequence of media confusion and outright deception aiming to deliberately misrepresent anti-aging medical care, the reality of the clinical practice of hormone replacement therapy has become muddled. A recent *Sports Illustrated* article states[5] that: "In the sports world, the term 'anti-aging' has often come to signify therapy that uses hormones – usually testosterone and HGH – and … DHEA." This erroneous definition grossly misrepresents the legal and ethical physiological use of hormones and supplements as being synonymous with the inappropriate use of hormones for sports enhancement. The

A4M is squarely opposed to this myopic interpretation of “anti-aging” and urges reference to the official definition of anti-aging medicine as presented above.

Any use of performance enhancing drugs or hormones banned from professional sports constitutes inappropriate misuse. It is a violation of the A4M Physician Member Code of Ethics to prescribe for the explicit purposes of performance enhancement. The A4M does not endorse or condone the use of any illicit substances for sports cheating. However, the A4M does support the continued availability of such substances to adult patients with objectively assessed hormone deficiencies. Such judicious use of HRT does not equate to a banned drug issue.

A4M’s physician co-founders Dr. Robert Goldman, MD, PhD, DO, FAASP, Chairman; and Dr. Ronald Klatz, MD, DO, President, are co-authors of *Death In the Locker Room* (1984), a first-ever expose of the illicit use of anabolic steroids in sports, and *Grow Young with HGH* (1997), a best-selling book that explored the clinical benefits of judicious and appropriate HGH therapy in deficient adults. *Death in the Locker Room* is widely regarded as the seminal text on the dangers of anabolic and performance enhancing substances in sports. *Death in the Locker Room* was the first book to alert the public and the medical community to such issues, and the book subsequently led directly to much of the drug testing, control, and educational programs now in-place across a number of professional sports and on the global level.

Statute[6] 21 U.S.C. § 333(e), a provision of the Food, Drug, and Cosmetic Act (FDCA), states, in pertinent part, that "whoever knowingly distributes, or possesses with intent to distribute, human growth hormone for any use in humans other than the treatment of a disease or other recognized medical condition, where such use has been authorized by [FDA] and pursuant to the order of a physician, is guilty of an offense punishable by not more than 5 years in prison." We need to take a critical look at the historical context and legislative intent of a law before we interpret it. The law did not originally address HGH. The 1988 law was written and passed regarding anabolic steroids. The legislative history of the statute shows an intent to focus on steroid trafficking to athletes, particularly adolescent athletes, amid increasing reports of amateur and professional sports doping and concerns about the 1988 Summer Olympics (at which, ironically, Canadian sprinter Ben Johnson's steroid positive ignited a global firestorm).

Dr. Goldman served as Special Adviser & Lecturer to the US Drug Enforcement Agency (DEA) Demand Reduction Education Programs nationally, as well as to the US Olympic Committee, spearheading the design of drug policy and testing procedures. In his activities with the DEA, Dr. Goldman was directly involved in an advisory capacity with the process that led to the creation of the Anabolic Steroid Control Act of 1990. “The Anabolic Steroid Control Act was never intended to restrict practicing physicians involved in the clinical treatment of hormone deficiency syndromes,” comments[7] Dr. Goldman, who explains that: “Rather, this law was specifically directed to prevent the trafficking of anabolic steroids to athletes.”

The Anabolic Steroid Control Act of 1990 lifted steroids out of the FDCA and into the Controlled Substances Act. Congress was presented with the option of making HGH into a controlled substance, too. However, following expert medical testimony that HGH lacks the adverse psychological and physical effects of steroids, Congress chose not to take such a drastic approach to HGH.[8,9] Instead, Congress took the lesser approach of inserting HGH, to replace steroids, in the FDCA law that was written to stop trafficking to cheating athletes. In fact, HGH was inserted as an afterthought, with no penalties mentioned, as editorial

comment; there was no intention to criminalize its judicious use in the clinical setting by trained physicians. The focus of lawmakers and Congress has always been to address non-medical use, i.e., improper use by competitive elite athletes, sports people and teenagers. It is A4M's view that the JAMA commentary[4] fails to understand or appreciate such legislative history and legislative purpose. A4M is advised that one of the authors of the JAMA commentary stated to United Press International (UPI) in reference to the statute, "They basically put in language that made it crystal clear that it is illegal to use growth hormone as an anti-aging intervention".[10] This is a very odd and A4M believes, an incorrect statement, considering the fact that when the law was written, there were no anti-aging doctors or profession in existence. In fact, the anti-aging medical profession did not even exist until five years after the 1988 statute was enacted. The concept of HGH s an anti-aging drug did not exist until the problem of Rudman's study.[12]

The Anabolic Steroid Control Act never intended to infringe upon physician freedoms to prescribe hormone therapy when clinically appropriate. It was specifically intended to prevent steroid trafficking in professional sports. Whereas education should have been a primary goal in implementing the Anabolic Steroid Control Act, instead an enforcement environment that granted limitless power unto itself was created. A multi-million dollar industry of drug testing was born and subsequently flourishes.

DISINFORMATION CAMPAIGN

History is replete with examples of medical pioneers whose innovations and foresight were trivialized, ignored, challenged, or violently opposed by the establishment, only to ultimately become accepted by society at-large. Leopold Auenbrugger was ridiculed for percussing and auscultating his patients' chests; Ignaz Semmelweiss' recommendation for doctors to wash their hands before each patient landed him in a mental asylum; and more recently, cardiologists denied Nathan Pritikin's program for dietary modification to modulate cardiovascular risk until after his death. Given time and objective, undeniable evidence, scientific truths are ultimately borne out. In the words of Dr. Augenbrugger, "It has always been the fate of those who have illustrated the arts and sciences by their discoveries to be beset by envy, malice, hatred, destruction, and calumny."

Misguided Attacks on HRT

Statute[6] 21 U.S.C. § 333(e), a provision of the Food, Drug, and Cosmetic Act (FDCA), supports the use of hormone replacement in mature, clinically GH-deficient adults as both treatment of a disease and a medically authorized use granted by the FDA. Any implication that the statute was intended to target medical hormone replacement by ethical doctors in the new and emerging field of anti-aging medicine is therefore incorrect and misleading.

To obfuscate the truth, critics of the anti-aging medical science offer deliberately misleading claims concerning HRT with the specific and ultimate goal to severely restrict the use of hormone therapy. Most notably, the JAMA commentary[4] purported to address the legality of Human Growth Hormone (HGH, GH) treatment by physicians for growth hormone deficient (GHD) patients. The commentary, however, was flawed by a number of incorrect, misplaced references and studies, and multiple basic scientific errors.

In the May-June 2009 issue[1] of the prestigious *Archives of Gerontology and Geriatrics*, an international journal integrating experimental, clinical, and social studies on aging published by Elsevier, founder and Editor-in-Chief Prof. Dr. Imre Zs.-Nagy expresses his opinions on the use of the HGH as an anti-aging medical intervention. Prof. Dr. Nagy's Editorial points out the main clinical results of HGH replacement therapy (hGHRT) in light of the "Membrane

Hypothesis of Aging" (MHA), which he submits as offering a solid basis for the interpretation of the observed beneficial effects of HGH. Prof. Dr. Zs.-Nagy's profile of the sharp and protracted conflict of views between the gerontological establishment and the A4M exposes a "disregard by certain individuals bearing some of the most prestigious affiliations in the gerontological establishment, for truth, academic integrity, and scientific professionalism." Dr. Zs.-Nagy submits that: "[T]he gerontological elite has … sought to obfuscate the facts of the anti-aging medical movement. I submit that the reason for this is nothing less than an abject fear by the gerontological elite to avert their loss of control, power, prestige, and position in the multi-billion dollar industry of gerontological medicine. "'

Elite athlete and professional sports/medical writer Monica Mollica observes[11] that: "For reasons that are not readily apparent, there appears to be a conservative political movement that opposes the use of testosterone in older men. Continuing, Ms. Mollica observes that: "The political climate is working against testosterone replacement therapy in older men despite overwhelming scientific data supporting this appropriate pursuit as a strategy to prolong healthy longevity."
`

HGH

On July 5, 1990, Daniel Rudman, M.D., a pioneer researcher in the use of HGH, and his colleagues at the Medical College of Wisconsin made medical history with an article[12] in the *New England Journal of Medicine.* It detailed the first clinical trial of elderly men on HGH therapy, which compared the effects of 6 months of HGH injections on 12 men, aged 61 to 81 years, with an age-matched control group. The result made headlines all over the world. Those taking the hormone injections gained an average of 8.8% in lean body mass and lost 14% fat, without diets or exercise. Their skin became thicker and firmer and the lumbar bones of the spine increased. In other words, HGH had virtually turned their flabby, frail, bodies into their sleeker, stronger, younger selves. In language rarely used in conservative medical journals, the researchers wrote: "The effects of 6 months of HGH on lean body mass and adipose-tissue mass were equivalent in magnitude to the changes incurred during 10 to 20 years of aging."

HGH is one of the most studied compounds in medicine with almost 100,000 journal references currently in PubMed. The majority of these data demonstrate the positive benefits of HGH therapy in multi-year studies, well beyond the typical 6-12 month study protocols. [13,14]

Growth hormone replacement therapy has been shown to improve muscle strength and mobility, cognitive function, cardiovascular disease, osteoporosis, immune function, body composition, obesity and sarcopenia, fibromyalgia, Crohn's disease, other illnesses, and quality of life issues.[15,16,17,18,19,20,21]

Low GH[22] is associated with decreased longevity in humans, with more than 20 years decreased lifespan with low GH.[23] Older men with higher IGF-1 do not show the same decrease in lean body mass and increase in fat mass. "GH determines life's potential."[24] Childhood or adult GH deficiency is associated with 2-3 times increase in mortality.[25]

Low GH[22] and its downstream hormone IGF-1 are associated with poor health and quality of life outcomes. The June 2012 issue[26] of *The Journals of Gerontology: Series A* published a series of articles documenting the clinical benefits of IGF-1. Of note, Higashi et al[27] provide "a comprehensive update on IGF-1's ability to modulate vascular oxidative stress and to limit atherogenesis and the vascular complications of aging." Further, Ungvari et al[28] cite the "cardiovascular protective effects of insulin-like growth factor (IGF)-1" [to] "[provide] a

landscape of molecular mechanisms involved in cardiovascular alterations in patients and animal models with … adult-onset IGF-1 deficiency," submitting that: "Microvascular protection conferred by endocrine and paracrine IGF-1 signaling" suggest "its implications for the pathophysiology of cardiac failure and vascular cognitive impairment, and the role of impaired cellular stress resistance in cardiovascular aging."

The "2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines" reports[29] that treating GH deficiency in patients with chronic heart failure beneficially affects the primary endpoint of peak oxygen consumption, which showed "remarkable" increases of 7.1 ml/kg/m in GH-treated patients, as compared to a decrease of 1.8 ml/kg/m among control subjects. In that left ejection fraction rose by 10% in the GH-treated patients (declined 2% in controls); with a greater effect on left ventricular and systolic volume index of -22 ml/m2 (as compared to increase of 8 ml/m2 in controls), the American College of Cardiology Foundation/American Heart Association Task Force writes that: "The improvements … are consolidated predictors of survival." Notably, there were no major adverse events among the GH-treated patients.

As stated by Savine: "If mean IGF-1 of 300 is mean normal for 20-30 year olds, almost all men and women over the age of 40 have an IGF-1 deficit."[30] Most patients beyond age 60 have total 24 hour HGH secretion rates indistinguishable from those of hypopituitary patients with organic pituitary gland lesions.[30] Therefore the A4M submits that the empirical data suggests that when treating Adult Growth Hormone Deficiency (AGHD, GHD), physicians are treating a documented deficiency disease and not performing off-label treatment as the JAMA commentary[4] authors suggest. In fact, HGH deficiency is associated with significantly decreased longevity in human siblings. Longevity and healthy aging are directly related to GH/IGF-1 levels.[31] As Savine points out, "Life without GH is poor in quantity and quality."[30]

When AGHD is treated with GH, there are usually increases in GH, IGF-1 and IGF Binding Protein 3 (IGFBP-3) which all have a role in clinical results. Although IGF-1 is pro-mitotic and taken out of context could promote cancer, IGFBP-3 is anti cancer.[32] The mechanism is explained by stimulation of anti-cancer gene p53. Teenagers with the highest GH and IGF-1 have low rates of cancer. When treating with GH a balance is produced between IGF-1 and IGFBP-3.[33] A central question in GHRT is "Does GHRT increase the risk of cancer." Multiple studies and reviews have concluded that there is no increase in cancer risk compared to the general population. Jenkins[34] review is aptly titled, "Does Growth Hormone cause cancer?" and provides the conclusion:

> "Extensive studies of the outcome of GH replacement in childhood cancer survivors show no evidence of an excess of de novo cancers, and more recent surveillance of children and adults treated with GH has revealed no increase in observed cancer risk."

Moltich's[35] review has similar conclusions:

> "Although there has been some concern about an increased risk of cancer, reviews of existing, well-maintained databases of treated patients have shown this theoretical risk to be nonexistent"

With regard for the potential for an increased cancer risk with HGH treatment, peer-reviewed literature suggests the opposite. HGH treatment may up-regulate binding proteins of IGF, specifically IGF-6; this has been noted in studies to prevent many types of cancer, such as

prostate, ovarian, brain and endometrial.[36,37,38,39,40,42] It is also well documented that cancer survivor children who received HGH did not exhibit any increased cancer risks. In fact, there are no peer reviewed long-term clinical studies that document human cancer risks from HGH administration.[38,39,40] To the contrary, cancer mortality and recurrence has been found to be reduced, or survival time increased in cancer patients on HGH. Patients deficient in HGH are reported to have a 400% increase in cancer mortality and a 200% increase of cancer incidence.[41,42] Noted was also a reduction by 50% of cancer risk to patients with long term HGH replacement (60 months).[21] Additionally, the Growth Hormone Research Society has stated that "Current labeling for GH states that active malignancy is a contraindication. ... There are no data to support this labeling. Current knowledge does not warrant additional warning about cancer risk."[43] However, caution should always be exercised in patients with a history of cancer; and HGH therapy is not for every patient.

Ruiz-Torres et al[24] completed a study that compared ageing parameters of young (up to 39 years) and old (over 70 years) individuals having similar insulin-like growth factor-1 (IGF-1) blood levels. In follow-up, the researchers studied the decline in IGF-1 levels, comparing its behavior in the first half with that in the second half of adult life. The investigators concluded that: “GH secretion in adulthood plays a determinant role not only for some regressive manifestations, but also for life potential.”

Media reports about the federal law concerning HGH have created unnecessary confusion, and some reports have confused non-medical over-the-counter homeopathic sprays and nutritional products with pharmaceutical-grade, FDA-approved injection medications for AGHD patients. It is A4M's opinion that such misleading journalism incorrectly equates sports and homeopathic nutritional supplements sold through websites with pharmaceutical-grade injectable HGH prescribed for patients with diagnosed AGHD. Such poor presentations of the science and commentary, in A4M's view, have erroneously suggested that the replacement of HGH in aging adults is illegal, and has led to sensationalized headlines. Patients are not given HGH for a diagnosis or treatment of "anti-aging," but for on-label use for AGHD syndrome, a diagnosed disease. It should be noted, that before initiating HGH supplementation, anti-aging physicians first encourage the increase of growth hormone by increasing exercise, enhancing sleep cycles, balancing other hormone deficiencies and decreasing of sugar intake, as evaluated by Gardner, et al.[44]

In a landmark court case[45], James Forsythe, MD, HMD won a clear and unanimous victory that reaffirmed the right of a physician to prescribe HGH to adults with deficiency conditions, including aging and arthritis. Dr. Forsythe comments[46] that**:** “It is a perversion of the law for state licensing boards to mistreat and harass physicians for this legal, just, and appropriate use of this lifesaving medication – human growth hormone**.”**

DHEA

Dehydroepiandrosterone (DHEA) is the most abundant steroid in the human body and is involved in the manufacture of testosterone, estrogen, progesterone, and corticosterone.

There is evidence to suggest that DHEA may stimulate human growth hormone (HGH). Morales et al[47] published results of a double blind, placebo-controlled, crossover study involving 71 women and 13 men, ages of 40 to 70 years. Subjects took 50 mg of DHEA for three months, followed by a placebo for three months. While subjects were receiving DHEA, their levels of DHEA and DHEA-S rose to that of a young adult within 2 weeks of DHEA replacement and were sustained throughout the 3 months of the study. Furthermore 84% of women and 67% of men reported an improved sense of both physical and psychological well-being, including improved sleep quality, increased energy levels, improved ability to

handle stress, and increased sense of relaxation. Five of the volunteers also noted improvement in chronic joint pain and mobility. The researchers also found that DHEA caused a significant rise in IGF-1 levels, although it did not affect the 24-hour measurement of HGH levels. They speculate that restoring the levels of DHEA may stimulate the liver to produce more IGF-1 or generate more HGH receptors. In other words, we may find that the anti-aging benefits attributed to DHEA may actually be due to the stimulation of the HGH-IGF-1 system.

When[22] DHEA levels are in an optimal range, there can be less risk of developing atherosclerosis. Rabijewski[48] found that DHEA could lower insulin levels and decrease the risk for developing type II diabetes. DHEA also decreases the risk of cancer because it enhances the immune system response. DHEA is also thought to be neuroprotective.

Prof. Etienne-Emile Baulieu, world known researcher and endocrinologists at INSERM in Paris, former president of the French Academy of science,Honorary member of College of France, known for his work on contraception and on steroid hormones was the first to synthesize DHEA in the sixties. Prof. Baulieu conducted numerous conclusive researches on the efficiency and benefits of DHEA. His findings underline the systematic positive results of administrating DHEA in his experimental and clinical studies, especially in men. His findings demonstrate that 50 mg of DHEA in 280 participants during a year had significantly improved their bone mass, skin thickness and pigmentation, as well as the libido in both men and women, the general physical and mental well-being were improved too.[49,50] In an interview for a study on anti-aging medicine, Prof. Baulieu declares: “One of the most important effects of DHEA has not yet received enough attention: it acts on the receptors of neurotransmitters. There are very encourageing research on the well being and improvement of memory in old age”[51]

Testosterone

Testosterone is the main hormone produced in the testicles and secreted by the testes. Testosterone deficiency has pleiotropic deleterious effects. There is increased cardiovascular system dysfunction, which can lead to the increased incidence of AMI’s and strokes. Citing separately published data finding that: “serum testosterone levels were proved to be an independent negative predictor for developing arterial stiffness, assessed from the peak systolic and end diastolic diameters of the common carotid artery and simultaneous brachial artery blood pressure,” Kelly and Jones[62] submit that: “testosterone has demonstrated anti-inflammatory effects clinically and [testosterone replacement therapy] can improve atherosclerosis assessed non-invasively in hypogonadal men and in animal studies.”

Testosterone[22] optimization is anti-inflammatory. Testosterone prevents cytokine production and initiates the acute phase response, which elevates C-reactive protein, serum amyloid A and fibrinogen. Testosterone also prevents the formation of the adhesion molecules vascular cell adhesive molecule (VCAM) and intercellular adhesive molecule, (CD 54/ICAM), which are necessary components of the process of atherosclerosis. Thus, testosterone replacement is a very powerful anti-inflammatory treatment that can help to prevent atherosclerosis. Testosterone has also been shown to be of benefit in thetreatment of chronic heart failure. Pugh et al.[53] found that testosterone increases cardiac output, decreases left ventricular load, and has no adverse cardiovascular effects. Malkin et al.[54] show that testosterone replacement moderates inflammatory cytokines and improves heart failure outcomes. Turhan et al.[55] found that men with low free testosterone levels have greater than 3 times the risk for the development of coronary artery disease.

There[22] is a common misconception that testosterone has adverse cardiovascular effects. However, the opposite has been shown with current research. The lower the free testosterone level the more likely coronary artery disease will be present. Testosterone replacement therapy (TRT) improves ST depression and dilates coronary arteries. TRT also may improve lipids and low testosterone is associated with dyslipidemia. English et al. found that low-dose transdermal testosterone therapy improves angina threshold in men with chronic stable angina. Rosano et al.[56] found that "Short-term administration of testosterone induces a beneficial effect on exercise-induced myocardial ischemia in men with coronary artery disease." The same researchers also concluded that intracoronary testosterone has direct dilating effects on the coronary arteries. Finally, Hak et al.[57] found that low levels of endogenous androgens increase the risk of atherosclerosis in elderly men.

Testosterone[22] can be a very powerful tool for the control of insulin resistance. Replacement doses decrease insulin resistance. Low levels of testosterone play a role in the development of type 2 diabetes. Low testosterone is associated with metabolic syndrome, hypertension, type II diabetes, fibromyalgia, and coronary artery disease. Boyanov et al.[58] studied the effect of testosterone supplementation in men with type 2 diabetes, visceral obesity, and partial androgen deficiency. Subjects received testosterone undecanoate, and the results reflect that supplementary testosterone reduced hemoglobin A1C levels by 17.3%, led to a decrease in visceral obesity, and improved symptoms of androgen deficiency including erectile dysfunction. Observing that: "There is strong evidence that a low testosterone level and clinical hypogonadism have a high prevalence n men with metabolic syndrome and/or type 2 diabetes," Muraleedharan and Jones[59] conclude that: "Testosterone deficiency is a risk factor in itself for the subsequent development of the metabolic syndrome and type 2 diabetes."

Testosterone[22] is the major predictor of skeletal mass, and it is synergistic with growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Bhasin et al.[60] show that testosterone can improve strength even without exercise, but there is a marked improvement if testosterone is taken in combination with exercise. Declining testosterone levels are associated with accelerated osteoporosis, decreased muscle mass, and anemia – i.e., frailty.

Numerous studies have documented testosterone's positive effects on body composition. Mudali and Dobs[61] write: "Studies in hypogonadal men have shown that testosterone replacement is effective in increasing muscle mass and strength and decreasing fat mass…Current evidence suggests that testosterone replacement may be effective in reversing age-dependent body composition changes and associated morbidity." LeBlanc et al[62] analyzed data collected on 1,183 men, ages 65 years and older, following the subjects for 4.5 years. Body composition was measured using dual energy x-ray absorptiometry (DXA) scans and physical performance was measured through a series of exercises that assessed grip strength, lower extremity power, walking speed and the ability to rise from a chair without the use of arms. Results showed that higher levels of testosterone were associated with reduced loss of lean muscle mass in older men, especially in those who were losing weight. In these men, higher testosterone levels were also associated with less loss of lower body strength. The study authors concluded: "Higher endogenous testosterone is associated with reduced loss of lean mass and lower extremity function in older men losing weight. Endogenous testosterone may contribute to healthy aging." Kovacheva et al[63] report that testosterone supplementation reverses sarcopenia in aging via regulation of myostatin and "multiple signal transduction pathways in sarcopenia," concluding that: 'Testosterone reverses sarcopenia through stimulation of cellular metabolism and survival pathway together with inhibition of death pathway."

Testosterone[22] levels correlate with cognitive function, and TRT can improve cognitive function. Moffat et al.[64] found that serum free testosterone concentration can be used to predict memory performance and cognitive status in elderly men. Gouras et al[65] showed that testosterone replacement therapy prevents the production of beta amyloid precursor protein in men, which suggests that testosterone replacement may play a role in the prevention of Alzheimer's disease. A pilot study by Tan[66] on the effects of testosterone in hypogonadal aging male patients with Alzheimer's disease revealed that mental status of those given testosterone replacement therapy improved over one year, whereas the mental status of those given a placebo declined. Janowsky et al[67] found that increasing testosterone to 150% of baseline levels in older men resulted in a significant enhancement of spatial cognition. A review of testosterone and cognition in elderly men, Holland et al[68] concluded that: "Results from cell culture and animal studies provide convincing evidence that testosterone could have protective effects on brain function. Testosterone levels are lower in Alzheimer's disease cases compared to controls, and some studies have suggested that low free testosterone (FT) may precede Alzheimer's disease onset...Positive associations have been found between testosterone levels and global cognition, memory, executive functions, and spatial performance in observational studies."

Studies have shown that men who have their testosterone levels restored with TRT are less likely to suffer from depression, are less moody, more sociable, and have more energy. O'Connor et al[69] investigated the effects of TRT on self- and partner-reported aggression and mood. Eight hypogonadal men received 200 mg intramuscular testosterone biweekly for 8 weeks. Results showed that TRT led to significant reductions in negative mood, tension, anger, and fatigue. Aydogan et al[70] assessed the relationship with testosterone levels and psychological symptoms in young male patients with congenital hypogonadotropic hypogonadism (CHH). 39 young male patients with CHH and 40 age-matched healthy males were enrolled in the study. Results showed that hypogonadal participants had more severe symptoms of sexual dysfunction, anxiety, depression, and worse quality of life. However, 6 months of TRT led to improvements in anxiety and depression scores and the life qualities of participants. TRT also improves sexual function. Khera et al[71] investigated if 12-months of treatment with a testosterone gel improved sexual function in hypogonadal men, as measured by the Brief Male Sexual Function Inventory (BMSFI). Results showed that the mean total BMSFI score significantly increased from baseline at 12 months (27.4 ± 10.3 to 33.8 ± 9.8, $P < 0.001$) and at each visit in all domains (sex drive/libido, erectile function, ejaculatory function, level of bother). Regression analysis indicated that increased total BMSFI score was significantly associated with increased total testosterone levels at 6 months. The authors concluded: "In hypogonadal patients, 12-month administration of topical testosterone gel resulted in increased total testosterone and free testosterone levels and significantly improved sexual function."

A Cochrane systematic study reviewed the benefits of testosterone for peri- and postmenopausal women. The authors concluded that "there is evidence that adding testosterone to hormone therapy has a beneficial effect on sexual function in postmenopausal women. There was a reduction in HDL cholesterol associated with the addition of testosterone to the hormone therapy regimens. Due to lack of targeted research, it is difficult to estimate the effect of testosterone on sexual function in association with any individual hormone treatment regimen."[72]

Rhoden[22] et al.[73] point out that benign prostatic hyperplasia (BPH) symptoms are not exacerbated with testosterone supplementation. Cooper et al.[74] studied the effect of exogenous testosterone on prostate volume, serum and semen prostate specific antigen (PSA) levels in healthy young men. Participants were given testosterone intramuscularly at

doses of 100, 250, or 500 mg a week. Serum testosterone increased, and there was no change in prostate volume or serum and semen PSA. Morales[75] and Prehn[76] both concluded that there is no evidence to suggest that exogenous androgens promote the development of prostate cancer. Morley[77] states that "There is no clinical evidence that the risk of either prostate cancer or BPH increases with testosterone replacement therapy." A collaborative analysis published in the *Journal of the National Cancer Institute* in 2008 found that there was no association between the risk of prostate cancer and any hormone measured, including testosterone, DHT, estradiol and others. Gould et al.[78] review of 15 studies of testosterone replacement, up to 15 years in duration, showed no increase of prostate cancer risk. Agarwal[79] and Sarosdy[80] found that testosterone treatment studies of patients with prostate cancer after radical prostatectomy and brachytherapy have shown no recurrences or significant increases of PSA. Morgantaler's[81] study reported dramatic evidence on the safety profile of TRT: 13 testosterone deficient men with biopsy proven prostate cancer were treated with TRT. After 2.5 years repeat biopsies were done and no cancer was found in 54%, there was also no local progression or metastasis found.

Attacks on Compounding Pharmacies

Compounding by pharmacists has been a foundational aspect of the practice of pharmacy. While today the majority of prescription medication is mass-produced by pharmaceutical companies, many patients require custom-made preparations that are prescribed by their physician and compounded by a trained pharmacist.

Compounding pharmacies are strictly regulated the respective state boards of pharmacy. Presently, U.S. Senate Bill S.959 would transfer control of compounding pharmacies to the Food and Drug Administration (FDA). This legislation would give sole authority of the FDA to determine what medications could be used in the practice of compounding pharmacy. Knowing its long time antipathy to bio-identical hormones, you can rest assured that the FDA would inevitably ban compounded bio-identical hormones. This has been its plan since the late 1980s. A series of federal court cases has prevented this. Despite this pending legislation, courts have repeatedly upheld pharmacists' rights to compound despite repeated attempts by the FDA to challenge the activity. In May 2006, a U.S. District court judge ruled that the compounding of ingredients to create a customized medication in accordance with a valid prescription does not create a new drug subject to the FDA's approval process (see Medical Center Pharmacy et al. v. Gonzales et al.). Additionally, the U.S. Supreme Court has held as unconstitutional FDA's repeated attempts to regulate pharmacist compounding.

Attacks on Credentialed Physicians

The American Board of Anti-Aging & Regenerative Medicine (ABAARM) issues Board Certification to individuals with M.D. (Doctor of Medicine), D.O. (Doctor of Osteopathic Medicine), Doctors of Podiatric Medicine (DPM), and M.B.B.S. (Bachelor of Medicine/Bachelor of Science) degrees. The American Board of Anti-Aging Health Practitioners (ABAAHP) issues Diplomate Certification to Doctors of Chiropractic (DC), Doctors of Dentistry (DDS), Naturopathic Doctors (ND), Registered Pharmacists (RPh), scientists (PhD and similar), Registered Nurses, Nurse Practitioners, and Physician Assistants, and Licensed Acupuncturists (L.Ac.).

Through ABAARM and ABAAHP, the A4M is one of approximately 270 specialist medical societies and medical boards, only 24 of which in total have been approved by the American Board of Medical Specialties (the "ABMS"). A self-appointed organization, ABMS most recently approved a medical specialty – nuclear medicine – in 1985, 28 years ago as of this writing. In a field of over 270 specialist medical societies, ABMS approval is an arduous, time intensive, and resource depleting process. The A4M is one of nearly 250 societies that

have yet to receive ABMS approval,. Statements that anti-aging medicine is not yet an ABMS-recognized medical specialty mischaracterize the reality of gaining such approval and to infer – improperly – a lack of credibility on the part of A4M.

Currently, A4M's educational programming awards category 1 AMA/Physician's Recognition Award (PRA) physician credits, the highest level available for physicians and surgeons. The content of A4M's academic congresses are closely monitored and supervised by AMA-approved CME accreditation bodies. A4M's educational programming has consistently received the highest ratings and excellent reviews for the quality of medical educational content by peer-reviewed organizations. A4M's educational programming has received recognition and support of national governments and universities worldwide.

HORMONE REPLACEMENT THERAPY

History

Hormone replacement therapies with controlled substances such as testosterone and growth hormone have been used since many years. The first testosterone treatment of testosterone deficiency in adult men started around 1940 and since then, for more than 40 years growth hormone has been administered to treat short stature children and since 1985 with the safer, not contaminated recombinant growth hormone, product of biotechnology. In the latter 1980's, the first clinical trial of adults with growth hormone deficiency were published, and since the beginning of the 1990s, growth hormone treatment of adult patients started in private medical practice.

The concept of Interventional Endocrinology acknowledges the fact that not everyone experiences symptoms of deficiency – relative or absolute - at the same levels. Therefore, taking a comprehensive medical history and physical can act to substantiate the application of replacement/supplementation protocols, in accordance with accepted standards of care. Clear documentation in this regard helps support the physician's approach in treating the patient.

Safety & Efficacy

To-date, no adverse effects of hormone replacement therapies administered to adults with diagnosed deficiency(ies) have been reported to the US FDA's Adverse Event Reporting System (FAERS), the national database providing post-marketing safety surveillance for drug and therapeutic biologic products. Likewise, as of this writing, the US CDC's Medication Safety Program contains no reports of adverse effects relating to HRT.

HGH therapy has been in use for over 40 years on adults and children[82], with one of the best safety records in modern pharmacia and whose dose in adults is typically only 1/5 to 1/7 of the pediatric dose and under the strict supervision of an endocrinologist or anti-aging specialist. As of this writing, the US National Library of Medicine's PubMed database lists over 100,000 peer-reviewed citations on HGH therapy; not a single death or permanent life threatening morbidity has been reported in its use of AGHD in otherwise healthy but AGHD patients.

The side effects of GH replacement therapy, if any, are usually minor and are reversible by decreasing the dose or in a few cases discontinuing the treatment. Significant side effects are rarely seen in clinical practice. Also, when the same total dose is divided daily over a week-long period (instead of administering 3 days a week) side effects are diminished or absent. If side effects do occur, it has been clinically demonstrated that they disappear with cessation of treatment.

The Clinical Anti-Aging Setting

Most traditional endocrinologists have had no intense training in treatment of testosterone and growth hormone deficiencies. They generally have excellent training in the treatment of diabetes, but lack of interest and expertise in how to treat testosterone and adult growth hormone deficiencies and some other hormone deficiencies that may accelerate aging. Because of this lack of knowledge, many of them have rejected these treatments and confused them with the improper use at excessive doses by sports athletes searching to improve their performance. The A4M, its numerous worldwide affiliated scientific and medical societies, and befriended organizations, do not approve the improper use of these substance in sports, but do point to the right of every patient who is suffering from one of these deficiencies to get relief from their complaints by the adequate hormone treatment.

Critics of the anti-aging medical science do acknowledge that HGH prescribing is perfectly legal in connection with (1) "treatment of a disease" or (2) an "other recognized medical condition" that has been authorized by FDA. At no time has Congress evinced any intent to restrict ethical physicians from prescribing HGH to mature or elderly adults for medical reasons within their sound judgment. Nothing in the statute dictates to physicians how to diagnose the indications for diseases which may be treated by HGH. Any inference that the statute was intended to prohibit physicians from prescribing HGH for hormone replacement purposes in GH-deficient adults is, in A4M's view, misplaced.

The therapeutic value of HGH was validated by a study[83] conducted in Stockholm, Sweden. Data concerning visits to the doctor, number of days in hospital, and amount of sick leave were obtained from patients included in KIMS (Pharmacia International Metabolic Database), a large pharmacoepidemiological survey of hypopituitary adults with GHD, for 6 months before GH treatment and for 6-12 months after the start of treatment. Assistance required with normal daily activities was recorded at baseline and after 12 months of GH therapy. Quality of life (QoL) (assessed using a disease-specific questionnaire, QoL-Assessment of GHD in Adults) and satisfaction with physical activity during leisure time were also assessed. For the total group (n = 304), visits to the doctor, number of days in hospital, and amount of sick leave decreased significantly ($P < 0.05$) after 12 months of GH therapy. Patients also needed less assistance with daily activities, although this was significant ($P < 0.01$) only for the men. QoL improved after 12 months of GH treatment ($P < 0.001$), and both the amount of physical activity and the patients' satisfaction with their level of physical activity improved after 12 months ($P < 0.001$). In conclusion, GH replacement therapy, in previously untreated adults with GHD, produces significant decreases in the use of healthcare resources, which are correlated with improvements in QoL.

CONCLUDING REMARKS

Repeatedly since the genesis of the anti-aging medical movement in 1991, the media has sought to demonize the use of hormone replacement therapies in healthy but deficient adults. Relying on partisan – and often misinformed – critics, the media fuel and encourage hysteria among the public, which thereby results in a climate of misguided federal and state actions that seek to restrict these safe, proven, life-enhancing therapies.

Attempts to criminalize the practice of medicine where variations to State Board-favored traditional care threaten the continued advancement of innovative medicine. In these situations, there are no injured patients and no victims yet criminal proceedings are waged against progressive health professionals. State officials abuse their authority in recasting minor administrative issues as criminal acts; this is unjust and may be considered as criminal abuse of their publicly elected positions. Sensationalization by media confuses the public,

with false allegations suggesting that HRT in clinically documented cases of adult deficiency syndromes equates to the abuse of performance-enhancing anabolic steroids.

The American Academy of Anti-Aging Medicine (A4M) is resolute in defending the rights of the patient working in conjunction with their physician in choosing any and all justifiable therapies, drugs and interventions which can be shown to improve either the quality or duration of the human lifespan or the form and function of the individual's physiology in order to achieve greater vitality and health at every age. It is in fact the physician's duty to act as an advocate for the patient's right to obtain the full lawful measure of scientific medical therapeutics necessary for optimum health and personal freedom of choice in healthcare.

The observation by George Orwell (1903-1950), English novelist, in the prognostic classic novel *1984*, that: "War is peace. Freedom is slavery. Ignorance is strength" predicts that In a world where lies are supported by the establishment, to stand firm for truth is a dangerous and revolutionary action. Physicians of conscience and good will must unite to take back the future – or all freedoms, including freedom of choice in healthcare – will be lost forever.

APPENDIX A. LITERATURE REVIEW

This section presents a selection of published peer-reviewed studies that document the life-enhancing and/or life extending benefits of HRT in aging adults. For further references, see the A4M's White Paper "Guidance for Physicians on Hormone Replacement Therapy"; A4M, May 2007; available at: http://www.worldhealth.net/white-papers-official-statements/

HGH

Aberg ND. Growth hormone increases connexin-43 expression in the cerebral cortex and hypothalamus. Endocrinology 2000 Oct; 141(10):3879-86

Abs R. Update on the diagnosis of GH deficiency in adults. Eur J Endocrinol. 2003 Apr; 148 Suppl 2:S3-8.

Adamopoulos S et al. Growth hormone administration reduces circulating proinflammatory cytokines and soluble Fas/soluble Fas ligand system in patients with chronic heart failure secondary to idiopathic dilated cardiomyopathy. Am Heart J 2002 Aug;144(2):359-64

Aimaretti G et al. Diagnostic reliability of a single IGF-I measurement in 237 adults with total anterior hypopituitarism and severe GH deficiency.Clin Endocrinol (Oxf). 2003 Jul; 59(1):56-61

Albert SG et al. Low-dose recombinant human growth hormone as adjuvant therapy to lifestyle modifications in the management of obesity.Clin Endocrinol Metab. 2004 Feb; 89(2):695-701.

Aleman et al. Insulin-Like Growth Factor-I and Cognitive Function in Healthy Older Men J Clin Endocrinol Metab 84:471–475, 1999

Andreassen et al. Concentrations of the acute phase reactants high-sensitive C-reactive protein and YKL-40 and of interleukin-6 before and after treatment in patients with acromegaly and growth hormone deficiency. Clin Endocrinol (Oxf). 2007 Aug 28

Baffa R et al. Low serum insulin-like growth factor 1 (IGF-1): a significant association with prostate cancer. Tech Urol 2000 Sep; 6(3):236-239

Bartke A et al. Consequences of growth hormone (GH) overexpression and GH resistance. Neuropeptides 2002 Apr;36(2-3):201

Baum HB et al. Effects of physiologic growth hormone therapy on bone density and body composition in patients with adult-onset growth hormone deficiency. A randomized, placebo-controlled trial. Ann Intern Med 1996 Dec 1; 125(11):883-90

Bengtsson BA, Edén S, Lönn L, et al. Treatment of adults with growth hormone (GH) deficiency with recombinant human GH. J Clin Endocrinol Metab. 1993;76:309-317.

Bennett R Growth hormone in musculoskeletal pain states.Curr Rheumatol Rep. 2004 Aug; 6(4):266-73.
Bennett RM et al. A randomized, double-blind, placebo-controlled study of growth hormone in the treatment of fibromyalgia Am J Med. 1998 Mar; 104(3):227-31.
Besson A et al. Reduced longevity in untreated patients with isolated growth hormone deficiency. J Clin Endocrinol Metab. 2003 Aug; 88(8):3664-7.
Biller BM et al. Sensitivity and specificity of six tests for the diagnosis of adult GH deficiency. J Clin Endocrinol Metab. 2002 May; 87(5):2067-79.
Blackman M et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA November 13, 2002. Vol 288 No 18.
Bocchi EA et al. Growth hormone for optimization of refractory heart failure treatment. Arq Bras Cardiol 1999 Oct; 73(4):391-8
Bogarin R et al. Growth hormone treatment and risk of recurrence or progression of brain tumors in children: a review. Childs Nerv Syst. 2009 Jan 14
Boguszewski CL, Meister LH, Zaninelli DC, Radominski RB. One year of GH replacement therapy with a fixed low-dose regimen improves body composition, bone mineral density and lipid profile of GH-deficient adults. Eur J Endocrinol. 2005;152:67-75.
Bohdanowicz-Pawlak A et al. Risk factors of cardiovascular disease in GH-deficient adults with hypopituitarism: a preliminary report. Med Sci Monit. 2006 Feb; 12(2):CR75-80.
Borson-Chazot F. et al. Decrease in Carotid Intima-Media Thickness after One Year Growth Hormone (GH) Treatment in Adults with GH Deficiency J Clin Endocrinol Metab 84: 1329–1333, 1999
Branski LK et al. Randomized Controlled Trial to Determine the Efficacy of Long-Term Growth Hormone Treatment in Severely Burned Children., Ann Surg. 2009 Sep 2
Burgess W et al. The immune-endocrine loop during aging: role of growth hormone and insulin-like growth factor-I. Neuroimmunomodulation 1999 Jan-Apr; 6(1-2):56-68
Caidahl K, Edén S, Bengtsson BA. Cardiovascular and renal effects of growth hormone. Clin Endocrinol (Oxf). 1994;40:393-400.
Cappola AR et al. Association of IGF-I levels with muscle strength and mobility in older women. J Clin Endocrinol Metab 2001 Sep; 86(9):4139-46
Cappola et al. Insulin-like growth factor I and interleukin-6 contribute synergistically to disability and mortality in older women JCEM, 2003 May; 88(5):2019-25.
Cenci MC, Soares DV, Spina LD, Brasil RR, Lobo PM, Michmacher E, Vaisman M, Boguszewski CL, Conceição FL. Comparison of two dose regimens of growth hormone (GH) with different target IGF-1 levels on glucose metabolism, lipid profile, cardiovascular function and anthropometric parameters in gh-deficient adults. Growth Horm IGF Res. 2012;22:116-121.
Chan et al. Plasma insulin-like growth factor-I and prostate cancer risk: a prospective study. Science Vol 279 January 1998
Cherbonnier C et al. Potentiation of tumour apoptosis by human growth hormone via glutathione production and decreased NF-kappaB activity. Br J Cancer. 2003 Sep 15;89(6):1108-15
Christiansen, J. Influence of growth hormone and androgens on body composition in adults. Horm Res. 1996; 45(1-2):94-8
Colao A et al. Beginning to end: Cardiovascular implications of growth hormone (GH) deficiency and GH therapy. Growth Horm IGF Res. 2006 May 9
Colao A et al. Effect of growth hormone (GH) and insulin-like growth factor I on prostate diseases: an ultrasonographic and endocrine study in acromegaly. J Clin Endocrinol Metab 1999 Jun; 84(6):1986-91
Colao A et al. Impaired cardiac performance in elderly patients with growth hormone deficiency J Clin Endocrinol Metab 1999 Nov; 84(11):3950-5

Colao A, di Somma C, Cuocolo A, Spinelli L, Tedesco N, Pivonello R, Bonaduce D, Salvatore M, Lombardi G. Improved cardiovascular risk factors and cardiac performance after 12 months of growth hormone (GH) replacement in young adult patients with GH deficiency. J Clin Endocrinol Metab. 2001;86:1874-1881.
Colao A.Bone loss is correlated to the severity of growth hormone deficiency in adult patients with hypopituitarism. J Clin Endocrinol Metab 1999 Jun; 84(6):1919-24
Collier SR et al. Growth hormone responses to varying doses of oral arginine.Growth Horm IGF Res. 2005 Apr; 15(2):136-9.
Cook DM.Shouldn't adults with growth hormone deficiency be offered growth hormone replacement therapy?Ann Intern Med 2002 Aug 6;137(3):197-201
Cook, D et al. Route of Estrogen Administration Helps to Determine Growth Hormone (GH) Replacement Dose in GH-Deficient Adults. J Clin Endocrinol Metab 1999Nov; 84: (11): 3956–3960,
Corpas E et al. Oral arginine-lysine does not increase growth hormone or insulin-like growth factor-I in old men. J Gerontol 1993 Jul; 48(4):M128-33
Cuatrecasas G et al. Growth hormone as concomitant treatment in severe fibromyalgia associated with low IGF-1 serum levels. BMC Musculoskelet Disord. 2007 Nov 30:
Cuatrecasas G, Alegre C, Fernandez-Solà J, Gonzalez MJ, Garcia-Fructuoso F, Poca-Dias V, Nadal A, Cuatrecasas G, Navarro F, Mera A, Lage M, Peinó R, Casanueva F, Liñan C, Sesmilo G, Coves MJ, Izquierdo JP, Alvarez I, Granados E, Puig-Domingo M. Growth hormone treatment for sustained pain reduction and improvement in quality of life in severe fibromyalgia. Pain. 2012 Jul;153(7):1382-9.
Drake W et al Optimizing growth hormone replacement therapy by dose titration in hypopituitary adults. J Clin Endocrinol Metab 1998 Nov; 83(11):3913-9 Fazio et al. A preliminary study of GH in the treatment of dilated cardiomyopathy. NEJM 1996:334:809-814
Elbornsson M, Götherström G, Franco C, Bengtsson BÅ, Johannsson G, Svensson J. Effects of 3-year GH replacement therapy on bone mineral density in younger and elderly adults with adult-onset GH deficiency. Eur J Endocrinol. 2012 Feb;166(2):181-9.
Fiebig HH et al. No evidence of tumor growth stimulation in human tumors in vitro following treatment with recombinant human growth hormone Anticancer Drugs 2000 Sep;11(8):659-64
Follin C, Thilén U, Ahrén B, Erfurth EM. Improvement in cardiac systolic function and reduced prevalence of metabolic syndrome after two years of growth hormone (GH) treatment in GH-deficient adult survivors of childhood-onset acute lymphoblastic leukemia. J Clin Endocrinol Metab. 2006 May;91(5):1872-5.
Franco C et al. Growth hormone treatment reduces abdominal visceral fat in postmenopausal women with abdominal obesity: a 12-month placebo-controlled trial. J Clin Endocrinol Metab. 2005 Mar; 90(3):1466-74
Franco C, Andersson B, Lönn L, Bengtsson BA, Svensson J, Johannsson G. Growth hormone reduces inflammation in postmenopausal women with abdominal obesity: a 12-month, randomized, placebo-controlled trial. J Clin Endocrinol Metab. 2007 Jul;92(7):2644-7.
French RA et al. Age-Associated Loss of Bone Marrow Hematopoietic Cells Is Reversed by GH and Accompanies Thymic Reconstitution Endocrinology Vol. 143, No. 2 690-699, Jan 2002
Frohman LA. Controversy about treatment of growth hormone-deficient adults: a commentary. Ann Intern Med. 2002 Aug 6;137(3):202-4.
Garten A, Schuster S, Kiess W. The insulin-like growth factors in adipogenesis and obesity. Endocrinol Metab Clin North Am. 2012 Jun;41(2):283-95,

Genth-Zotz S et al. Recombinant growth hormone therapy in patients with ischemic cardiomyopathy: effects on hemodynamics, left ventricular function, and cardiopulmonary exercise capacity. Circulation. 1999 Jan 5-12; 99(1):18-21
Ghigo E et al. Diagnosis of adult GH deficiency. Growth Horm IGF Res. 2008 Feb; 18(1):1-16.
Gibney et al. The effects of 10 years of GH in adult GH deficient patients J Endocrin Metab 1999 August
Gilchrist FJ et al. The effect of long-term untreated growth hormone deficiency (GHD) and 9 years of GH replacement on the quality of life (QoL) of GH-deficient adults. Clin Endocrinol (Oxf) 2002 Sep; 57(3):363-70
Gillberg, P. et al. Two Years of Treatment with Recombinant Human Growth Hormone Increases Bone Mineral Density in Men with Idiopathic Osteoporosis J Clin Endocrinol Metab 2002 87: 4900-4906
Gotherstrom G et al. A prospective study of 5 years of GH replacement therapy in GH-deficient adults: sustained effects on body composition, bone mass and metabolic indices. J Clin Endocrinol Metab 2001 Oct; 86(10):4657-65
Giustina A, Barkan A, Chanson P, Grossman A, Hoffman A, Ghigo E, Casanueva F, Colao A, Lamberts S, Sheppard M, Melmed S; Pituitary Society; European Neuroendocrine Association. Guidelines for the treatment of growth hormone excess and growth hormone deficiency in adults. J Endocrinol Invest. 2008 Sep;31(9):820-38. Review
Harris, et al. Cytokines, insulin-like growth factor 1, sarcopenia, and mortality in very old community-dwelling men and women: the Framingham Heart Study. Am J Med. 2003 Oct 15; 115(6):429-35.
Hedstrom M. Hip fracture patients, a group of frail elderly people with low bone mineral density, muscle mass and IGF-I levels. Acta Physiol Scand 1999 Dec; 167(4):347-50
Yusuke Higashi, Sergiy Sukhanov, Asif Anwar, Shaw-Yung Shai, Patrice Delafontaine. “Aging, Atherosclerosis, and IGF-1.” J Gerontol A Biol Sci Med Sci (2012) 67A (6): 626-639.
Ho KK et al. Regulating of growth hormone sensitivity by sex steroids: implications for therapy. Front Horm Res. 2006;35:115-28
Hong J et al.; IGFBP-3 mutants that do not bind IGF-I or IGF-II stimulate apoptosis in human prostate cancer cells. J Biol Chem 2002 Jan 9, 2002
Ingermann AR, Yang YF, Han J, Mikami A, Garza AE, Mohanraj L, Fan L, Idowu M, Ware JL, Kim HS, Lee DY, Oh Y. Identification of a novel cell death receptor mediating IGFBP-3-induced anti-tumor effects in breast and prostate cancer. J Biol Chem. 2010 Sep 24;285(39):30233-46.
Isgaard J et al.GH improves cardiac function in rats with experimental MI. Eur J Clin Invest 1997;27:517-
Isley WL. Growth hormone therapy for adults: not ready for prime time?Ann Intern Med 2002 Aug 6;137(3):190-6
Janssen, Y et al. A Switch from Oral (2 mg/Day) to Transdermal (50 mg/Day) 17b-Estradiol Therapy Increases Serum Insulin-Like Growth Factor-I Levels in Recombinant Human Growth Hormone (GH)-Substituted Women with GH Deficiency. J. Clin Endo Metab. 85: January 2000
Jenkins PJ, Mukherjee A, Shalet SM. Does growth hormone cause cancer? Clin Endocrinol (Oxf). 2006 Feb;64(2):115-21.
Johannsson G et al. GH treatment of abdominally obese men reduces abdominal fat mass, improves glusoce and lipoprotein metabolism and reduces diastolic BP. J Clin Endocinol Metab 1997;82:727-734
Johansen et al. Ipamorelin a new ghrp induces longitudinal bone growth in rats. GH and IGF Research 1999, 9 106-113

Johnsen P. et al. Insulin-Like Growth Factor (IGF) I, -II, and IGF Binding Protein-3 and Risk of Ischemic Stroke J Clin Endocrinol Metab 2005 90: 5937-5941;
Kelley KW, Brief S, Westly HJ, Novakofski J, Bechtel PJ, Simon J, Walker EB. GH3 pituitary adenoma cells can reverse thymic aging in rats. Proc Natl Acad Sci U S A. 1986;83:5663-5667.
Khansari DN et al. Effects of long-term, low-dose growth hormone therapy on immune function and life expectancy of mice. Mech Ageing Dev 1991 Jan; 57(1):87-100
Kishimoto I, Tokudome T, Hosoda H, Miyazato M, Kangawa K. Ghrelin and cardiovascular diseases. J Cardiol. 2012 Jan;59(1):8-13.
Kurek R et al. The significance of serum levels of insulin-like growth factor-1 in patients with prostate cancer BJU Int 2000 Jan; 85(1):125-9
Lang CH et al. Cytokine inhibition of JAK-STAT signaling: a new mechanism of growth hormone resistance. Pediatr Nephrol. 2004 Nov 10
Laughlin GA et al. The prospective association of serum insulin-like growth factor I (IGF-I) and IGF-binding protein-1 levels with all cause and cardiovascular disease mortality in older adults: the Rancho Bernardo Study. J Clin Endocrinol Metab. 2004 Jan; 89(1):114-20
Laughlin GA, Barrett-Connor E, Criqui MH, Kritz-Silverstein D. The prospective association of serum insulin-like growth factor I (IGF-I) and IGF-binding protein-1 levels with all cause and cardiovascular disease mortality in older adults: the Rancho Bernardo Study. J Clin Endocrinol Metab. 2004 Jan;89(1):114-20.
Leal-Cerro A The growth hormone (GH)-releasing hormone-GH-insulin-like growth factor-1 axis in patients with fibromyalgia syndrome. J Clin Endocrinol Metab. 1999 Sep; 84(9):3378-81.
Liu H, Bravata DM, Olkin I, Nayak S, Roberts B, Garber AM, Hoffman AR. Systematic review: the safety and efficacy of growth hormone in the healthy elderly. Ann Intern Med. 2007;146:104-115.
Liu QL, Wang YS, Wang JX. Effect of growth hormone on the immune function of dendritic cells. Chin Med J (Engl). 2010;123:1078-1083.
Longobardi, S et al Effects of two years of growth hormone (GH) replacement therapy on bone metabolism and mineral density in childhood and adulthood onset GH deficient patients. J Endocinol Invest, May 1999
Major J et al. Insulin-Like Growth Factor-I and Cancer Mortality in Older Men The Journal of Clinical Endocrinology & Metabolism Vol. 95, No. 3 1054-1059 March 2010
Marcell TJ et al. Oral arginine does not stimulate basal or augment exercise-induced GH secretion in either young or old adults. Gerontol A Biol Sci Med Sci 1999 Aug; 54(8):M395-9
Mitsi AC et al. Early, intracoronary growth hormone administration attenuates ventricular remodeling in a porcine model of myocardial infarction. Growth Horm IGF Res. 2006 Apr; 16(2):93-100
Mitsi AC et al. Early, selective growth hormone administration may ameliorate left ventricular remodeling after myocardial infarction. Med Hypotheses. 2005; 64(3):582-5
Molitch ME. Diagnosis of GH deficiency in adults--how good do the criteria need to be? J Clin Endocrinol Metab. 2002 Feb;87(2):473-6.
Moyle GJ, Daar ES, Gertner JM, Kotler DP, Melchior JC, O'brien F, Svanberg E; Serono 9037 Study Team. Growth hormone improves lean body mass, physical performance, and quality of life in subjects with HIV-associated weight loss or wasting on highly active antiretroviral therapy. J Acquir Immune Defic Syndr. 2004 Apr 1;35(4):367-75.
Muniyappa R et al. Long-Term Testosterone Supplementation Augments Overnight Growth Hormone Secretion in Healthy Older Men. Am J Physiol Endocrinol Metab. 2007

Munzer T et al., Effects of GH and/or sex steroid administration on abdominal subcutaneous and visceral fat in healthy aged women and men. J Clin Endocrinol Metab 2001 Aug; 86(8):3604-10
Nam SY et al. Growth Hormone and Adipocyte Function in Obesity.Horm Res 2000 Jul; 53 Suppl S1:87-97
Nam SY et al. Low-dose growth hormone treatment combined with diet restriction decreases insulin resistance by reducing visceral fat and increasing muscle mass in obese type 2 diabetic patients. Int J Obes Relat Metab Disord 2001 Aug;25(8):1101-7.
Nam SY, Kim KR, Cha BS, Song YD, Lim SK, Lee HC, Huh KB. Low-dose growth hormone treatment combined with diet restriction decreases insulin resistance by reducing visceral fat and increasing muscle mass in obese type 2 diabetic patients. Int J Obes Relat Metab Disord. 2001 Aug;25(8):1101-7.
Napolitano LA, Schmidt D, Gotway MB, et al. Growth hormone enhances thymic function in HIV-1-infected adults. J Clin Invest. 2008;118:1085-1098.
Nguyen CT, Aaronson A, Morrissey RP, Agarwal M, Willix RD, Schwarz ER. Myths and truths of growth hormone and testosterone therapy in heart failure. Expert Rev Cardiovasc Ther. 2011;9:711-720.
Niikura, T et al. Insulin-Like Growth Factor I (IGF-I) Protects Cells from Apoptosis by Alzheimer's V642I Mutant Amyloid Precursor Protein through IGF-I Receptor in an IGF-Binding Protein-Sensitive Manner The Journal of Neuroscience, March 15, 2001, 21(6):1902-1910
Nyberg F. Growth Hormone in the Brain: Characteristics of Specific Brain Targets for the Hormone and Their Functional Significance. Front Neuroendocrinol 2000 Oct; 21(4):330-348
Perrot, A. et al. Growth Hormone Treatment in Dilated Cardiomyopathy J Card. Surg 2001; 16:127-131
Pfeifer M et al. Growth Hormone (GH) Treatment Reverses Early atherosclerotic Changes in GH-Deficient Adults J Clin Endocrinol Metab 84: 453–457, 1999
Popovic V, et al Growth Horm IGF Res. 2005 Jun; 15(3):177-84. 2005 Mar 21. Hypopituitarism following traumatic brain injury
Popovic, V et al. The effectiveness of arginine + GHRH test compared with GHRH + GHRP-6 test in diagnosing growth hormone deficiency in adults. Clin Endocrinol (Oxf). 2003 Aug; 59(2):251-7
Ren J et al. Insulin-like growth factor I as a cardiac hormone: physiological and pathophysiological implications in heart disease. J Mol Cell Cardiol 1999 Nov;31(11):2049-61
Rosén T, Bengtsson BA. Premature mortality due to cardiovascular disease in hypopituitarism. Lancet. 1990;336:285-288.
Rousseau N et al. Effect of aging on growth hormone-induced insulin-like growth factor-I secretion from cultured rat chondrocytes Growth Regulation 7 (1) 1997
Rudman D, Feller AG, Nagraj HS, Gergans GA, Lalitha PY, Goldberg AF, Schlenker RA, Cohn L, Rudman IW, Mattson DE. Effects of human growth hormone in men over 60 years old. N Engl J Med. 1990;323:1-6.
Ruiz-Torres A et al. Ageing and longevity are related to growth hormone/insulin-like growth factor-1 secretion. Gerontology. 2002 Nov-Dec; 48(6):401-7
Ruiz-Torres A. and Soares de Melo Kirzner M. “Ageing and Longevity Are Related to Growth Hormone/Insulun-Like Growth Factor-1 Secretion.” Gerontology 2002; 48:401-507.
Sattler F et al. Testosterone and Growth Hormone Improve Body Composition and Muscle Performance in Older Men. JCEM 2009 94:1991-2001 March 17
Sattler F et al. Testosterone Threshold Levels and Lean Tissue Mass Targets Needed to Enhance Skeletal Muscle Strength and Function: The HORMA Trial. J Gerontol A Biol Sci Med Sci. 2010 Nov 8.

Savine R. et al Growth hormone replacement for the somatopause. Horm Res 2000; 53 Suppl 3:37-41
Savino W, Smaniotto S, Mendes-da-Cruz DA, Dardenne M. Growth hormone modulates migration of thymocytes and peripheral T cells. Ann N Y Acad Sci. 2012;1261:49-54.
Schernhammer ES et al. Insulin-like growth factor-I, its binding proteins (IGFBP-1 and IGFBP-3), and growth hormone and breast cancer risk in The Nurses Health Study II. Endocr Relat Cancer. 2006 Jun; 13(2):583-592
Schneider HJ, Klotsche J, Wittchen HU, et al. Effects of growth hormone replacement within the KIMS survey on estimated cardiovascular risk and predictors of risk reduction in patients with growth hormone deficiency. Clin Endocrinol (Oxf). 2011;75:825-830.
Scirè G, Del Bianco C, Spadoni GL, Cianfarani S. Growth hormone therapy does not alter the insulin-like growth factor-I/insulin-like growth factor binding protein-3 molar ratio in growth hormone-deficient children. J Endocrinol Invest. 2008 Feb;31(2):153-8.
Sesmilo G et al. Effects of growth hormone administration on inflammatory and other cardiovascular risk markers in men with growth hormone deficiency. A randomized, controlled clinical trial. Ann Intern Med 2000 Jul 18; 133(2):111-22
Sesmilo G. et al. Effects of GH Administration on Homocysteine Levels in Men with GH Deficiency: A Randomized Controlled Trial. The Journal of Clinical Endocrinology & Metabolism Vol. 86, No. 4 1518-1524, 2001
Shalet SM, Brennan BM, Reddingius RE. Growth hormone therapy and malignancy. Horm Res 1997; 48 Suppl 4:29-32
Slonim AE et al. A preliminary study of growth hormone therapy for Crohn's disease. N Engl J Med 2000 Jun 1; 342(22):1633-
Soares DV, Spina LD, de Lima Oliveira Brasil RR, Lobo PM, Salles E, Coeli CM, Conceição FL, Vaisman M. Two years of growth hormone replacement therapy in a group of patients with Sheehan's syndrome. Pituitary. 2006;9(2):127-35.
Stochholm, K et al. Mortality and GH Deficiency a Nationwide Study. European Journal of Endocrinology. (2007)157 9-18
Strassberger C et al. How robust are laboratory measures of growth hormone status? Hormone Research 2005; 64:1-
Sugimoto T et al. Effect of recombinant human growth hormone in elderly osteoporotic women. Clin Endocrinol (Oxf) 1999 Dec; 51(6):715-724
Svensson J et al. Body composition and quality of life as markers of the efficacy of growth hormone replacement therapy in adults.Horm Res 2001;55 Suppl 2:55-60
Svensson J, Mattsson A, Rosén T, Wirén L, Johannsson G, Bengtsson BA, Koltowska Häggström M; Swedish KIMS National Board. Three-years of growth hormone (GH) replacement therapy in GH-deficient adults: effects on quality of life, patient-reported outcomes and healthcare consumption. Growth Horm IGF Res. 2004;14:207-215.
Swerdlow A. et al. Growth Hormone Treatment of Children with Brain Tumors and Risk of Tumor Recurrence. The Journal of Clinical Endocrinology & Metabolism Vol. 85, No. 12, December 2000
Takala J et al. Increased mortality associated with GH treatment in critically ill adults. NEJM 1999; 341:785-
Thum T et al. Growth hormone treatment improves markers of systemic nitric oxide bioavailability via insulin-like growth factor-1. J Clin Endocrinol Metab. 2007 Aug 28
Tivesten, A The Growth Hormone Secretagogue Hexarelin Improves Cardiac Function in Rats after Experimental Myocardial Infarction. Endocrinology, January 2000, p. 60-66 Vol. 141, No. 1
Toogood A. et al. Growth Hormone Replacement Therapy in the Elderly with Hypothalamic-Pituitary Disease: A Dose-Finding Study. J Clin Endocrinol Metab 84: 131–136, 1999
Torella D et al. Cardiac stem cell and myocyte aging, heart failure, and insulin-like growth factor-1 overexpression. Circ Res. 2004 Mar 5;94(4):514-24

Zoltan Ungvari and Anna Csiszar. "The Emerging Role of IGF-1 Deficiency in Cardiovascular Aging: Recent Advances." J Gerontol A Biol Sci Med Sci (2012) 67A (6): 599-610.
Valimaki MJ et alEffects of 42 months of GH treatment on bone mineral density and bone turnover in GH-deficient adults. Eur J Endocrinol 1999 Jun; 140(6):545-54
van Dam PS Somatropin therapy and cognitive function in adults with growth hormone deficiency: a critical review. Treat Endocrinol. 2006; 5(3):159-70
Van Der Lely et al. Use of human GH in elderly patients with accidental hip fracture. Eur J Endocrinol 2000 Nov; 143(5):585-592
Wang P et al. The role of endotoxin, TNF-alpha, and IL-6 in inducing the state of growth hormone insensitivity. World J Gastroenterol 2002 Jun; 8(3):531-6 AIM:
Wren AM et al. The novel hypothalamic peptide ghrelin stimulates food intake and growth hormone secretion, Endocrinology 2000 Nov;141(11):4325-8
Yancy CW, Jessup M, Bozkurt B, Masoudi FA, et al; ACCF/AHA Task Force Members. "2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines." J Am Coll Cardiol. 2013 Jun 5.

DHEA

Akishita M, Hashimoto M, Ohike Y, Ogawa S, Iijima K, Eto M, Ouchi Y. Association of plasma dehydroepiandrosterone-sulfate levels with endothelial function in postmenopausal women with coronary risk factors. Hypertens Res. 2008; 31:69-74.
Baulieu E.E., Thomas G., Legrain S., Lahlou N., Roger M., Debuire B., Faucounau V., Girard L., Hervy M.P., Latour F., Leaud M.C., Mokrane A., Pitti-Ferrandi H., Trivalle C., de Lacharriere O., Nouveau S., Rakoto-Arison B., Souberbielle J.C., Raison J., Le Bouc Y., Raynaud A., Girerd X., Forette F. (2000). Dehydroepiandrosterone (DHEA), DHEA sulfate, and aging: contribution of the DHEAge Study to a sociobiomedical issue. Proc Natl Acad Sci USA, 97(8):4279–4284.
Baulieu E.E. (1996). Dehydroepiandrosterone (DHEA): a fountain of youth? J Clin Endocrinol Metabo, 81:3147–3151.
Barrett-Connor E, Khaw KT, Yen SS. A prospective study of dehydroepiandrosterone sulfate, mortality, and cardiovascular disease. N Engl J Med. 1986;315:1519-1524.
Barrett-Connor E, Goodman-Gruen D. Dehydroepiandrosterone sulfate does not predict cardiovascular death in postmenopausal women. The Rancho Bernardo Study. Circulation. 1995;91:1757-1760.
Chiu KM, Schmidt MJ, Havighurst TC, Shug AL, Daynes RA, Keller ET, Gravenstein S. Correlation of serum L-carnitine and dehydro-epiandrosterone sulphate levels with age and sex in healthy adults. Age Ageing. 1999;28:211-216.
Ciolino H, MacDonald C, Memon O, Dankwah M, Yeh GC. Dehydroepiandrosterone inhibits the expression of carcinogen-activating enzymes in vivo. Int J Cancer. 2003;105:321-325.
Green JE, Shibata MA, Shibata E, Moon RC, Anver MR, Kelloff G, Lubet R. 2-difluoromethylornithine and dehydroepiandrosterone inhibit mammary tumor progression but not mammary or prostate tumor initiation in C3(1)/SV40 T/t-antigen transgenic mice. Cancer Res. 2001;61:7449-7455.
de Heredia FP, Cerezo D, Zamora S, Garaulet M. Effect of dehydroepiandrosterone on protein and fat digestibility, body protein and muscular composition in high-fat-diet-fed old rats. Br J Nutr. 2007;97:464-470.
Ho HY, Cheng ML, Chiu HY, Weng SF, Chiu DT. Dehydroepiandrosterone induces growth arrest of hepatoma cells via alteration of mitochondrial gene expression and function. Int J Oncol. 2008;33:969-977.

Hursting SD, Perkins SN, Haines DC, Ward JM, Phang JM. Chemoprevention of spontaneous tumorigenesis in p53-knockout mice. Cancer Res. 1995;55:3949-3953.
Kumar P, Taha A, Sharma D, Kale RK, Baquer NZ. Effect of dehydroepiandrosterone (DHEA) on monoamine oxidase activity, lipid peroxidation and lipofuscin accumulation in aging rat brain regions. Biogerontology. 2008;9:235-246. Erratum in: Biogerontology. 2008;9:283-284.
Morales AJ, Nolan JJ, Nelson JC, Yen SS. Effects of replacement dose of dehydroepiandrosterone in men and women of advancing age. J Clin Endocrinol Metab. 1994;78:1360-1367. Erratum in: J Clin Endocrinol Metab 1995;80:2799.
Page JH, Ma J, Rexrode KM, Rifai N, Manson JE, Hankinson SE. Plasma dehydroepiandrosterone and risk of myocardial infarction in women. Clin Chem. 2008;54:1190-1196.
Rabijewski M, Zgliczyński W. Positive effects of DHEA therapy on insulin resistance and lipids in men with angiographically verified coronary heart disease--preliminary study]. Endokrynol Pol. 2005 Nov-Dec;56(6):904-10.
Rao KV, Johnson WD, Bosland MC, Lubet RA, Steele VE, Kelloff GJ, McCormick DL. Chemoprevention of rat prostate carcinogenesis by early and delayed administration of dehydroepiandrosterone. Cancer Res. 1999;59:3084-3089.
Reiter WJ, Pycha A, Schatzl G, Pokorny A, Gruber DM, Huber JC, Marberger M. Dehydroepiandrosterone in the treatment of erectile dysfunction: a prospective, double-blind, randomized, placebo-controlled study. Urology. 1999;53:590-594; discussion 594-5.
Stuckelberger A. (2008). Anti-Ageing Medicine : Myths and Chances. ETH Verlag, Zurich, Switzerland.
Yang S, Fu Z, Wang F, Cao Y, Han R. Anti-mutagenicity activity of dehydroepiandrosterone. Zhonghua Zhong Liu Za Zhi. 2002;24:137-140. Chinese.

Testosterone

Agarwal PK et al. Testosterone replacement therapy after primary treatment for prostate cancer. J Urol. 2005 Feb; 173(2):533-6.
Alexander GM, Swerdloff RS, Wang C, et al. Androgen-behavior correlations in hypogonadal men and eugonadal men. II. Cognitive abilities. Hormones and Behavior 1998; 33(2):85-94.
Algarte-Genin M et al. Prevention of Prostate Cancer by Androgens: Experimental paradox or clinical reality? European Urology 46 (Sept 2004) 285-295
Araujo Ab et al Prevalence and incidence of androgen deficiency in middle-aged and older men: estimates from the Massachusetts Male Aging Study. J Clinical Endocrinol Metabolism 2004 Dec; 89(12):5920-6.
Arnlov J et al. Endogenous sex hormones and cardiovascular disease incidence in men. Ann Intern Med. 2006 Aug 1; 145(3):176-84
Aydogan U, Aydogdu A, Akbulut H, Sonmez A, Yuksel S, Basaran Y, Uzun O, Bolu E, Saglam K. Increased frequency of anxiety, depression, quality of life and sexual life in young hypogonadotropic hypogonadal males and impacts of testosterone replacement therapy on these conditions. Endocr J. 2012 Aug 31.
Barrett-Connor E et al. Endogenous sex hormones and cognitive function in older men. J Clin Endocrinol Metab 1999 Oct; 84(10):3681-5
Basaria et al. November 2001 Anabolic-Androgenic Steroid Therapy in the Treatment of Chronic Diseases. The Journal of Clinical Endocrinology & Metabolism Vol. 86, No. 11 5108-5117
Bhasin S et al. Testosterone therapy in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2006 Jun; 91(6):1995-2010.

Bhasin S. et al. Testosterone replacement increases fat-free mass and muscle size in hypogonadal men. J Clin Endocrinol Metab. 1997 Feb; 82(2):407-13.
Bhasin S. The dose-dependent effects of testosterone on sexual function and on muscle mass and function. Mayo Clin Proc. 2000 Jan; 75 Suppl: S70-5
Boyanov MA et al. Testosterone supplementation in men with type 2 diabetes, visceral obesity and partial androgen deficiency. Aging Male. 2003 Mar;6(1):1-7.
Burris A et al. A long-term, prospective study of the physiologic and behavioral effects of hormone replacement in untreated hypogonadal men. J Androl 1992 Jul-Aug;13(4):297-304
Caminiti G et al. Effect of long-acting testosterone treatment on functional exercise capacity, skeletal muscle performance, insulin resistance, and baroreflex sensitivity in elderly patients with chronic heart failure a double-blind, placebo-controlled, randomized study. J Am Coll Cardiol. 2009 Sep 1;54(10):919-27
Caretta N et al. Erectile dysfunction in aging men: testosterone role in therapeutic protocols. J Endocrinol Invest. 2005; 28 (11 Suppl Proceedings):108-11
Cassidenti D et al. Effects of sex steroids on skin 5 alpha-reductase activity in vitro Obstetrics & Gynecology 1991; 78:103-107
Channer KS, Jones TH Cardiovascular effects of testosterone: implications of the "male menopause"? Heart. 2003 Feb; 89(2):121-2.
Chen C et al. Cancer Epidemiol Biomarkers Prev. Endogenous sex hormones and prostate cancer risk: a case-control study nested within the Carotene and Retinol Efficacy Trial. 2003 Dec; 12(12):1410-6.
Cooper CS et al. Effect of exogenous testosterone on prostate volume, serum and semen prostate specific antigen levels in healthy young men J Urol 1998 Feb; 159(2):441-3
Daniell HW et al. Hypogonadism in men consuming sustained-action oral opioids. J Pain. 2002 Oct; 3(5):377-84.
Dimitrakakis C et al. Breast cancer incidence in women using testosterone in addition to usual hormone therapy. Menopause 11 (5) 2004
Edinger KL et al. Testosterone's anti-anxiety and analgesic effects may be due in part to actions of its 5alpha-reduced metabolites in the hippocampus. Psychoneuroendocrinology. 2005 Jun; 30(5):418-30
El-Sakka AI et al. Prostatic specific antigen in patients with hypogonadism: effect of testosterone replacement. J Sex Med. 2005 Mar; 2(2):235-40,
Endogenous Sex Hormones and Prostate Cancer: A Collaborative Analysis of 18 Prospective Studies Endogenous Hormones and Prostate Cancer Collaborative Group. J Natl Cancer Inst 2008 100: 170-183
English KM et al. Low-dose transdermal testosterone therapy improves angina threshold in men with chronic stable angina: A randomized, double-blind, placebo-controlled study. Circulation 2000 Oct 17; 102(16):1906-11
Fink B et al. The 2nd-4th digit ratio (2D:4D) and neck circumference: implications for risk factors in coronary heart disease. Int J Obes (Lond). 2006 Apr; 30(4):711-4
Foresta C et al. Reduced Number of Circulating Endothelial Progenitor Cells in Hypogonadal Men. Journal of Clinical Endocrinology & Metabolism 91(11):4599–4602
Fukui, M et al. Diabetes Care 26:1869–1873, June, 2003
Gould DC, Kirby RS Testosterone replacement therapy for late onset hypogonadism: what is the risk of inducing prostate cancer?Prostate Cancer Prostatic Dis. 2006;9(1):14-8
Gouras GK et al. Proc Natl Acad Sci U S A 2000 Feb 1; 97(3):1202-5
Gray A, Feldman HA, McKinlay JB, Longcope C. Age, disease, and changing sex hormone levels in middle-aged men: results of the Massachusetts Male Aging Study. J Clin Endocrinol Metab. 1991;73:1016-1025.
Gunawardena, K et al. Testosterone is a potential augmentor of antioxidant induced apoptosis in human prostate cancer cells. Cancer Detect Prev. 2002; 26(2):105-13

Habib FK, et al. Serenoa repens (Permixon) inhibits the 5alpha-reductase activity of human prostate cancer cell lines without interfering with PSA expression. Int J Cancer. 2005 Mar 20; 114(2):190-4.
Hak, Elisabeth et al. Low Levels of Endogenous Androgens Increase the Risk of Atherosclerosis in Elderly Men: The Rotterdam Study. The Journal of Clinical Endocrinology & Metabolism Vol. 87, 2002, No. 8 3632-3639
Hatzoglou A. et al. Membrane androgen receptor activation induces apoptotic regression of human prostate cancer cells in vitro and in vivo. (Journal of Clinical Endocrinology & Metabolism 2004, 10.1210/jc.2004-0801)
Hau M et al. Testosterone reduces responsiveness to nociceptive stimuli in a wild bird. Horm Behav. 2004 Aug; 46(2):165-70.
Hoffman MA. Is low serum free testosterone a marker for high grade prostate cancer? J Urol 2000 Mar; 163(3):824-7
Hogervorst E et al. Low free testosterone is an independent risk factor for Alzheimer's disease. Exp Gerontol. 2004 Nov-Dec; 39(11-12):1633-9.
Holland J, Bandelow S, Hogervorst E. Testosterone levels and cognition in elderly men: a review. Maturitas. 2011;69:322-337.
Iczkowski, K. et al. The Dual 5 alpha reductase inhibitor dutasteride induces atrophic changes and decreases cancer volume in the human prostate. Urology 65:76-82, 2005
Jankowska EA. Circulating estradiol and mortality in men with systolic chronic heart failure. JAMA. 2009 May 13; 301(18):1892-901.
Janowsky JS. Thinking with your gonads: testosterone and cognition. Trends Cogn Sci. 2006 Feb;10(2):77-82.
Jeong, HJ et al. Inhibition of aromatase activity by flavinoids. ArchPharm Res. 1999 Jun; 22(3):309-12
Jones TH, Arver S, Behre HM, et al; TIMES2 Investigators. Testosterone replacement in hypogonadal men with type 2 diabetes and/or metabolic syndrome (the TIMES2 study). Diabetes Care. 2011;34:828-837.
Daniel M Kelly and T Hugh Jones. “Testosterone: a vascular hormone in health and disease,” J Endocrology 217:3 R47–R71.
Keogh E Can a sexually dimorphic index of prenatal hormonal exposure be used to examine cold pressor pain perception in men and women? : Eur J Pain. 2006 Apr 4
Khaw KT, Barrett-Connor EJ. Blood pressure and endogenous testosterone in men: an inverse relationship. Hypertens. 1988 Apr; 6(4):329-32.
Khaw KT. et al. Endogenous testosterone and mortality due to all causes, cardiovascular disease, and cancer in men. Circulation. 2007; 116:2694-2701
Khera M, Bhattacharya RK, Blick G, Kushner H, Nguyen D, Miner MM. Improved sexual function with testosterone replacement therapy in hypogonadal men: real-world data from the Testim Registry in the United States (TRiUS). J Sex Med. 2011;8:3204-3213.
Korbonits M, Slawik M A comparison of a novel testosterone bioadhesive buccal system, striant, with a testosterone adhesive patch in hypogonadal males J Clin Endocrinol Metab. 2004 May; 89(5):2039-43
Korenman SG, Morley JE, Mooradian AD, et al. 1990 Secondary hypogonadism in older men: its relationship to impotence. J Clin Endocrinol Metab. 71:963–969.
Ekaterina L. Kovacheva, Amiya P. Sinha Hikim, Ruoqing Shen, Indranil Sinha, Indrani Sinha-Hikim. “ Testosterone Supplementation Reverses Sarcopenia
in Aging through Regulation of Myostatin, c-Jun NH2-Terminal Kinase, Notch, and Akt Signaling Pathways.” Endocrinology, Feb. 2010; 151(2):628–638.
Kupelian V et al. Low sex hormone-binding globulin, total testosterone, and symptomatic androgen deficiency are associated with development of the metabolic syndrome in nonobese men. J Clin Endocrinol Metab. 2006 Mar; 91(3):843-50.

Laaksonen DE et al. Sex hormones, inflammation and the metabolic syndrome: a population-albased study.Eur J Endocrinol. 2003 Dec; 149(6):601-8
Laaksonen DE et al. Testosterone and Sex Hormone-Binding Globulin Predict the Metabolic Syndrome and Diabetes in Middle-Aged Men.Diabetes Care. 2004 May;27(5):1036-1041
LeBlanc ES, Wang PY, Janowsky JS, Neiss MB, Fink HA, Yaffe K, Marshall LM, Lapidus JA, Stefanick ML, Orwoll ES; Osteoporotic Fractures in Men (MrOS) Research Group. Association between sex steroids and cognition in elderly men. Clin Endocrinol (Oxf). 2010 Mar;72(3):393-403.
LeBlanc ES, Wang PY, Lee CG, et al. Higher testosterone levels are associated with less loss of lean body mass in older men. J Clin Endocrinol Metab. 2011;96:3855-3863.
Leder BZ et al. Effects of aromatase inhibition in elderly men with low or borderline-low serum testosterone levels.J Clin Endocrinol Metab. 2004 Mar; 89(3):1174-80.
Lunenfeld B Endocrinology of the aging male. Minerva Ginecol. 2006 Apr; 58(2):153-70
Maggio M et al. Correlation between testosterone and the inflammatory marker soluble interleukin-6 receptor (sIL-6r) in older men.J Clin Endocrinol Metab. 2005 Nov 1
Makinen J et al. Increased carotid atherosclerosis in andropausal middle-aged men.J Am Coll Cardiol. 2005 May 17; 45(10)
Malkin CJ et al. Testosterone as a protective factor against atherosclerosis--immunomodulation and influence upon plaque development and stability. J Endocrinol. 2003 Sep; 178(3):373-80
Malkin CJ et al. Testosterone replacement in hypogonadal men with angina improves ischaemic threshold and quality of life. Heart. 2004 Aug; 90(8):871-6.
Malkin CJ et al. Testosterone therapy in men with moderate severity heart failure: a double-blind randomized placebo controlled trial. Eur Heart J. 2005 Aug 10
Malkin CJ et al. The effect of testosterone replacement on endogenous inflammatory cytokines and lipid profiles in hypogonadal men J Clin Endocrinol Metab. 2004 Jul; 89(7):3313-8.
Marks LS et al. Effect of testosterone replacement therapy on prostate tissue in men with late-onset hypogonadism: a randomized controlled trial JAMA. 2006 Nov 15; 296(19):2369-71.
Moffat SD, Resnick SM. Long-term measures of free testosterone predict regional cerebral blood flow patterns in elderly men.Neurobiol Aging. 2006 May 11
Morales A. Monitoring androgen replacement therapy: testosterone and prostate safety.J Endocrinol Invest. 2005; 28(3 Suppl):122-7
Morales A.Androgen replacement therapy and prostate safety.Eur Urol 2002 Feb; 41(2):113-20
Morgentaler A et al. Testosterone therapy in men with untreated prostate cancer. Journal of Urology 2011 Apr;185(4)9.
Morgentaler A Testosterone and Prostate Cancer: An Historical Perspective on a Modern Myth. Eur Urol. 2006 Jul 26
Morgentaler A Testosterone replacement therapy and prostate risks: where's the beef? Can J Urol. 2006 Feb; 13 Suppl 1:40-3.
Morgentaler A. et al Two years of testosterone therapy associated with decline in prostate-specific antigen in a man with untreated prostate cancer. J Sex Med. 2009 Feb; 6(2):574-7.
Morgentaler, M. Guideline for Male Testosterone therapy. A clinician’s perspective. J. Clin Endo Metab. 92 (2) 416-417, 2007 no abstract available
Morley J. Testosterone and frailty. Clin Geriatr Med 1997 Nov;13(4):685-95
Morley JE. Testosterone replacement and the physiologic aspects of aging in men.Mayo Clin Proc. 2000 Jan; 75 Suppl: S83-7
Mudali S, Dobs AS Effects of testosterone on body composition of the aging male. Mech Ageing Dev. 2004 Apr; 125(4):297-304

Mudali S, Dobs AS. Effects of testosterone on body composition of the aging male. Mech Ageing Dev. 2004;125:297-304.
Muller M et al. Endogenous sex hormones and progression of carotid atherosclerosis in elderly men. Circulation. 2004 May 4; 109(17):2074-9.
Muniyappa R et al. Long-Term Testosterone Supplementation Augments Overnight Growth Hormone Secretion in Healthy Older Men. Am J Physiol Endocrinol Metab. 2007
Vakkat Muraleedharan and T. Hugh Jones. "Review: Testosterone and the metabolic syndrome," Therapeutic Advances in Endocrinology and Metabolism 2010 1: 207.
Nathan L et al. Testosterone inhibits early atherogenesis by conversion to estradiol: critical role of aromatase. Proc Natl Acad Sci U S A. 2001 Mar 13;98(6):3589-93
Nettleship JE, Jones RD, Channer KS, Jones TH. Testosterone and coronary artery disease. Front Horm Res. 2009;37:91-107.
O'Connor DB, Archer J, Hair WM, Wu FC. Exogenous testosterone, aggression, and mood in eugonadal and hypogonadal men. Physiol Behav. 2002;75:557-566.
Oettel M et al. Progesterone: the forgotten hormone in men? Aging Male. 2004 Sep; 7(3):236-57
Padero MC et al. Androgen supplementation in older women: too much hype, not enough data. J Am Geriatr Soc 2002 Jun; 50(6):1131-40
Pantuck AJ et al. Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen following Surgery or Radiation for Prostate Cancer.Clin Cancer Res. 2006 Jul 1;12(13):4018-4026
Phillips GB Relationship between serum sex hormones and coronary artery disease in postmenopausal women. Arterioscler Thromb Vasc Biol. 1997 Apr; 17(4):695-701
Phillips GB. Is atherosclerotic cardiovascular disease an endocrinological disorder? The estrogen-androgen paradox. J Clin Endocrinol Metab. 2005 May;90(5):2708-11
Prehn RT. On the prevention and therapy of prostate cancer by androgen administration. Cancer Res 1999 Sep 1; 59(17):4161-4
Pugh PJ, Jones RD, West JN, Jones TH, Channer KS. Testosterone treatment for men with chronic heart failure. Heart. 2004 Apr;90(4):446-7.
Rao et al. Effect of testosterone on threshold of pain.Indian J Physiol Pharmacol. 1981 Oct-Dec; 25(4):387-8.
Rhoden EL, Averbeck MA. [Prostate carcinoma and testosterone: risks and controversies]. Arq Bras Endocrinol Metabol. 2009 Nov;53(8):956-62.
Rosano GM et al. Acute anti-ischemic effect of testosterone in men with coronary artery disease. Circulation 1999 Apr 6; 99(13):1666-70
Sarosdy MF. Testosterone replacement for hypogonadism after treatment of early prostate cancer with brachytherapy. Cancer. 2007 Feb 1;109(3):536-41
Schmidt M et al. Androgen conversion in osteoarthritis and rheumatoid arthritis synoviocytes--androstenedione and testosterone inhibit estrogen formation and favor production of more potent 5alpha-reduced androgens. Arthritis Res Ther. 2005; 7(5):R938-48.
Schmidt M, Renner C, Loffler G. Progesterone inhibits glucocorticoid-dependent aromatase induction in human adipose fibroblasts. J Endocrinol. 1998 Sep;158(3):401-7
Schubert M et al. Intramuscular testosterone undecanoate: pharmacokinetic aspects of a novel testosterone formulation during long-term treatment of men with hypogonadism. J Clin Endocrinol Metab. 2004 Nov; 89(11):5429-34.
Shores MM et al. Low serum testosterone and mortality in male veterans. Arch Intern Med. 2006 Aug 14; 166(15):1660-5
Sinha-Hikim I et al. Effects of testosterone supplementation on skeletal muscle fiber hypertrophy and satellite cells in community-dwelling older men. J Clin Endocrinol Metab. 2006 Aug; 91(8):3024-33.
Somboonporn W., Davis S., Seif M.W. and Bell R. (2005). Testosterone for peri- and postmenopausal women. Cochrane Database of Systematic Reviews, Issue 4.

Stattin P et al. High levels of circulating testosterone are not associated with increased prostate cancer risk: a pooled prospective study. Int J Cancer. 2004 Jan 20; 108(3):418-24
Svartberg J. Epidemiology: testosterone and the metabolic syndrome. Int J Impot Res. 2006 Jul 20
Tan RS A pilot study on the effects of testosterone in hypogonadal aging male patients with Alzheimer's disease. Aging Male. 2003 Mar; 6(1):13-7.
Tilakaratne A, Soory M. Effects of the anti-androgen finasteride on 5 alpha-reduction of androgens in the presence of progesterone in human gingival fibroblasts. J Periodontal Res. 2000 Aug; 35(4):179-85
Travison TG et al. A population-level decline in serum testosterone levels in American men. J Clin Endocrinol Metab. 2006 Oct 24
Tsujimura A et al. Treatment with human chorionic gonadotropin for PADAM: a preliminary report. Aging Male. 2005 Sep-Dec; 8(3-4):175-9
Turhan S et al. The association between androgen levels and premature coronary artery disease in men. Coron Artery Dis. 2007 May; 18(3):159-62.
Turna B et al. Women with low libido: correlation of decreased androgen levels with female sexual function index. Int J Impot Res. 2004 Dec 09
van den Beld et al. Measures of bioavailable serum testosterone and estradiol and their relationships with muscle strength, bone density, and body composition in elderly men J Clin Endocrinol Metab 2000 Sep;85(9):3276-82
Vermeulen A. Androgens in the aging male. J Clin Endocrinol Metab. 1991. 73:221–224.
Vigna GB et al. Testosterone replacement, cardiovascular system and risk factors in the aging male. J Endocrinol Invest. 2005; 28(11 Suppl Proceedings):69-74
Webb CM et al. Effects of testosterone on coronary vasomotor regulation in men with coronary heart disease. Circulation. 1999 Oct 19; 100(16):1690-6.
Yeap BB et al Higher serum free testosterone is associated with better cognitive function in older men, while total testosterone is not. The Health In Men Study. Clin Endocrinol (Oxf). 2008 Mar; 68(3):404-12
Yeap BB et al In men older than 70 years, total testosterone remains stable while free testosterone declines with age. The Health in Men Study. Eur J Endocrinol. 2007 May;156(5):585-94
Yeap BB et al Low free testosterone concentration as a potentially treatable cause of depressive symptoms in older men. Arch Gen Psychiatry. 2008 Mar; 65(3):283-9.
Yeap BB et al. Lower testosterone levels predict incident stroke and transient ischemic attack in older men. J Clin Endocrinol Metab. 2009 Jul; 94(7):2353-9.
Yeap BB et al. Are declining testosterone levels a major risk factor for ill-health in aging men? Int J Impot Res. 2009 Jan-Feb; 21(1):24-36.
Yeap BB et al. Lower serum testosterone is independently associated with insulin resistance in non-diabetic older men. The Health In Men Study. Eur JEndocrinol. 2009 Aug 18.
Yeap BB et al. Serum testosterone levels correlate with haemoglobin in middle-aged and older men. Intern Med J. 2008 Aug 16.
Yeap BB et al. Healthier lifestyle predicts higher circulating testosterone in older men: the Health In Men Study. Clin Endocrinol (Oxf). 2009 Mar; 70(3):455-63.
Yeap BB et al. Lower sex hormone-binding globulin is more strongly associated with metabolic syndrome than lower total testosterone in older men: the Health in Men Study. Eur J Endocrinol. 2008 Jun; 158(6):785-92.
Yeap BB et al. Luteinizing hormone levels are positively correlated with plasma amyloid-beta protein levels in elderly men. J Alzheimers Dis. 2008 Jun; 14(2):201-8.
Yeap BB et al. Testosterone and ill-health in aging men. Nat Clin Pract Endocrinol Metab. 2009 Feb; 5(2):113-21.

Zitzmann M Hormone substitution in male hypogonadism Mol Cell Endocrinol 2000 Mar 30; 161(1-2):73-88

REFERENCES

1. Zs.-Nagy I. “Is consensus in anti-aging medical intervention an elusive expectation or a realistic goal?” Archives of Gerontology and Geriatrics, Volume 48 Issue 3; May-June 2009, 271-276.
2. Interview with Tanjung Subrata, MD, 16 September 2013.
3. Interview with Tim Bolen, 30 July 2013.
4. Perls TT, Reisman NR, Olshansky SJ. "Provision or Distribution of Growth Hormone for 'Anti-Aging': Clinical and Legal Issues." JAMA. 2005 Oct 26;294(16):2086-90.
5. Epstein D. “US sprinter Tyson Gay linked to anti-aging specialist,” SI.com; 16 July 2013.
6. Paragraph excerpted from White Paper “Guidance for Physicians on Hormone Replacement Therapy”; A4M, May 2007; available at: http://www.worldhealth.net/white-papers-official-statements/
7. Interview with Robert Goldman, M.D., Ph.D., D.O., FAASP, 27 July 2013.
8. Statement of Louis Underwood, M.D., "Abuse of Steroids in Amateur and Professional Athletics," Hearing Before the Subcommittee on Crime/ House Committee on the Judiciary, March 22, 1990).
9. Interview with Rick Collins, JD, CSCS, www.steroidlaw.com, September 2013.
10. Mitchell, S.; HGH illegal as anti-aging treatment: United Press International (UPI), Oct. 25, 2005.
11. Mollica M. “Testosterone Replacement Therapy – Why Is It So Controversial?”; http://www.brinkzone.com/bodybuilding/testosterone-replacement-therapy-why-is-it-so-controversial/; July 20, 2012.
12. Rudman D, Feller AG, Nagraj HS, Gergans GA, Lalitha PY, Goldberg AF, Schlenker RA, Cohn L, Rudman IW, Mattson DE. Effects of human growth hormone in men over 60 years old. N Engl J Med. 1990;323:1-6.
13. Gotherstrom G., et.al. "A prospective study of 5 years of GH replacement therapy in GH-deficient adults: sustained effects on body composition, bone mass, and metabolic indices" Journal of Clinical Endocrinology and Metabolism, 86 (10): 4657-65, Oct. 2001.
14. Gibney J, et. al., "The Effects of 10 Years of Recombinant Human Growth Hormone, (GH) in Adult GH-Deficient Patients", The Journal of Clinical Endocrinology and Metabolism, Volume 84, Number 8, August 1999.
15. Cappola AR et al. Association of IGF-I levels with muscle strength and mobility in older women. J Clin Endocrinol Metab 2001 Sep;86(9):4139-46.
16. Aleman A. et al. Insulin-Like Growth Factor-I and Cognitive Function in Healthy Older Men J Clin Endocrinol Metab 84:471475, 1999.
17. Sugimoto T et al. Effect of recombinant human growth hormone in elderly osteoporotic women. Clin Endocrinol (Oxf) 1999 Dec;51(6):715-724.
18. Napoli R et al. J Am Coll Cardiol 2002 Jan 2;39(1):90-5.
19. Johannsson G et al. GH treatment of abdominally obese men reduces abdominal fat mass, improves glucose and lipoprotein metabolism and reduces diastolic BP. J Clin Endocinol Metab 1997;82:727-734.
20. Albert SG et al. Low-dose recombinant human growth hormone as adjuvant therapy to lifestyle modifications in the management of obesity. Clin Endocrinol Metab. 2004 Feb;89(2):695-701.
21. Nam SY et al. Low-dose growth hormone treatment combined with diet restriction decreases insulin resistance by reducing visceral fat and increasing muscle mass in obese type 2 diabetic patients.

22. Paragraph excerpted from Rothenberg R, et al. "Hormone Optimization: Evidence Based Practical Management." In Encyclopedia of Clinical Anti-Aging Medicine & Regenerative Biomedical Technologies, A4M, 2012, pp. 281-342.
23. Besson A et al. Reduced longevity in untreated patients with isolated growth hormone deficiency. J Clin Endocrinol Metab. 2003 Aug; 88(8):3664-7.
24. Ruiz-Torres A. and Soares de Melo Kirzner M. "Ageing and Longevity Are Related to Growth Hormone/Insulun-Like Growth Factor-1 Secretion." Gerontology 2002; 48:401-407.
25. Stochholm, K et al. Mortality and GH Deficiency a Nationwide Study. European Journal of Endocrinology. (2007)157 9-18
26. The Journals of Gerontology:Series A, Vol. 67A, Issue 6; June 2012; http://biomedgerontology.oxfordjournals.org/content/67A/6.toc
27. Yusuke Higashi, Sergiy Sukhanov, Asif Anwar, Shaw-Yung Shai, Patrice Delafontaine. "Aging, Atherosclerosis, and IGF-1." J Gerontol A Biol Sci Med Sci (2012) 67A (6): 626-639.
28. Zoltan Ungvari and Anna Csiszar. "The Emerging Role of IGF-1 Deficiency in Cardiovascular Aging: Recent Advances." J Gerontol A Biol Sci Med Sci (2012) 67A (6): 599-610.
29. Yancy CW, Jessup M, Bozkurt B, Masoudi FA, et al; ACCF/AHA Task Force Members. "2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines." J Am Coll Cardiol. 2013 Jun 5.
30. Savine R. et al. Growth hormone replacement for the somatopause. Horm Res 2000;53 Suppl 3:37-4
31. Wuster C, Melchinger U, Eversmann T, Hensen J, Kann P, von zur Muhlen A, Ranke MB, Schmeil H, Steinkamp H, Tuschy U. Reduced incidence of side-effects of growth hormone substitution in 404 patients with hypophyseal insufficiency. Results of a multicenter indications Study. Med Klin 1998 Oct 15;93(10):585-91.
32. Ingermann AR, Yang YF, Han J, Mikami A, Garza AE, Mohanraj L, Fan L, Idowu M, Ware JL, Kim HS, Lee DY, Oh Y. Identification of a novel cell death receptor mediating IGFBP-3-induced anti-tumor effects in breast and prostate cancer. J Biol Chem. 2010 Sep 24;285(39):30233-46.
33. Scirè G, Del Bianco C, Spadoni GL, Cianfarani S. Growth hormone therapy does not alter the insulin-like growth factor-I/insulin-like growth factor binding protein-3 molar ratio in growth hormone-deficient children. J Endocrinol Invest. 2008 Feb;31(2):153-8.
34. Jenkins PJ, Mukherjee A, Shalet SM. Does growth hormone cause cancer? Clin Endocrinol (Oxf). 2006 Feb;64(2):115-21.
35. Molitch ME. Diagnosis of GH deficiency in adults--how good do the criteria need to be? J Clin Endocrinol Metab. 2002 Feb;87(2):473-6.
36. Svensson J, et al. J Clin Endocrinol Metab. 2004;89(7):3306-12.
37. Eiser C, et al. Growth Hormone Treatment and Quality of Life among Survivors of Childhood Cancer. Horm Res. 2005; 633(6):300-4.
38. Zumkeller W, et al. _Expression and synthesis of insulin-like growth factor-binding proteins in human glioma cell lines. Int J Oncol. 1998 Jan;12(1)129-35.
39. Gielen SC, et al. Steroid-modulated proliferation of human endometrial carcinoma cell lines: any role for insulin-like growth factor signaling? J Soc Gynecol Investig. 2005 Jan;12(1):58-64.
40. Bach LA, Headey SJ, Norton RS. IGF-binding proteins the pieces are falling into place. Trends Endocrinol Metab. 2005 July;16(5):228-34.
41. Swerdlow AJ, et al. J Clin Endocrinol Metab 2000;85(12):4444-9.
42. Tacke J, et al. JPEN J Parenter Enteral Nutr 2000;24(3):140-4.

43. Critical Evaluation of the Safety of Recombinant GH Administration: Statement from the Growth Hormone Research Society, J Clin Endo Metab, May 2001.
44. Gardner et al. "Effects of dietary carbohydrate on fasting levels of human growth hormone and cortisol," Proceedings of the Soc for Exper Biol and Med, 1982, 36-40.
45. US District Court, District of Nevada Case #3:06-CR-147-BES-VPC, USA vs. James W. Forsythe.
46. Interview with James Forsythe, M.D., HMD, 18 September 2013.
47. Morales AJ, Nolan JJ, Nelson JC, Yen SS. Effects of replacement dose of dehydroepiandrosterone in men and women of advancing age. J Clin Endocrinol Metab. 1994;78:1360-1367. Erratum in: J Clin Endocrinol Metab 1995;80:2799.
48. Rabijewski M, Zgliczyński W. Positive effects of DHEA therapy on insulin resistance and lipids in men with angiographically verified coronary heart disease--preliminary study]. Endokrynol Pol. 2005 Nov-Dec;56(6):904-10.
49. Baulieu E.E., Thomas G., Legrain S., Lahlou N., Roger M., Debuire B., Faucounau V., Girard L., Hervy M.P., Latour F., Leaud M.C., Mokrane A., Pitti-Ferrandi H., Trivalle C., de Lacharriere O., Nouveau S., Rakoto-Arison B., Souberbielle J.C., Raison J., Le Bouc Y., Raynaud A., Girerd X., Forette F. (2000). Dehydroepiandrosterone (DHEA), DHEA sulfate, and aging: contribution of the DHEAge Study to a sociobiomedical issue. Proc Natl Acad Sci USA, 97(8):4279–4284.
50. Baulieu E.E. (1996). Dehydroepiandrosterone (DHEA): a fountain of youth? J Clin Endocrinol Metabo, 81:3147–3151.
51. Stuckelberger A. (2008). Anti-Ageing Medicine : Myths and Chances. ETH Verlag, Zurich, Switzerland. e-book in open access: http://www.vdf.ethz.ch/service/3225/9783728132253_anti-ageing-medicine_oa.pdf
52. Daniel M Kelly and T Hugh Jones. "Testosterone: a vascular hormone in health and disease," J Endocrology 217:3 R47–R71.
53. Pugh PJ, Jones RD, West JN, Jones TH, Channer KS. Testosterone treatment for men with chronic heart failure. Heart. 2004 Apr;90(4):446-7.
54. Malkin CJ et al. The effect of testosterone replacement on endogenous inflammatory cytokines and lipid profiles in hypogonadal men J Clin Endocrinol Metab. 2004 Jul; 89(7):3313-8.
55. Turhan S et al. The association between androgen levels and premature coronary artery disease in men. Coron Artery Dis. 2007 May; 18(3):159-62.
56. Rosano GM et al. Acute anti-ischemic effect of testosterone in men with coronary artery disease. Circulation 1999 Apr 6; 99(13):1666-70
57. Hak, Elisabeth et al. Low Levels of Endogenous Androgens Increase the Risk of Atherosclerosis in Elderly Men: The Rotterdam Study. The Journal of Clinical Endocrinology & Metabolism Vol. 87, 2002, No. 8 3632-3639
58. Boyanov MA et al. Testosterone supplementation in men with type 2 diabetes, visceral obesity and partial androgen deficiency. Aging Male. 2003 Mar;6(1):1-7.
59. Vakkat Muraleedharan and T. Hugh Jones. "Review: Testosterone and the metabolic syndrome," Therapeutic Advances in Endocrinology and Metabolism 2010 Oct;1(5):207-23.
60. Bhasin S. et al. Testosterone replacement increases fat-free mass and muscle size in hypogonadal men. J Clin Endocrinol Metab. 1997 Feb; 82(2):407-13.
61. Mudali S, Dobs AS. Effects of testosterone on body composition of the aging male. Mech Ageing Dev. 2004 Apr; 125(4):297-304
62. LeBlanc ES, Wang PY, Janowsky JS, Neiss MB, Fink HA, Yaffe K, Marshall LM, Lapidus JA, Stefanick ML, Orwoll ES; Osteoporotic Fractures in Men (MrOS) Research Group. Association between sex steroids and cognition in elderly men. Clin Endocrinol (Oxf). 2010 Mar;72(3):393-403.

63. Ekaterina L. Kovacheva, Amiya P. Sinha Hikim, Ruoqing Shen, Indranil Sinha, Indrani Sinha-Hikim. " Testosterone Supplementation Reverses Sarcopenia in Aging through Regulation of Myostatin, c-Jun NH2-Terminal Kinase, Notch, and Akt Signaling Pathways." Endocrinology, Feb. 2010; 151(2):628–638.
64. Moffat SD, Resnick SM. Long-term measures of free testosterone predict regional cerebral blood flow patterns in elderly men.Neurobiol Aging. 2006 May 11
65. Gouras GK et al. Proc Natl Acad Sci U S A 2000 Feb 1; 97(3):1202-5
66. Tan RS. A pilot study on the effects of testosterone in hypogonadal aging male patients with Alzheimer's disease. Aging Male. 2003 Mar; 6(1):13-7.
67. Janowsky JS. Thinking with your gonads: testosterone and cognition. Trends Cogn Sci. 2006 Feb;10(2):77-82.
68. Holland J, Bandelow S, Hogervorst E. Testosterone levels and cognition in elderly men: a review. Maturitas. 2011;69:322-337.
69. O'Connor DB, Archer J, Hair WM, Wu FC. Exogenous testosterone, aggression, and mood in eugonadal and hypogonadal men. Physiol Behav. 2002;75:557-566.
70. Aydogan U, Aydogdu A, Akbulut H, Sonmez A, Yuksel S, Basaran Y, Uzun O, Bolu E, Saglam K. Increased frequency of anxiety, depression, quality of life and sexual life in young hypogonadotropic hypogonadal males and impacts of testosterone replacement therapy on these conditions. Endocr J. 2012 Aug 31.
71. Khera M, Bhattacharya RK, Blick G, Kushner H, Nguyen D, Miner MM. Improved sexual function with testosterone replacement therapy in hypogonadal men: real-world data from the Testim Registry in the United States (TRiUS). J Sex Med. 2011;8:3204-3213.
72. Somboonporn W., Davis S., Seif M.W. and Bell R. (2005). Testosterone for peri- and postmenopausal women. Cochrane Database of Systematic Reviews, Issue 4.
73. Rhoden EL, Averbeck MA. [Prostate carcinoma and testosterone: risks and controversies]. Arq Bras Endocrinol Metabol. 2009 Nov;53(8):956-62.
74. Cooper CS et al. Effect of exogenous testosterone on prostate volume, serum and semen prostate specific antigen levels in healthy young men J Urol 1998 Feb; 159(2):441-3
75. Morales A. Monitoring androgen replacement therapy: testosterone and prostate safety.J Endocrinol Invest. 2005; 28(3 Suppl):122-7
76. Prehn RT. On the prevention and therapy of prostate cancer by androgen administration. Cancer Res 1999 Sep 1; 59(17):4161-4
77. Morley JE. Testosterone replacement and the physiologic aspects of aging in men.Mayo Clin Proc. 2000 Jan; 75 Suppl: S83-7
78. Gould DC, Kirby RS Testosterone replacement therapy for late onset hypogonadism: what is the risk of inducing prostate cancer?Prostate Cancer Prostatic Dis. 2006;9(1):14-8
79. Agarwal PK et al. Testosterone replacement therapy after primary treatment for prostate cancer. J Urol. 2005 Feb; 173(2):533-6.
80. Sarosdy MF. Testosterone replacement for hypogonadism after treatment of early prostate cancer with brachytherapy. Cancer. 2007 Feb 1;109(3):536-41
81. Morgentaler A et al. Testosterone therapy in men with untreated prostate cancer. Journal of Urology 2011 Apr;185(4)9.
82. Abramow M., Corvilain J.: Metabolic effects of human growth hormone in adults and children. J Ann Endocrinol (Paris) March-April 1963, 145-56.
83. Hernberg-Stahl E, Luger A, Abs R, Bengtsson BA, Feldt-Rasmussen U, Wilton P, Westberg B, Monson JP; KIMS International Board., KIMS Study Group. Pharmacia International Metabolic Database, "Healthcare consumption decreases in parallel with improvements in quality of life during GH replacement in hypopituitary adults with GH deficiency," J Clin Endocrinol Metab. 2001 Nov;86(11):5277-81.

CONTRIBUTING PHYSICIANS & SCIENTISTS

Martin Dayton, D.O.; Medical Director, Dayton Medical Center (Florida, USA)
Robert M. Goldman, M.D., Ph.D., D.O.; Co-Founder & Chairman, American Academy of Anti-Aging Medicine; Co-Founder & Chairman, World Anti-Aging Academy of Medicine
Brad Grant D.O., past Pres., Osteopathic Physicians and Surgeons of California
James Forsythe, M.D., HMD; private practice (Nevada, USA)
Steven F. Hotze, M.D.; Director, Texas for Physicians' and Patients' Rights; Chief Executive Officer, Hotze Health & Wellness Center (Texas, USA)
Ronald M. Klatz, M.D., D.O.; Co-Founder & President, American Academy of Anti-Aging Medicine
Hans Kugler, Ph.D.; President & Founder, International Academy of Anti-Aging Medicine
A.Tina Miranda, M.D., MBA, private practice (Florida, USA)
Iris Breuer Mueller, M.D.; Psychiatrist, The Cantonal Hospital of Lucerne, Switzerland; University of Zurich, Switzerland
Emil K. Schandl, M.S., Ph.D., M.D., (MA), FNACB, SC(ASCP), CC(NRCC), LNC, CLD (FL, NY, CA); Director, American Metabolic Laboratories, Clinical Laboratory
C. Norman Shealy, M.D., Ph.D.; President, Holos Institutes of Health., Inc. (Missouri, USA)
Astrid Stuckelberger, MSc, Ph.D., Docent; Faculty of Medicine, University of Geneva, Switzerland; Secretary-General, International Association of Gerontology and Geriatrics – European Region; President, Geneva International Network on Aging; Expert on Aging at the United Nations and European Commission

ENDORSING ORGANIZATIONS

American Academy of Anti-Aging Medicine (A4M)
Academy of Anti-Aging Medicine - China
Asia-Oceania Federation of Anti-Aging Medicine (AOFAAM)
AustralAsian Academy of Anti-Aging Medicine (A5M)
European Society of Anti-Aging Medicine (ESAAM)
German Society of Anti-Aging Medicine (GSAAM)
German Society of Hemotoxicology
Hellenic Academy of Antiaging Medicine
Indonesian Society of Anti-Aging Medicine
International Academy of Anti-Aging Medicine
Japan Anti-Aging Medical Spa Association (JAMSA)
Japanese Society of Clinical Anti-Aging Medicine (JSCAM)
Korea Anti-Aging Academy of Medicine (KA3M)
LatinoAmerican Federation of Anti-aging Societies
Romanian Association of Anti Aging Medicine
Sociedad de Medicine Antievejenimiento y Longevidad de Gran Canaria
Society for Anti-Aging & Aesthetic Medicine Malaysia (SAAAMM)
South African Academy of Anti-Aging & Aesthetic Medicine (SA5M)
Spanish Society of Anti-Aging
Thai Academy of Anti-Aging Medicine
Anti Aging Research and Education Society, Turkey
Center for Study of Anti-Aging Medicine - UDAYANA University, Indonesia
Ukrainian Association of Preventive & Anti-Aging Medicine
World Anti-Aging Academy of Medicine (WAAAM)

DISCLAIMER

This Position Paper is intended to articulate the general policy positions of certain officers and directors of The American Academy of Anti-Aging Medicine (A4M), its numerous worldwide affiliated scientific and medical

societies, and befriended organizations, and also to provide general information to practitioners and the public. This Position Paper is not intended to necessarily reflect the views of A4M's members or the members of A4M''s affiliated organizations. This Position Paper is also not intended to provide specific regulatory or legal advice at either the state or federal level. As state laws vary widely and individual circumstances may vary, readers are advised to consult their own legal counsel for guidance in meeting both state and federal requirements in their specific medical practice. In no event shall A4M, its parents, subsidiaries, affiliates and their respective members, directors, officers, employees, stockholders and agents be liable to you or any other entity for any and all damages including but not limited to direct, compensatory, indirect, incidental, consequential, special, exemplary or punitive damages (including, without limitation, damages for loss of profits, business interruption, loss of information and loss of business opportunities) arising out of or relating to (1) the use of or inability to use the above information, or (2) reliance on the content of this Position Paper; or (3) errors, inaccuracies, omissions, contained within the above materials; or (4) the satisfaction of any government regulation requiring disclosure of information on prescription or "off-label" drug products with regard to the information contained within this Position Paper. Because some jurisdictions may not permit each of these disclaimers and limitations, the above limitation may not apply to you. A4M and its parents, subsidiaries, affiliates and their respective members, directors, officers, employees, stockholders and agents further do not warrant the accuracy or completeness of the information, text, links or other items contained within this Position Paper. A4M may make changes to this Position Paper at any time without notice; however, A4M makes no commitment to update this Position Paper.