GH Replacement therapy for Adult GH Deficiency
Current Literature and Clinical Practice
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GH Replacement therapy for Adult GH Deficiency

Current Literature and Clinical Practice

Ron Rothenberg MD
• Physiology
• What data on GH Replacement Therapy (GHRT) is in the medical literature in the past few years?
• Does GHRT increase the risk of cancer?
• Are there significant side effects to GHRT?
• What are the practical aspects of GHRT based on medical literature and clinical experience?
• GH and inflammation?
Type Growth Hormone into Pubmed

• February 11, 2008:
  • 56,192 citations

• January 29, 2009
  • 89,413 citations

• November 11, 2010
  • 95,360 citations
• Exponential decline in GH release after 18-21
• 14% decline per decade after puberty
• Negative correlation of GH release and BMI
• GH has half life of 14 minutes
• IGF-1 has half life of < 10 minutes
IGFBP’s

- 6 IGF Binding Proteins
- Inhibit and Enhance IGF Actions
- IGF-1 + IGFBP-3 + Acid Labile Subunit = Ternary Complex
- Half-Life of Ternary Complex = 15 hours
- IGFBP-3 has independent actions and inhibits cancer through p53
Low IGF-1 – poor muscle strength and mobility in women 70-79

- Low IGF-1:
- Poor knee extensor muscle strength
- Slow walking speed
- Difficulty with mobility tasks

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
GH deficiency = decreased longevity in humans

• Patients with absent GH-1 gene compared to siblings
• Males, 56 vs. 75 yr (P < 0.0001)
• Females, 46 vs. 80 yr (P < 0.0001)
Ageing and Longevity are related to GH/IGF-1

- Old males with higher IGF-1 do not show age related decrease in Testosterone, LBM and increase in fat mass
- GH determines life potential

Adult GHD and Mortality

- Mortality increased childhood onset/adult onset GHD
- Hazard Ratio
  - Males 1.9
  - Females 3.4

Is GH RT a “Fountain of Youth”? 

- No 
- If we were to stay perfect why alter a perfect system 
- Since we are on a “programmed course of destruction”, GHRT is a way to help to maintain Quality of Life 
- Treat if patient has AGHD 
- Risk/Benefit analysis 
- Work in Progress 

AGHD

- Neurocognitive decline

GH Replacement

- Improved memory, alertness and concentration
GH and the brain

- GH exerts profound effects on CNS
- Improves
  - Cognitive capabilities
  - Memory
  - Alertness
  - Motivation, Work Capacity
- GH receptors present in the brain
  - Hypothalamus, choroid plexus, hippocampus
- GH crosses BBB

GH and the Brain

• IGF-1 correlated with cognitive function in men average age 69
• GH deficiency correlated with
  –poor emotional and psychosocial functioning

GH and Alzheimer’s

- IGF-I exerts cytoprotection against A beta amyloid induced neuronal cell death

GH Cognitive Review

- GH and IGF-1 cross BBB and have brain receptors especially in hippocampus and amygdala, fronto-parietal cortex
- Effects are mediated by an interaction with the NMDA receptor, and may lead to neuronal regeneration and increased neurotransmitter activity.
- GH and IGF-1 correlated with cognitive function in multiple studies
- In GHD GHRT improves processing speed and attention
AGHD

- Reduced bone density

GH Replacement

- Reversal of osteoporosis

Bone density significantly improved with GH therapy
• Increases formation and strength of cortical bone.
• Synergistic effect with exercise
• Lower IGF in Hip Fx patients


• 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

GH Rx Hip Fx

- Double blind, controlled,
- 6 weeks Rx
- 20 micro grams/kg/day
- > 75 years old, IGF returned to 50 year old level
- Return to pre-fracture living: 94 vs. 75%
- Statistically Significant, well tolerated

GH and bone density

- 18 month study - men
- Increase bone density, bone turnover, lean body mass
- Body fat decreased
- Low incidence of side effects

AGHD
• Increased CV deaths

GH Replacement
• Increased CV function
• Improves lipid profile?
• Reverses atherosclerosis
• Reduced carotid intima thickness
• Improves dilated cardiomyopathy

Gibney et al. The effects of 10 years of GH in adult GH deficient patients
J Endocrin Metab 1999 August
GHD - increased cardiovascular risk

- Abnormal body composition,
- Unfavorable lipid profile,
- Increased fibrinogen
- Increased C-reactive protein levels,
- Insulin resistance,
- Early atherosclerosis
- Endothelial dysfunction
- Impaired left ventricular (LV) performance

Colao A et al. Beginning to end: Cardiovascular implications of growth hormone (GH) deficiency and GH therapy. *Growth Horm IGF Res.* 2006 May 9
GHRT reverses risks

- Reduces body fat and visceral adipose tissue
- Reduces low-density lipoprotein cholesterol and triglyceride levels
- Improves endothelial function
- Reduces intima media thickness
- Improves LV performance
Growth Hormone Treatment in Dilated Cardiomyopathy

- Double blind, placebo controlled
- 2 IU/day x 12 weeks
- GH induced increase in IGF-1 predicted change in ejection fraction
- IGF-1 increase > 80 pg/mL caused notable improvement in ejection fraction – 5%

GH, CHF, Exercise Capacity

• GH treatment 4 IU = 1.33 mg every other day
• Improved all parameters of Exercise Capacity

GH and Atherosclerosis

- GH normalized Intima Media thickness of carotid artery (IMT) by 3 months improvement continued 18 months
- IMT negatively correlated with IGF-1
- No significant change in lipids
- Direct effect on arterial wall via NO?

- 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
GH and Refractory Heart Failure

- GH Rx increased
- GH level
- IGF-1
- Ejection fraction 13% to 28%
- Dobutamine discontinued

IGF-1 inverse with BP

- Inverse with BP and
- 2 hour glucose and triglyceride levels
- Vasodilator, NO actions

GH and Homocysteine

• HC Decreased in GH treated (average 1.2 µmol/L, p = .047)
• Changes in HC were negatively correlated with changes in IGF-I.
  – Not with folate, vitamin B12, total T₃, C-reactive protein, interleukin-6, or insulin levels.

• 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
GH and coronary inflammation

- GH deficient adults have increased CV mortality
- Inflammatory markers are predictive of CV events
- C-Reactive Protein increased in GH deficiency
- With GH Replacement therapy
  - C Reactive protein decreased
  - Visceral and Subcutaneous fat decreased
  - No change in cholesterol, HDL

GH and CRP

- GH deficiency = Increased CRP
- GH treatment = Decreased CRP

- 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
Inflammatory Cytokines decreased IGF-1

- Growth hormone (GH) and insulin-like growth factor (IGF)-I are potent regulators of muscle mass in health and disease.
- Inflammation, TNF alpha produce catabolism thru inhibition of IGF-1.
GH, Heart Failure, Inflammation

- Proinflammatory cytokines contribute to chronic heart failure.
- 4 IU GH every other day
- Significant Decrease in TNF alpha and IL-6
- Significant clinical improvement and exercise capacity improvement
- 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
Lower IGF-1 = More CV disease

- Risk of IHD increased 38% for every 40 ng/dl decrease of IGF-1
- 3 x higher with lowest IGFBP-1
- IGF-1 stimulates NO production and increases blood flow
- Patients with GH deficiency have premature atherosclerosis
GH/IGF-1 and Immune System

- Connection between neuroendocrine and immune systems
- Aging, stress and nutrition effect GH/IGF-1
- IGF-1 needed for lymphocyte maturation and function
- IGF-1 restores age-related thymic involution in rodents
- IGF-1 restores damaged immune system
- Decline in T and B cells are restored by GH

Differentiative Actions

IGF-1

Cell Type

Pro B Cells (B220^-/IgM^-)

Pre B Cells (B220^+/IgM^-)

Mature B Cells (B220^+/IgM^+)

Proliferative Actions

Co-factor with IL-7, IL-3, KL
Thymic Involution

A. Control

B. IGF-1

C. GH

D. IGF-1 + GH
AGHD

• Abnormal Body fat and distribution

GH Replacement

• Increased Lean body mass and Decreased abdominal fat
• Decreases abdominal fat by up to 50%
GH and Body Composition

- GH deficiency
  - abnormal body composition
  - increase adipose mass and decrease in muscle mass
  - insulin resistance and decreased muscle strength

- Long term GH replacement normalizes these abnormalities

GH and obesity

- GH secretion impaired in obesity
- IGF-1 and BP’s may be normal due to secretion by adipocytes
- GH decreases adiposity
  - inhibits lipoprotein lipase
  - enhances lipolysis
  - improves dyslipidemia

Middle age men with low GH and abdominal obesity

- 9 months of GH treatment 9.5 micrograms/kg/day
  - Decreased fat, abdominal visceral 18% and subcutaneous 6%
  - Improved insulin sensitivity
  - Total Cholesterol, LDL, Triglycerides decreased
  - Diastolic BP decreased
- 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 Endocrinol Metab* 1997;82:727-734
GH +/- Sex Steroids and Subcutaneous and Visceral Fat

- HRT = Estraderm + Provera
- T = Testosterone Enanthate 100 mg q 2 weeks ("Testosterone Lite")
- GH = 20 micrograms/kg 3 x a week
- For 70 kg  20 x 70 = 1400 micrograms = 1.4 mg = 4.2 mg = 12.6 IU/week

Percent change in Visceral Fat
**GH Rx = fat loss and increased HDL**

- Obese men and women, Double blind, placebo controlled
- Diet and Exercise
- GH 0.2 to 0.4 in men or 0.6 mg /day in women x 6 months
- Body weight (from body fat) decreased 2.4 kg @ 6 months and persisted
- P=.04
- No adverse effects on glucose and insulin
- One drop out due to edema
- HDL increased 19% in GH group

GH and Obese postmenopausal women

- 40 postmenopausal women with abdominal obesity
- Randomized, double-blind, placebo-controlled, 12-month trial with GH (0.67 mg/d).
- Improved insulin sensitivity and reduced abdominal visceral fat and total and low-density lipoprotein cholesterol concentrations

Complimentary effects of T and GH


AGHD

• Impaired physical performance

GH Replacement

• Increased exercise capacity

AGHD

- Chronic fatigue, depression

GH Replacement

- Sense of well being
- Improved Quality of Life

Gibney et al. The effects of 10 years of GH in adult GH deficient patients. *J Endocrin Metab* 1999 August
GH and Quality of Life

- GH deficient adults
- GH RT improved Quality of Life
- Improved (all significant p values)
  - Energy
  - Vitality
  - Anxiety
  - Depression
  - Well-being
  - Self-control

- 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
Does GH cause cancer?

• “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.”

IGF, BPs and Breast CA

• “IGF-I, IGFBP-1, IGFBP-3, and GH levels were not associated with breast cancer risk”

• 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
Safety of GH and cancer

• GH treatment of adults with GHD is safe

• “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”

• 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
GH Replacement and cancer

- Tumor recurrence not greater than in patients not on GH
- No increase in cancer in children on GH replacement
- “No evidence of an increased risk of malignancy, recurrent or de novo.”

- Shalet SM, Brennan BM, Reddingius RE. Growth hormone therapy and malignancy. *Horm Res* 1997;48 Suppl 4:29-32
GH Replacement and cancer risk

- “There is no data to suggest that IGF-1 and IGF BP 3 modulate cancer risk in GH treated patients.”
- “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”
- No evidence that GH increases cancer recurrence or de novo cancer or leukemia
- Increased risk of cancer in hypopituitary adults

GH RT and Brain Tumor Recurrence

- Children with brain tumors, S/P Cranial Radiotherapy
- 180 treated with GH
- 891 not treated with GH
- In treated patients
  - Decreased risk of recurrence - 0.6 RR
  - Decreased risk of mortality - 0.5 RR
• Brain tumors most common solid neoplasm in children
• Life expectancy increasing – morbidity increasing – GH deficiency
• GH use increased exponentially
• No increased risk of tumor progression, recurrence or new CNS or non CNS tumor or leukemia
• Irradiation of hypothalamic pituitary axis for a tumor remote from the hypothalamic pituitary axis – most common cause of GH deficiency in these patients

• **Recurrence** rate was less in all studies

• **RR 0.6 to 0.8**

Low IGF-1 associated with Prostate Cancer

• IGF1 lower in Prostate Ca patients than controls: 125 vs. 158
• IGF1 higher 6 months after radical prostatectomy: 125 vs. 148
• No association of IGF1 and PSA
• IGF1 decreased with age
IGF and cancer mortality

• Positive association in men > 50 y/o
• No association in women
• No association with all cause mortality
• No IGF BP3 measurements
• p = .039

• Jacqueline M. Major, Gail A. Laughlin, Donna Kritz-Silverstein, Deborah L. Wingard and Elizabeth Barrett-Connor. 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
Anti-cancer effect of GH?

- GH stimulates glutathione production which decreases NFkB resulting in apoptosis of cancer cells.
Dx of GH Deficiency

- Phenotype – Clinical
- Provocation tests
  - L-arginine, GHRH, Insulin
  - Inconsistent, Impractical, Potentially dangerous
- IGF-1
  - Optimal range 290-500
  - Do not need to “chase” IGF-1
- 24 hour urine
  - Ref range (Meridian) 1065-4722 pg/24 hrs
  - Optimal range 5000 pg/24 hours
Dx AGHD

- Suspect in Brain Injuries (TBI, SAH, Tumors)
- Suspect in Cranial Irradiation
- Suspect in hypopituitarism
- Normal IGF-I levels do not rule out severe GHD
- Very low IGF-I levels in patients highly suspected for GHD – skip provocative tests

Stimulation tests

• Insulin hypoglycemia – dangerous
• GHRH + L-Arginine – GHRH no longer available
• Mentioned in package insert
• Explain why you considered stim tests and ruled out use
Dx of Adult GHD

• ITT (Insulin Tolerance Test) is the standard GH < 5 micrograms/l
• Hypoglycemia from ITT potentially dangerous
• IGF-1 < 84 96% predictive
• 1/3 of patients with GHD by ITT have “normal” IGF-1
• 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
Molitch, *JCEM* 2002

- IGF-1 < 84 microgram/l has 96% predictive value of DX of AGHD per stimulation test
- 3 or 4 other pituitary deficiencies and IGF-1 < 94 sensitivity 100% but specificity of only 30%
- 1/3 of patients with AGHD by stimulation test have IGF-1 in “normal” range
- “The stimulated GH levels currently used are somewhat arbitrary”
- “I am dubious about using only GH response to a provocative test as the criterion for labeling patients as having GHD”
IGF-1 for Endocrine dx AGHD

- Years: 20-40, 40-60, >60
- GHD: <74, <85, <74
- No GHD: 232, 166, 110
- Normal IGF-1 does not R/O AGHD

GH testing

• Variability in GH and IGF-1 testing
• “Biochemical testing should always be interpreted in a clinical context and never serve as stand alone criteria for establishing a diagnosis.”
• Strassberger C et al. How robust are laboratory measures of growth hormone status? *Hormone Research* 2005; 64:1-5
GHD Phenotype

• Increased truncal and visceral fat
• Decreased lean mass
• Osteopenia, glucose intolerance associated with insulin resistance
• Lipid profile consistent with increased atherogenic risk
• Decreased exercise capacity
• Altered cardiac structure and function
• Diminished quality of life.

Isolated GH deficiency

- Hypertension
- Fractures
- Dyslipidemia
- Obesity
- Type 2 Diabetes
- Poor Quality of Life
- GH Treatment improved above
GH Replacement - Side Effects

• Edema and Arthralgia
  – Related to low frequency high dose schedule
  – Related to giving mg/kg dose instead of gradual increase from low dose
  – Reversible with decrease of dose

• Vance M. et al. GH Therapy in Adults and Children. *NEJM* October 14, 1999
GH Estrogen, Testosterone

• “Estrogens should be administered by the parenteral route in women and testosterone be replaced in men to optimize the benefits of GH replacement.”

• Ho KK et al. Regulating of growth hormone sensitivity by sex steroids: implications for therapy. *Front Horm Res.* 2006;35:115-28
Female taking oral Estrogen

- HRT or BCP’s
  - No significant IGF-1 increase
  - No significant clinical improvement
  - Changing to transdermal estrogens: improved IGF-1 and clinical effects
- Less than effects in men
T Augments Overnight GH Secretion

- 100 mg T IM q 2 weeks x 26 weeks
- Total T increased 33%
- E2 increased 31%
- SHBG decreased 17%
- GH secretion increased 1.9 x
- IGF-1 increased 22%
- IGFBP-3 no change

GH RT and Insulin

• GH RT can increase insulin resistance
• Patients are not lifestyle compliant with zone diet and resistance and aerobic diet are most susceptible
• Testosterone RT attenuates this increased insulin resistance in men
• Insulin resistance can improve as well, especially after 1st month
• Caution diabetics on Insulin or oral hypoglycemics that their requirements might increase or decrease
GH decreases Insulin Resistance (Nam)

- Obese type II diabetics - 25 kcal/kg IBW diet
- GH 0.15mg/kg/week
  - For 100 kg pt = 15mg/week = 45 IU/week
- GH group vs Placebo Group
- Greater fat loss
- Greater Visceral fat decrease
- Increased Lean Body Mass
- Increased Glucose disposal rate
- Decreased Insulin in FFA
“Low-dose GH treatment combined with dietary restriction resulted not only in a decrease of visceral fat but also in an increase of muscle mass with a consequent improvement of the insulin resistance observed in obese type 2 diabetic patients.”

GH - Fibromyalgia

- IGF-1 < 250 “Functional GH deficiency”
- 0.8-1.4 mg/day
- Standard therapy with or without GH
- Significant improvement of Fibromyalgia parameters
- Cuatrecasas G et al. Growth hormone as concomitant treatment in severe fibromyalgia associated with low IGF-1 serum levels. *BMC Musculoskeletal Disorder.* 2007 Nov 30
Perioperative GH

- Improved muscle mass, muscle strength, fatigue
- Accelerated healing

GH and Burns

- Randomized prospective study
- GH (.1-.2 mg/kg/d) in massive burns
- Improved growth, lean body mass, less scarring and improved resting energy use
- CONCLUSION: long-term treatment GH enhanced recovery
- 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
GH and Brain Injury

- GH deficiency, is common among survivors of traumatic brain injury (TBI) tested several months or years following head trauma.
- Moderate-to severe head trauma or mild trauma
- Onset can evolve over years following injury.
- Assessment of the GH-IGF axis IGF-I, plus dynamic GH testing is indicated.
• Some degree of hypopituitarism is found in 35-40% of TBI patients
• Untreated TBI induced hypopituitarism contributes to the chronic neurobehavioral problems seen in many head-injured patients
• Subjects treated with GH experience significant improvements in concentration, memory, depression, anxiety and fatigue.
• Pituitary failure can occur even in minor head injuries and is poorly recognized.
TBI and SAH high risk for hypo-pit

- 1/3 to ½ have anterior pit. abnormalities
- GH/IGF in 15-20%
- Sx may mimic brain trauma
- May be psych sx
- Increase morbidity and mortality
“Appropriate hormone replacement therapy for those patients with both TBI and TBI-induced pituitary function impairment could, for the first time, allow treatment and correction of underlying causes of TBI sequelae rather than merely symptomatic treatment.”
Current GH Controversy

• Can Dx of AGHD be made without a stimulation test on the basis of clinical picture and IGF-1?

• Endocrine literature supports this idea

• 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

GH OTC “Secretagogues”

- OTC Products
  - Some may work to a limited extent
  - No published evidence in peer reviewed medical literature
  - Proprietary unpublished studies can claim increase in IGF-1
  - Do not contain significant amounts of GH
    - GH is Prescription Drug and cannot be sold OTC
    - Large molecule (191 AA) not bioavailable orally
Secretagogue

- True GH Secretagogues exist. (but we can’t get them yet)
  - Growth Hormone Releasing Peptides
    - Hexarelin
    - Ipamorelin
  - Hypothalamic and Pituitary action
    - Johansen et al. Ipamorelin a new ghrp induces longitudinal bone growth in rats. GH and IGF Research 1999, 9 106-113
- Ghrelin – secreted by the stomach
  - Endogenous ligand for GHRP receptor
  - Powerful orexigenic agent

Oral L-Arginine 5 g

- No Increase in GH
  - Young or old
  - Resting or exercise

GH and oral Arginine

- 5, 9, or 13 grams PO
- At 60 min up to 100% increase in GH
- Limited by GI side effects

GH and stem cells

- Improves quality and quantity of adult stem cells and endothelial progenitor cells
GH, NO, EPC

- CV disease = low NO bioavailability and Decreased EPC’s
- Healthy middle aged adults Rxed with GH
- Diastolic BP Decreased
- NO increased
- Increased circulating EPC’s
IGF-1 and cardiac stem cells

- IGF-1 prevents cardiac stem cell senescence and prevents aging cardiomyopathy

GH RT Algorithm

• Possible plan
  – Everything in this field is controversial
  – Many different approaches
• “Work in Progress”
  – Changes are continuously necessary
• Women need higher doses than men for same IGF-1 and clinical results
• Average male dose 0.4 mg/day
• Average female dose 0.6 mg/day
• **Time:** First thing in the morning or before bed. Avoid using when Insulin high after meals

• **Frequency:** single dose daily, no big deal if occasional doses are missed, BID might be slightly better

• **Ramp up doses**

• **mg x 3 = IU**

• **Take it easy with insulin resistance, maybe start Testosterone first in men**

• **How long to continue:** forever until something better comes along
Arguments against GH RT

• Cost
• Increased Insulin Resistance
• Side effects
• Not long enough studies
• Other ways to achieve same benefits

Arguments for GH RT

- Safe
- Less Morbidity and Mortality - CV Disease
- Body Composition: Bone, Muscle, Fat, Visceral Fat
- Less Inflammation
- Better QoL
- Less Sick Days
- Improved Exercise Capacity
“Growth hormone is essential for normal adult life, and without it life expectancy is shortened, energy and vitality reduced and the quality of this life is impaired. The medical case for GH replacement is now proven beyond any reasonable medical and scientific doubt.”
Adult Growth Hormone Deficiency

- **Suspect AGHD**
  - **Is pt > 40 y/o?**
    - **YES**
      - Get baseline IGF, consider stim test
    - **NO**
      - Get baseline IGF check yearly
  - **NO**
    - **YES**
      - Stim test positive?
    - **NO**
      - Is IGF in youthful range? 275-350 ng/ml?
        - **YES**
          - Consider AGHD with nl IGF- ie obesity
        - **NO**
          - Consider other rx testosterone,diet exercise,

- **GHRT**
  - Evaluate other hormones
  - **YES**
  - **NO**
  - **? GHRT**
Anti-aging workup, lab hormones, lifestyle, cancer screens negative?

YES

Start GH 0.2 mg/day
Lifestyle program
Balanced Hormones
Assess at 3 weeks

NO

Refer for Workup
GH Controversial
Cleared by Consult?
Urologist, Oncologist etc

YES

NO

Significant side effects?

YES

NO

Decrease dose to 0.1 mg/day

Increase dose to 0.4 mg/day

Significant side effects resolved?

NO

YES

D/C Treatment

Slowly ramp up

No GH
Adult Growth Hormone Deficiency

0.4 mg tolerated in 12 weeks?

IGF in youthful range

- YES
  - Keep dose at 0.4 mg

- NO
  - Too high
    - >500
      - Decrease dose to 0.2 mg
  - Too Low
    - <250
      - Increase dose to 0.6 mg

In 3 months
Titrate dose
Range 0.1-0.7 mg
Average 0.4 male
Average 0.6 female

Side effects
Glucose Insulin
q 3 months 1st year
q 6 months 2nd year
Side Effects?

- Edema
  - Decrease dose
  - Low dose diuretics
  - Resolved?
    - YES: Continue lower dose D/C diuretics Consider inc dose after 1 month
    - NO: D/C GH Consider lower dose after 1 month

- Arthralgia
  - Decrease dose
  - Anti-inflammatory
  - Resolved?
    - YES: Continue low dose D/C anti-inflammatories
    - NO: D/C GH Consider lower dose after 1 month
Adult Growth Hormone Deficiency

- Side effects?
  - Paresthesias
    - mild?
      - Cont GH
      - Decrease dose if patient distressed
    - severe?
      - Hold GH 1 week
      - Decrease dose
  - Resolved?
    - YES
      - Cont low dose
      - Consider increase in 1 month
    - NO
      - D/C GH
      - Consider lower dose after 1 month

- Glucose Intolerance
  - Hyperglycemia?
    - YES
      - Treat men with testosterone for free T in young range if no contraindication
    - NO
      - Decrease dose
  - Insulin?
    - YES
      - D/C GH
      - Consider restart
    - NO
      - Cont lower dose
      - Consider increase after 1-2 months

- Strict diet limiting high glycemic index carbs
- Exercise: Resistance and Aerobic
- Testosterone RX
- Lifestyle change