THE DIAGNOSIS OF ADULT GROWTH HORMONE DEFICIENCY AND ITS TREATMENT USING HGH SECRETAGOGUES (Peptides)

EXCELMALE
Your Men's Health Community

ADULT GROWTH HORMONE DEFICIENCY (AGHD)
Symptoms

Symptoms	Clinical Features
•Lack of positive wellbeing	•Increased body fat
•Depressed Mood	•Decreased muscle mass
•Increased anxiety	•Decreased bone density
•Social isolation	•Increases LDL cholesterol
•Decreased energy	•Decreased cardiac muscle
	•Decreased insulin sensitivity
	•Decreased sweating and thermoregulation
	•Increased plasma fibrinogen
	•Impaired cardiac function

Benefits of Increased IGF-1 Levels

- IGF-1 levels as high as 275 or greater are associated with the **reversal, improvement or prevention** of medical conditions:
  - Heart disease
  - Hypertension
  - Prostate cancer
  - Glucose intolerance
  - Osteoporosis
  - Lipodystrophy

Lipo Benefits of Higher IGF-1 Levels

- Obesity is associated with low IGF-1 levels
- Help statin drugs **lower LDL cholestorol**
- Study in JAMA showed that GH administration in patients with HIV significantly **reduced visceral fat and truncal obesity, triglycerides and diastolic BP**, correlating to an increase in IGF-1 from 146 to 267 after 12 months of treatment – Aug 6, 2008 Vol 300, No.5
- Egrifta (Tesamorelin) **FDA Approval** 2010

GH and Neurogenesis

- GH seems to be important for **neurogenesis** and **neuromodulation** throughout adulthood
- GH/IGF-1 deficiency with age may be implicated in the **loss of neurons**
- GH replacement may be effective in **supporting neurogenesis**, which may be the cause of its **cognitive enhancing effects**

GH and Malignancy

- **No studies** have proven a significant association between GH and malignancy
- GH replacement therapies need to be **monitored** by imaging, from ultrasounds to MRI scans as well as conventional blood and hormone testing to make sure that there are no side effects and related hormonal imbalances

GH/IGF-1 Major Findings

Head Trauma [1]	• ↓ IGF-1 after head trauma •GH deficiency may occur in as many as 33% of cases <u>Study:</u> Control mean IGF-1 222.2 Patient mean IGF-1: •Day 1 – 104.3 •Day 3 – 88.7 •Day 10 – 94.9
Brain Processing Speed, P300 Latency [2,3,4]	<u>Study 1:</u> Alzheimer's and the use of acetylcolinesterase inhibitors: rivastigmine ↑ GH release, ↑ P300 speed, 10 msec <u>Study 2:</u> Study at PATH Medical, N=1,545 •IGF-1 – 150, P300 – 360 msec •IGF-1 – 210, P300 – 338 msec <u>Study 3:</u> Sheehan's syndrome, N = 14 6 months of GH therapy. IGF-1 pre – 23 ng/ml, P300 pre – 353.30 msec IGF-1 post – 234 ng/ml, P300 post – 335.00 msec *This 211 point gain in IGF-1 = ↓ P300 latency, an approximate gain of 18 years in brain speed
Memory [5]	IGF-1 ↑ from 135 to 213 = improved cognitive function and memory in elderly patients
IQ [6]	In one study, every 100ng/ml ↑ in IGF-1 = ↑ in IQ by 7.0 points

GH/IGF-1 Major Findings

Personality, Psychiatric Health [7]	IGF-1 ↑ from 74.0 to 362.6 after 2 years of GH therapy = ↓ tension, ↓ anxiety, ↓ psychic complaints, ↑ short-term and long-term memory
Sarcopenia, Osteoporosis (Frame) [8]	12 months of GH replacement in 18 men: •IGF-1 pre – 138.1 ug/L, lumbar spine pre – 1.092 femur neck BMD pre – 0.886 g/cm² •IGF-1 post – 279.4, lumbar spine BMD post – 1.119, femur neck BMD post – 0.905
Lean Body Mass [9]	IGF-1 from 157 to 399 = ↑ lean body mass, ↓ visceral adiposity, ↑ calories burned at rest
Exercise [10]	During exercise, IGF-1 can go as high as 878 (sprinting), 1458 (endurance running). Exercise ↑ neurogenesis.
Atherosclerosis [11]	Atherosclerotic patients: •IGF-1 – 51.8 ug/L, intima-media thickness – 0.84 mm •After GH replacement: IGF-1 – 232.4, intima-media thickness – 0.75 mm
Insulin Sensitivity [12]	12 months GH replacement, N = 25 •IGF-1 pre – 103.5, fasting plasma insulin pre – 8.6, fasting plasma glucose pre – 4.4

Growth Hormone Production

- Growth Hormone Releasing Hormone (GHRH)
- Ghrelin (GHRP)
- Somatostatin

Somatostatin (SS)

- "SS" aka Growth Hormone Inhibiting Hormone (GHIH) or Somatotropin Release-Inhibiting Factor (SRIF)
- Produced primarily by hypothalamus
- Inhibits GH synthesis and release
- Makes hypothalamus resistant to stimulation by GHRH and hypoglycemia
- Responsible for pulsatile GH inhibition
- Decreases number of somatotropes, not amount of GH production by each
- Increases with age

Growth Hormone Releasing Hormone (GHRH)

- Produced by hypothalamus
- Stimulates GH synthesis and RELEASE
- Binds to the GHRH-R in pituitary
- Short half-life ~12 min
- Increases # of somatotropes AND amount of GH secreted from each
- No down regulation of GH

Sermorelin (GHRH)

- Geref—Sermorelin Acetate for Injection
- Analog of GHRH - First 29 amino acids
- Used for traditional GH stimulation testing
- T ½ 12 mins. IV or SC
- Injected SC qhs
- 30 years of data
- Upregulates own receptor
- Promotes non-REM slow wave sleep
- Effective dose approaches $ of rHGH

Growth Hormone Releasing Peptides (GHRP)

- Synthetic forms of Ghrelin
- GHRP-1, GHRP-2, GHRP-6, MK-0677, Hexarelin, Ipamorelin, Ghrelin
- Simple, short-chained amino acid complexes
- Bind to GHRP-R ➡ ⬆ GH
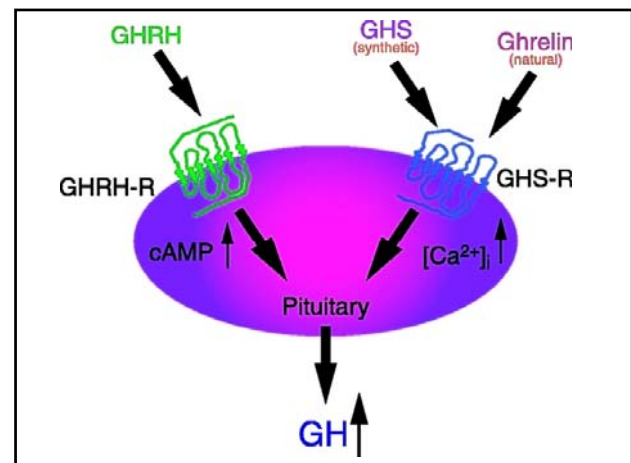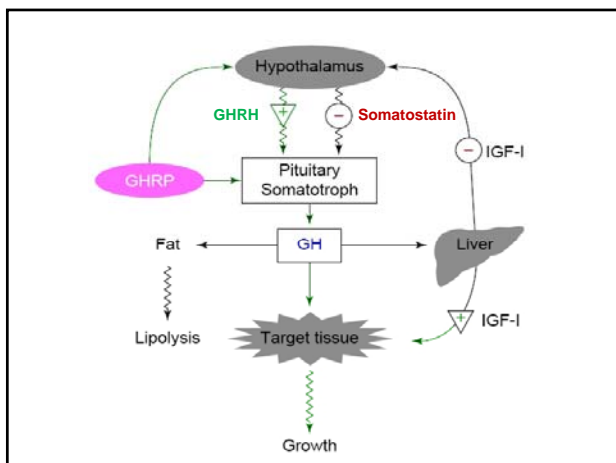- "Artificial amplification" b/c works with endogenous GHRH

GHRP-2

- More powerful version
- 1993
- Increases prolactin and cortisol
- Increases hunger and gastric emptying
- Cost effective

GHRP-6

- First potent GHRP developed (1980)
- Most studied of all GHRP's
- Does not increase Prolactin or Cortisol as much as GHRP-2
- Significantly increases hunger and gastric emptying
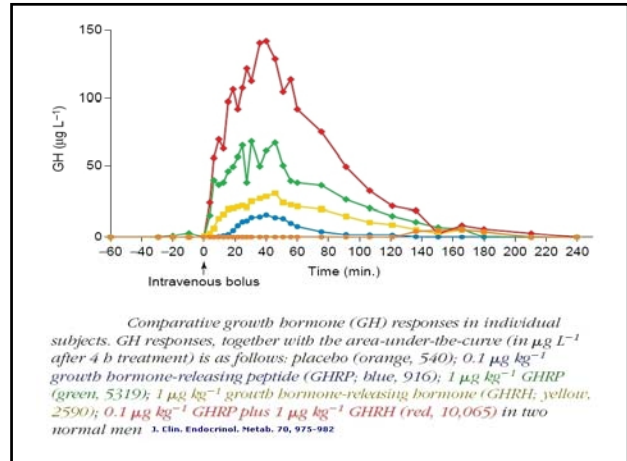- Cost effective

Effects of GHRP

- Bind to GHRP-R ("Ghrelin receptor") in pituitary to release GH
- Reduce inhibition by Somatostatin at pituitary
- Distinct and separate path than GHRH
- Stimulate GHRH production from hypothalamus
- Inhibit Somatostatin production from hypothalamus

GHRH and GHRP Synergy

- GHRPs will start a pulse, and acts synergistically with GHRPs, so there is no need to be concerned about administration timing if you co-administer GHRPs with Sermorelin.
- GHRPs Requires Endogenous Hypothalamic GHRH for Maximal GH Stimulation
  - NAUSHIRA PANDYA, ROBERTA DEMOTT-FRIBERG, CYRIL Y. BOWERS, ARIEL L. BARKAN, AND CRAIG A. JAFFE, Journal of Clinical Endocrinology and Metabolism 1998 Vol. 83, No. 4

Comparative growth hormone (GH) responses in individual subjects. GH responses, together with the area-under-the-curve (in μg L^{-1} after 4 h treatment) is as follows: placebo (orange, 540); 0.1 μg kg^{-1} growth hormone-releasing peptide (GHRP; blue, 916); 1 μg kg^{-1} GHRP (green, 5319); 1 μg kg^{-1} growth hormone-releasing hormone (GHRH; yellow, 2590); 0.1 μg kg^{-1} GHRP plus 1 μg kg^{-1} GHRH (red, 10,065) in two normal men J. Clin. Endocrinol. Metab. 70, 975-982

---

rHGH vs GHRH / GHRP

- GHRH / GHRP significantly **less expensive** than rHGH
- HGH **overdosing is minimized** or completely avoided with GHRH / GHRP
- Tissue exposure to HGH released by the pituitary under the influence of GHRH / GHRP is episodic not "square wave", **preventing tachphylaxis** by mimicking normal physiology
- By stimulating the pituitary, GHRH / GHRP **preserves more of the growth hormone neuroendocrine axis** which fails first during aging
- GHRH / GHRP **blocks the cascade of hypophyseal hormone failure** that occurs during aging, thereby **preserving youthful anatomy and physiology**
- GHRH / GHRP provides all the benefits of HGH replacement therapy and more, **YET IT'S OFF LABEL USE IS NOT PROHIBITED BY FEDERAL LAW**

GH Stimulation Testing

- Stimulation Tests are being **eliminated** due to their **invasiveness**, **lack of precision**, and **resulting deaths**
  - Insulin Tolerance Test
  - Glucagon Stimulation Test
- They are **time consuming**, **costly**, and **unsafe**
- GH Stimulation tests often have **misleading results**. E.g. children with renal failure, Prader-Willi syndrome, obesity, and Turner Syndrome
- **Quest Labs** says IGF-1 is sufficient to diagnose

IGF-1 as a Diagnostic Tool for AGHD

- Several studies show IGF-1 to be an effective independent diagnostic tool for AGHD
- JCEM: Referred to low IGF-1 as at or below 159
- JCEM study showed AGHD correlates with obese patients without pituitary disease

---

Sample Protocol

- GHRP-2/GHRP-6/Sermorelin
  - Weight gain and high GH Response (Inject 100/100/100 mcg before meals)
  - Increase 100/100/100 mcg up to 600/600/600 mcg total daily
- GHRP-2/Sermorelin
  - Best "bang for your buck" GH Response without significant weight gain (Inject 200/200 mcg SQ qhs)
  - Increase 100/100 mcg up to 600/600 mcg total daily
- Sermorelin
  - Weight Loss / Age Management (Inject 500 mcg SQ qhs)
  - Increase 500 mcg up to 1000 mcg total daily
- Patients will not start exhibiting the benefits of GHRT until at least **1 month** of being on their program and it usually takes about **3 months** to see the **full benefits** of the therapy.

GH Contraindications

- Pregnancy
- Malignancy
- History of Malignancy
- Diabetic proliferative retinopathy
- Sclerosing diseases of the liver and lungs
- Benign intracranial hypertension
- Uncontrolled diabetes

QUESTIONS?