Human Growth Hormone: What Can It Do For Your Growth, Human?

28 April 2008

Mark H. Davino, M.D.

Outline

- Objectives
- Introduction/Background
- HGH replacement in GH deficiency
- HGH in the elderly
- HGH in athletes
- Conclusion

Outline

- Objectives
- Introduction/Background
- HGH replacement in GH deficiency
- HGH in the elderly
- HGH in athletes
- Conclusion

Objectives

- To review the basics of human growth hormone (HGH) physiology
- To examine the effects of HGH replacement in GH deficient persons
- To understand the motivating factors driving the HGH industry to provide non-FDA approved use in the elderly and in athletes
- To determine the efficacy and safety of HGH supplementation in the elderly
- To examine the effects of HGH abuse by athletes and relatively healthy young individuals

Outline

- Objectives
- Introduction/Background
- HGH replacement in GH deficiency
- HGH in the elderly
- HGH in athletes
- Conclusion

Introduction/Background

- Growth Hormone is viewed as a performance enhancing drug abused by athletes
- Athletes serve as prominent role models
- Young patients model behavior after professional athletes
- Mitchell Report

Mitchell Report

- Roger Clemens

Mitchell Report

- Andy Pettitte

Yankees

Evil Empire

Introduction/Background

- Most abundantly produced hormone of the anterior pituitary gland
- Produced by somatotroph cells
- 22 kDa protein
- Product of 5 distinct genes all located on chromosome 17q22

Introduction/Background

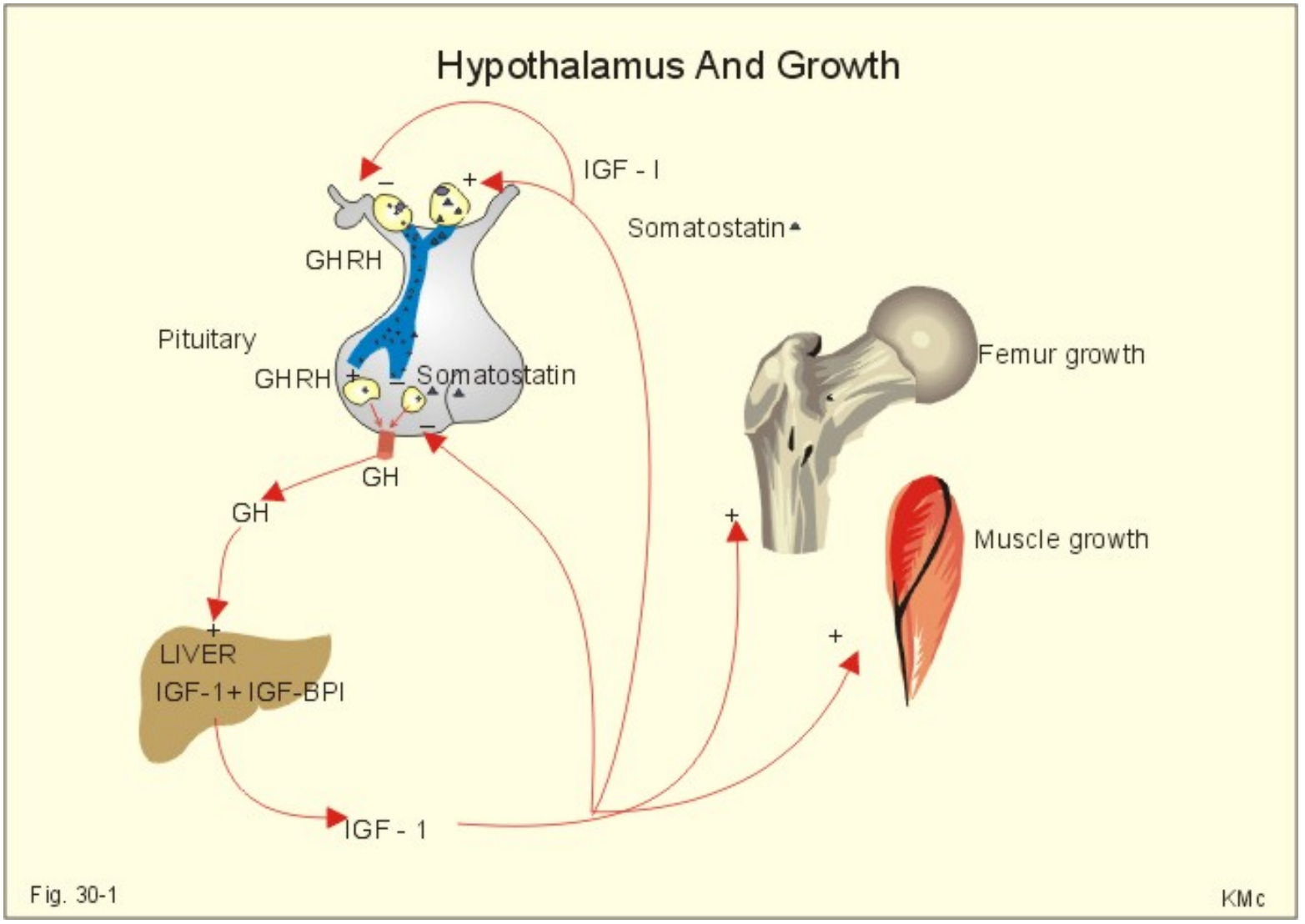
- Regulated by hypothalamic and peripheral factors
- Stimulators:
  - GHRH, hypoglycemia, ghrelin, exercise, sleep
- Inhibitors:
  - IGF-1, somatostatin, hyperglycemia

Growth Hormone Actions

- GH exerts anabolic effects
- Stimulation of protein synthesis
- Increased lipolysis and lipid oxidation
- Insulin antagonism
- Sodium and water retention
- Stimulation of bone growth

Growth Hormone Actions

- Stimulation of IGF-1 by hepatic cells
- IGF-1 binds specific receptors on target cells
- Target Cells:
  - Chondrocytes
  - Osteoblasts
  - Skeletal myoblasts
  - Keratinocytes
  - Astrocytes and glial cells


Hypothalamus And Growth
IGF - I
Somatostatin
GHRH
Pituitary
GHRH
Somatostatin
GH
GH
Femur growth
Muscle growth
LIVER
IGF-1+ IGF-BPI
IGF - 1
Fig. 30-1
KMc

Introduction/Background

- GH secretion is pulsatile, with higher peaks at night than during the day
- Immeasurable serum values b/w pulses
- 10 pulses lasting approximately 90 minutes
- Somatostatin maintains tonic inhibition of somatotrophic cells
- GHRH enables breakthrough activation

Introduction/Background

- Provacative Testing
- Insulin-Induced hypoglycemia
  - 0.1 U/kg of insulin; measure GH at 0, 15, 30, 60, 90, 120 minutes
  - Most sensitive but most dangerous
- Arginine
  - 0.5 g/kg (max 30 g); measure GH at 0, 30, 60, 90, 120 minutes
  - No side effects
- IGF-1 levels correlate well with GH secretion

Outline

- Objectives
- Introduction/Background
- HGH replacement in GH deficiency
- HGH in the elderly
- HGH in athletes
- Conclusion

Growth-Hormone Deficient Adults

- The effects of GH supplementation are well studied
- A review of over 20 clinical trials showed:
  - Increase in lean body mass (20/20)
  - Decrease in fat mass (13/14)
  - Increase in total body water (7/8)
  - Increase in extracellular water (3/4)
  - Increase in total body volume or plasma volume (2/3)
- Increase in bone mineral density in men

Growth-Hormone Deficient Adults

- Long-term effects of GH supplementation not as well studied
- Ter Maaten et al studied long term effects in a prospective study (50 men total; 12 were lost)
- 38 patients with GHD (mean age 28 +/- 4 yrs) followed for 3-5 years
- 12 patients had idiopathic GHD, 26 patients had complete pituitary failure (testosterone, ADH, hydrocortisone)
- All 38 patients had IGF-1 levels at least 2 SD below the accepted mean value for age

ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

Growth-Hormone Deficient Adults

- Outcomes measured:
  - anthropometry (height, weight, skin-fold thickness)
  - CT scanning of abdomen and upper leg
  - Bone densitometry
  - Echocardiography
  - Bicycle ergometry
- Initial GH dose of 9-27 µg/kg gradually tapered to 11 µg/kg with goal of attaining physiologic IGF-1 levels

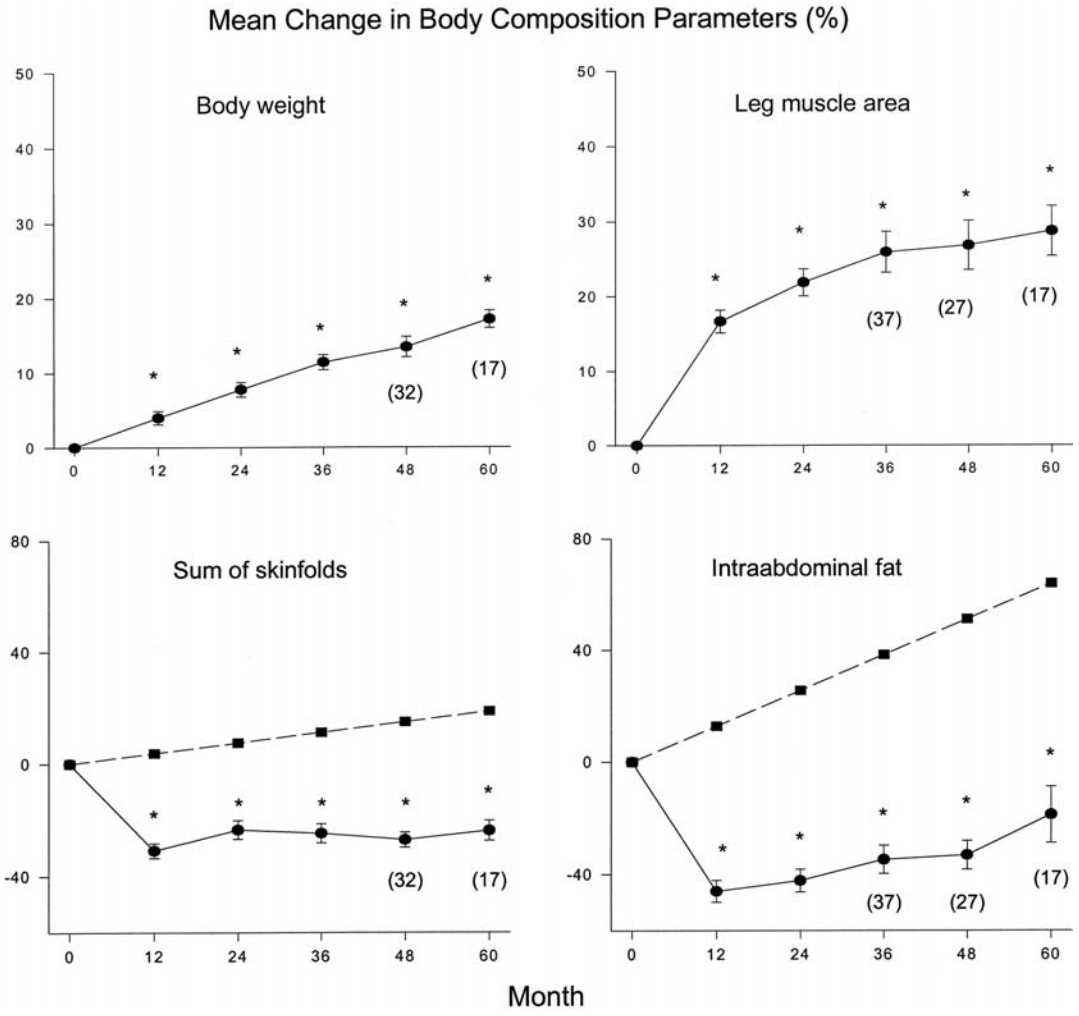
ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

Growth-Hormone Deficient Adults

- Subcutaneous fat decreased by 30.9% ($P < 0.001$)
  - Partial regain after 1 year
- Intra-abdominal fat decreased by 46% ($P < 0.001$)
  - Partial regain after 1 year
- Muscle mass of the leg increased progressively by 28.7% ($P < 0.001$)

ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

Growth-Hormone Deficient Adults



ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

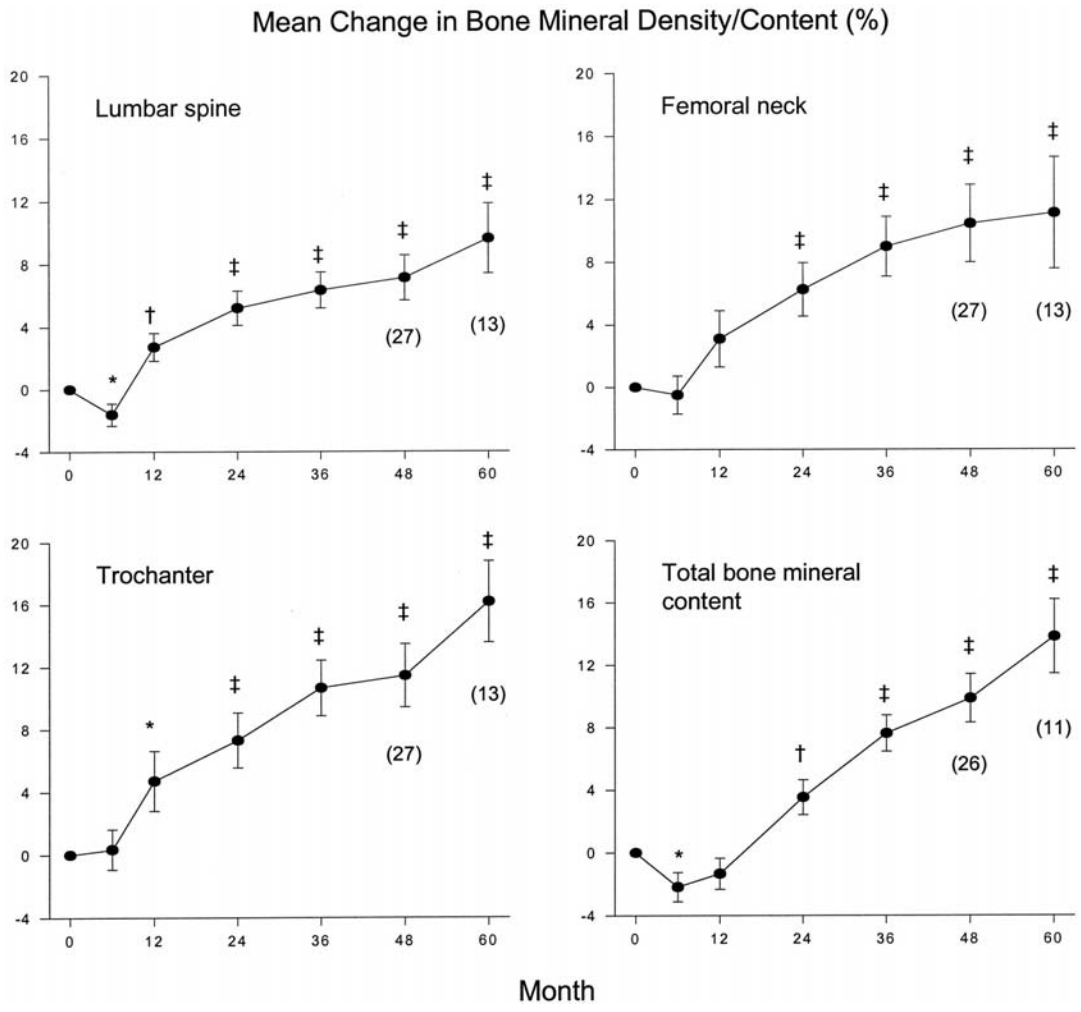
The Journal of Clinical Endocrinology & Metabolism

Growth-Hormone Deficient Adults

- Bone mineral density at the lumbar spine increased by 9.6% ($P < 0.001$)
- Bone mineral density at the femoral neck increased by 11.1% ($P < 0.001$)
- Bone mineral density at the trochanter increased by 16.2% ($P < 0.001$)

ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

Growth-Hormone Deficient Adults



ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

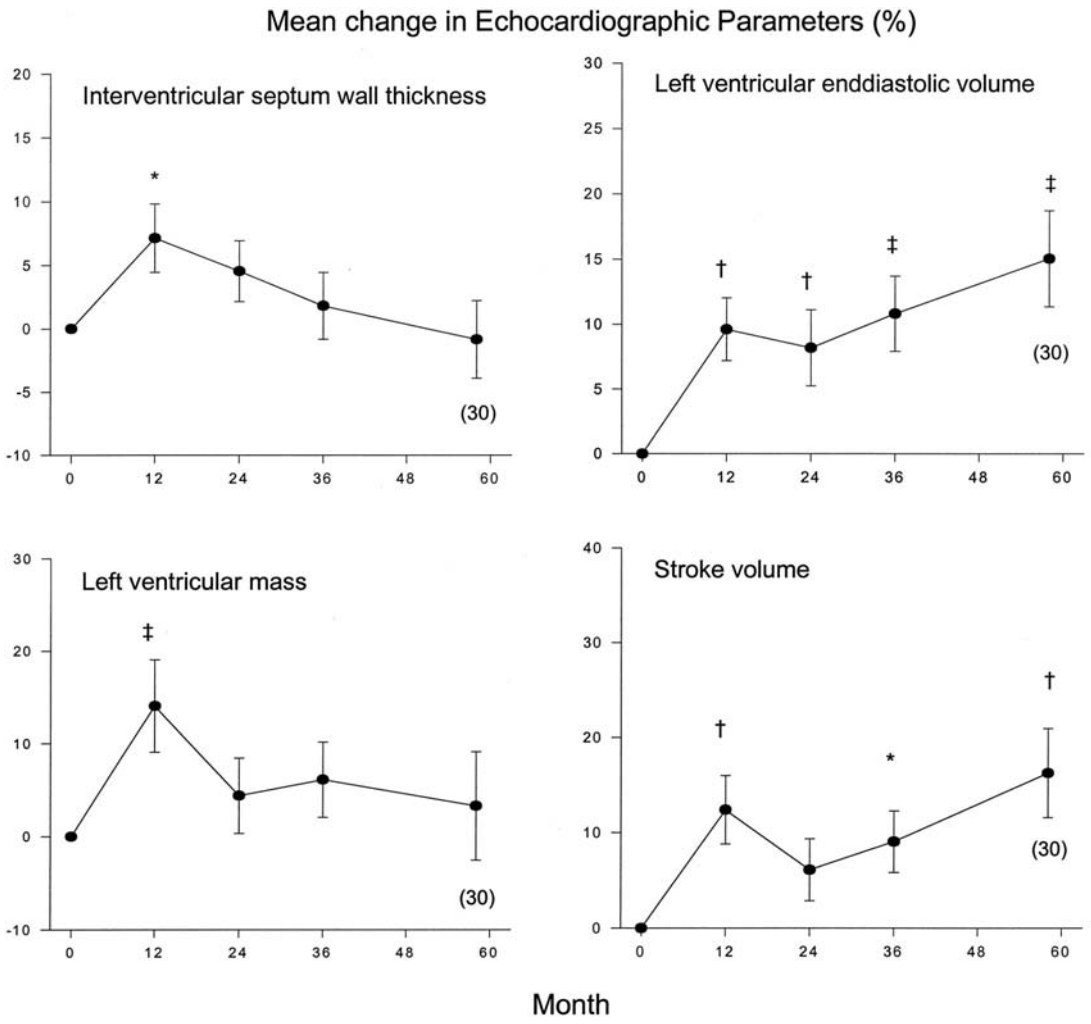
The Journal of Clinical Endocrinology & Metabolism

Growth-Hormone Deficient Adults

- Left ventricular mass surpassed baseline values after 1 year by 14.1% ($P < 0.001$), but returned to baseline values thereafter
- Stroke volume increased by 16.3% ($P = 0.002$)
- Cardiac output increased by 33.4% ($P < 0.001$)
- Ejection fraction did not change significantly
- 2 of 38 patients started antihypertensive treatment during 3rd year

ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

Growth-Hormone Deficient Adults



ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

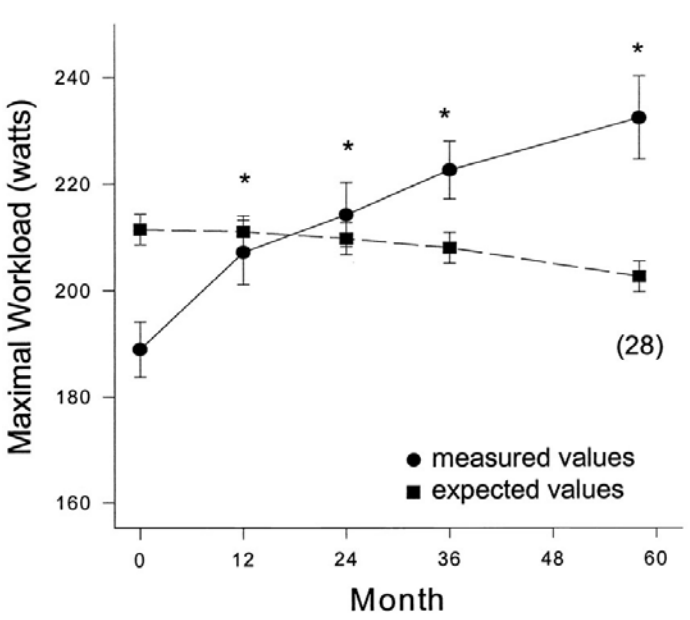
The Journal of Clinical Endocrinology & Metabolism

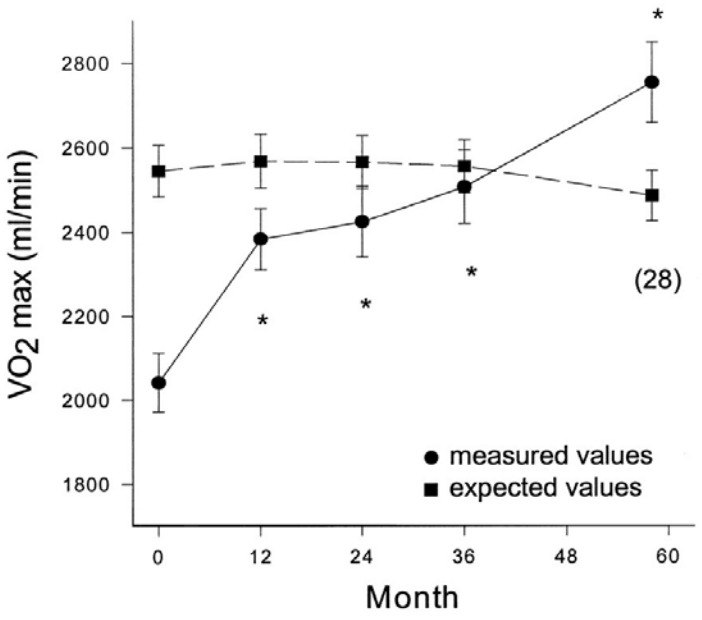
Growth-Hormone Deficient Adults

- In 34 of 38 patients, maximal work load and oxygen consumption increased throughout the study
  - Even exceeded predicted normal values at the end of the study
- 4 patients not evaluated (hip pain, insufficient cycle technique, legs too short to reach pedals, technical malfunctioning)

ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

Growth-Hormone Deficient Adults





ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

The Journal of Clinical Endocrinology & Metabolism

Growth-Hormone Deficient Adults

- Overall, GH replacement well tolerated
- Side effects:
  - Hypertension
  - Muscle and joint stiffness
  - Peripheral edema
  - Paresthesisas
  - Gynecomastia
  - Thirst

ter Maaten, J. C. et al. J Clin Endocrinol Metab 1999; 84:2373-2380

Outline

- Objectives
- Introduction/Background
- HGH replacement in GH deficiency
- HGH in the elderly
- HGH in athletes
- Conclusion

HGH in the Elderly

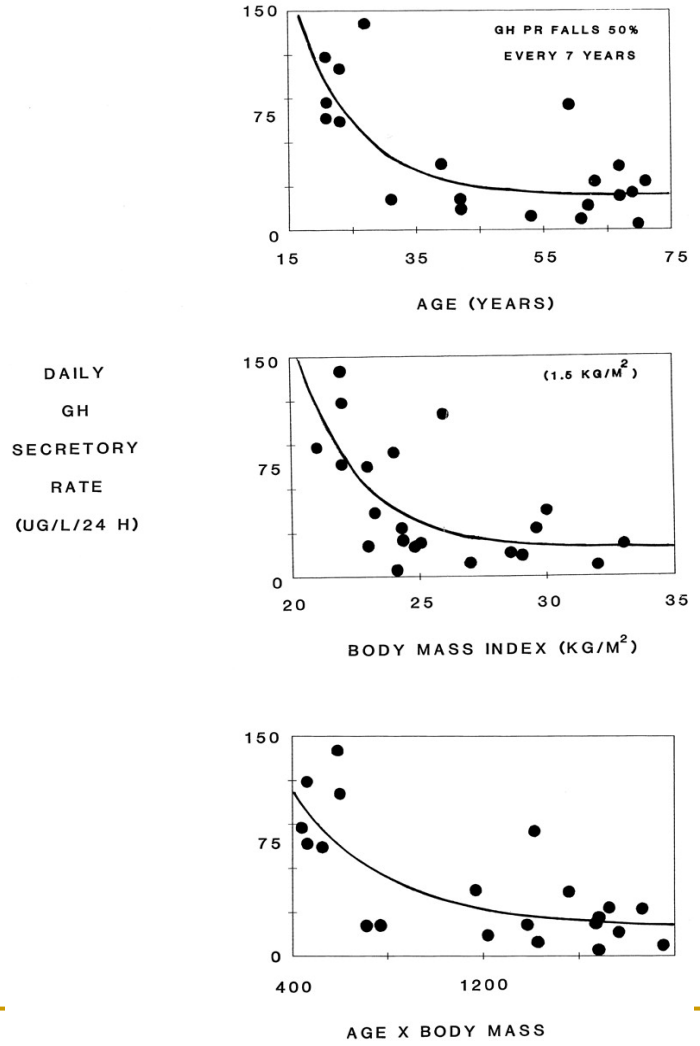
- The world's population continues to age each year and at unprecedented rates
- The percentage of older patients (age > 60) was 8% in 1950, 11% in 2007 and is projected to reach 21% by 2050
- Proportions more dramatic in developed countries
- By 2050, proportion is expected to reach 1/3 in the United States

World Assembly on Aging (Population Division; United Nations)

HGH in the Elderly

- GH levels, and thus IGF-1 levels, decline steadily in life after peaks in the neonatal period and in adolescence
- Less than 5% of healthy men 20 to 40 years old have plasma IGF-1 levels of < 350 U/L
- But 30% of healthy men over the age of 60 have levels < 350 U/L
- Parallel age-related decline in daily GH secretion and BMI

Parallel Age-Related Decline in Daily Growth Hormone Secretion and BMI



Giustina, A. et al. Endocr Rev 1998; 19:717-97

"Syringe of Youth?"

- One of the first RCTs involving HGH sought to elucidate the effects of GH supplementation in the aged population
- Rudman, et al published this trial in 1990 in *The New England Journal of Medicine*
- 21 healthy men aged 61 to 81 years old who had plasma IGF-1 levels less than 350 U/L were recruited from the community by newspaper advertisements

Rudman D, et al. Effects of Human Growth Hormone in Men Over 60 Years Old. N Engl J Med 1990; 323:1-6

"Syringe of Youth?"

- The subjects were randomly assigned in a 3:2 ratio to two study groups
- Neither group received any intervention for 6 month baseline period
- Group 1 received 0.03 mg/kg rHGH 3x weekly for 6 month treatment period
- Group 2 received no intervention during the analogous 6 month period

Rudman D, et al. Effects of Human Growth Hormone in Men Over 60 Years Old. N Engl J Med 1990; 323:1-6

Table 2. Clinical Characteristics of the Study Subjects.

Characteristic	Group 1 (N = 12)	Group 2 (N = 9)
Median age (range)	67 (61–73)	68 (65–81)
Percent of ideal body weight — median (range)	103 (94–120)	105 (99–117)
Medical conditions (no. of subjects)		
Degenerative joint disease	5	2
Benign prostatic hypertrophy	3	1
Glaucoma	1	1
Cataract	2	1
Arteriosclerotic heart disease*	3	1
Gallstones	0	1
Kidney stone	1	1
Hiatus hernia	0	1
Medications (no. of subjects)		
Nonsteroidal antiinflammatory drug	3	1
Pilocarpine eyedrops	1	1
Cimetidine	0	1

*Defined as a history of myocardial infarction or electrocardiographic abnormality ascribed to coronary artery disease.

Rudman D, et al. Effects of Human Growth Hormone in Men Over 60 Years Old. N Engl J Med 1990; 323:1-6

Table 1. Schedule of Tests during the Base-Line and Treatment Periods.

Test	Base-Line Period			Treatment Period					
	Mo 1	Mo 3	Mo 6	Mo 7	Mo 8	Mo 9	Mo 10	Mo 11	Mo 12
Physical examination	x	x	x	x	x	x	x	x	x
Hematology*	x	x	x	x	x	x	x	x	x
Urinalysis*	x	x	x	x	x	x	x	x	x
Blood chemistry*	x	x	x	x	x	x	x	x	x
Chest radiography	x		x						x
Electrocardiography	x		x						x
Echocardiography	x		x						x
Total body potassium†			x						x
Skin thickness‡			x						x
Bone density*§			x						x
Mandibular-height ratio*¶			x						x
Plasma IGF-I‖	x	x	x	x	x	x	x	x	x
Biosynthetic growth hormone**				x	x	x	x	x	x

*Tests included a complete blood count, hematocrit, blood indexes, and the measurement after an overnight fast of plasma glucose, urea nitrogen, creatinine, uric acid, sodium, potassium, chloride, carbon dioxide, phosphate, calcium, total protein, albumin, alkaline phosphatase, aspartate aminotransferase, lactic dehydrogenase, bilirubin, cholesterol, triglyceride high-density lipoprotein cholesterol, and glycosylated hemoglobin levels. Tests were performed at the North Chicago Veterans Affairs Medical Center laboratories.

†Total body potassium levels (lean body mass and adipose-tissue mass) were measured according to the method of Flynn et al.[15]

‡Calculated as the sum of the skin thicknesses of the right and left dorsal hand and right and left volar forearm measured with a Harpenden caliper according to the method of Lawrence and Shuster.[16]

§Measured according to the method of Nagraj et al.[17]

¶Measured according to the method of Goldberg et al.[18]

‖Measured at Nichols Laboratory, Los Angeles, according to the method of Furlanetto et al.[19]

**Administered to group 1 only.

Rudman D, et al. Effects of Human Growth Hormone in Men Over 60 Years Old. N Engl J Med 1990; 323:1-6

“Syringe of Youth?”

- In Group 1, the mean plasma IGF-1 levels rose to the “youthful” range of 500 to 1500 U/L during treatment
- In Group 2, the mean plasma IGF-1 levels did not change significantly

"Syringe of Youth?"

Table 3. Effect of the Administration of Human Growth Hormone on Plasma IGF-I Concentrations in Healthy Older Men.*

GROUP	PLASMA IGF-I								
	BASE-LINE PERIOD			TREATMENT PERIOD					
	mo 1	mo 3	mo 6	m o 7	mo 8	mo 9	mo 10	mo 11	mo 12
	units per liter								
Group 1	240±86	230±97	230±66	830±339†	680±180†	720±350†	810±305†	810±192†	910±312†
Group 2	240±69	240±126	240±108	200±126	220±123	240±177	180±126	240±186	300±201

*Values are means ±S D.

†P<0.05 for the comparison between groups.

“Syringe of Youth?”

- Six months of HGH supplementation in Group 1 resulted in:
  - 8.8% increase in lean body mass ($P < 0.05$)
  - 14.4% decrease in adipose-tissue mass ($P < 0.05$)
  - 1.6% increase in average lumbar vertebral bone density ($P < 0.05$)
- In Group 2, there were no significant changes

Table 4. Effect of the Administration of Human Growth Hormone on Weight, Lean Body Mass, Adipose-Tissue Mass, Skin Thickness, and Bone Density in Healthy Older Men.*

Variable	Group	End of Base-Line Period	End of Treatment Period	P Value†	Difference in Changes‡
Weight (kg)	1	77.2±11.4	78.2±12.1	0.26	+1.0 (1.4 to +3.4)
	2	83.3±11.1	83.3±9.7	0.97	
Lean body mass (kg)	1	53.0±7.4	57.7±9.1	0.0005	+3.7 (+0.7 to +6.6)
	2	54.2±7.1	55.2±7.3	0.17	
Adipose-tissue mass (kg)	1	24.1±5.0	20.6±5.6	0.05	2.4 (5.7 to +0.8)
	2	29.0±6.4	28.0±4.0	0.43	
Sum of skin thickness at four sites (mm)	1	9.9±1.2	10.6±1.5	0.07	+0.8 (0.1 to +1.7)
	2	9.3±0.9	9.23±0.80	0.69	
Bone density (g/cm^2)					
Mid-shaft radius	1	0.74±0.10	0.74±0.12	0.85	+0.04 (0.02 to +0.10)
	2	0.76±0.10	0.71±0.07	0.09	
Distal radius	1	0.37±0.07	0.36±0.08	0.12	0.004 (0.03 to +0.02)
	2	0.34±0.04	0.33±0.05	0.26	
Average, lumbar vertebrae 1–4	1	1.23±0.12	1.25±0.13	0.04	+0.006 (0.04 to +0.05)
	2	1.29±0.25	1.29±0.26	0.64	
Ward's triangle	1	0.70±0.14	0.69±0.13	0.15	0.018 (0.08 to +0.05)
	2	0.70±0.17	0.70±0.17	0.69	
Greater trochanter	1	0.85±0.13	0.85±0.13	0.72	+0.007 (0.05 to +0.03)
	2	0.81±0.15	0.81±0.13	0.55	
Femoral neck	1	0.92±0.15	0.91±0.14	0.53	0.029 (0.08 to +0.03)
	2	0.89±0.14	0.85±0.14	0.14	
Mandibular-height ratio	1	0.45±0.15	0.46±0.11	0.87	0.003 (0.07 to +0.06)
	2	0.47±0.12	0.47±0.12	0.98	

*Plus–minus values are means ±SD.

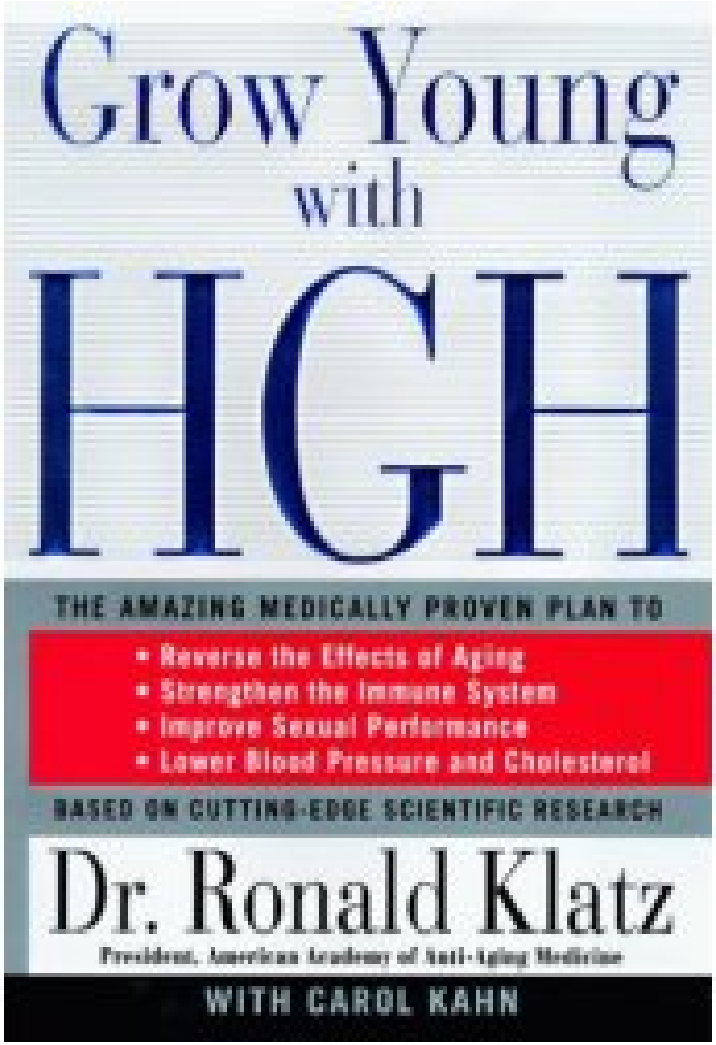
†P values are for the change from base line, by matched-pair t-test.

‡The difference in changes (12-month value minus 6-month value) is the average change in group 1 minus the average change in group 2. Values in parentheses are 95 percent confidence intervals, calculated by independent-sample, unequal-variance t-tests.

“Syringe of Youth?”

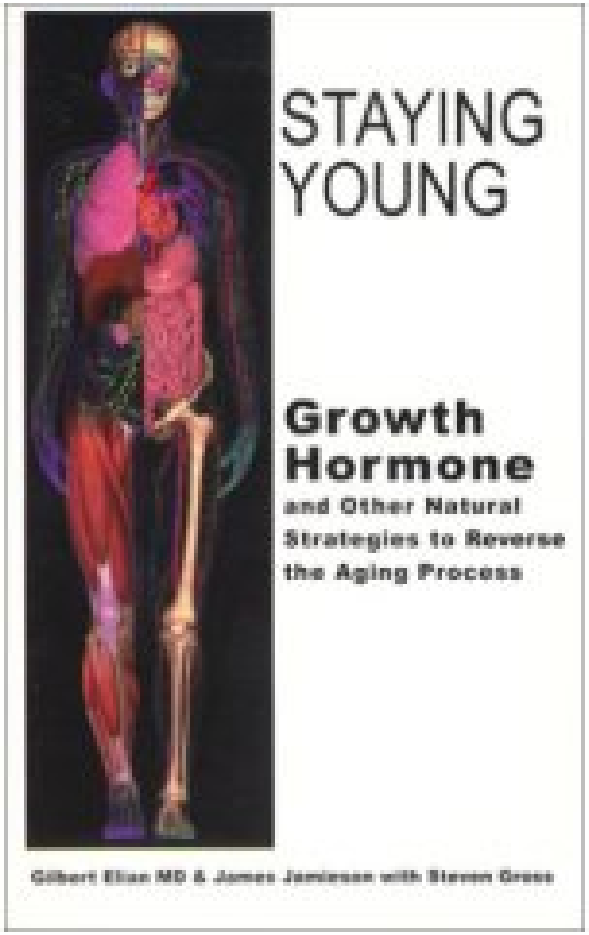
- Side effects:
  - Mean SBP increased (no anti-hypertensives initiated)
  - Fasting plasma glucose concentrations increased
  - No accumulation of ECW, edema, paresthesias or injection site pain observed
- Limitations:
  - Only men studied
  - Small study (n = 21)
  - Not blinded (bias)
  - No intention to treat analysis performed
  - IGF-1 levels lower than majority (2/3) of aged persons

Cashing in…



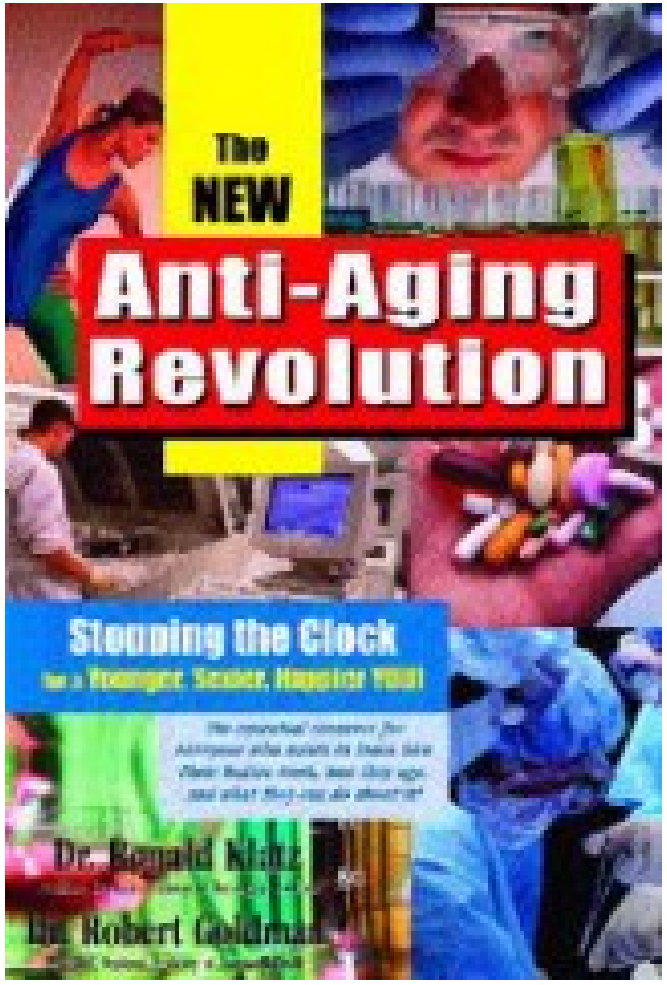
- Published in 1998 by Collins (New York)

Cashing in…



- Published in 1999 by Age Reversal Press (Boca Raton, FL)

Cashing in…



- Published in 2003 by Basic Health Publications (Laguna Beach, CA)

“Syringe of Youth?” Not so fast

- A more comprehensive, randomized, double-blinded, placebo-controlled trial published by Blackman et al in 2002
- This study further examined the efficacy and safety of GH supplementation, as well as coincident sex steroid replacement, in healthy U.S. community-dwelling men AND women (65 – 88 yrs old) over 26 weeks
- Non-smokers, non-etoh, neg stress, non-DM, IGF-1 levels less than 230 ng/ml

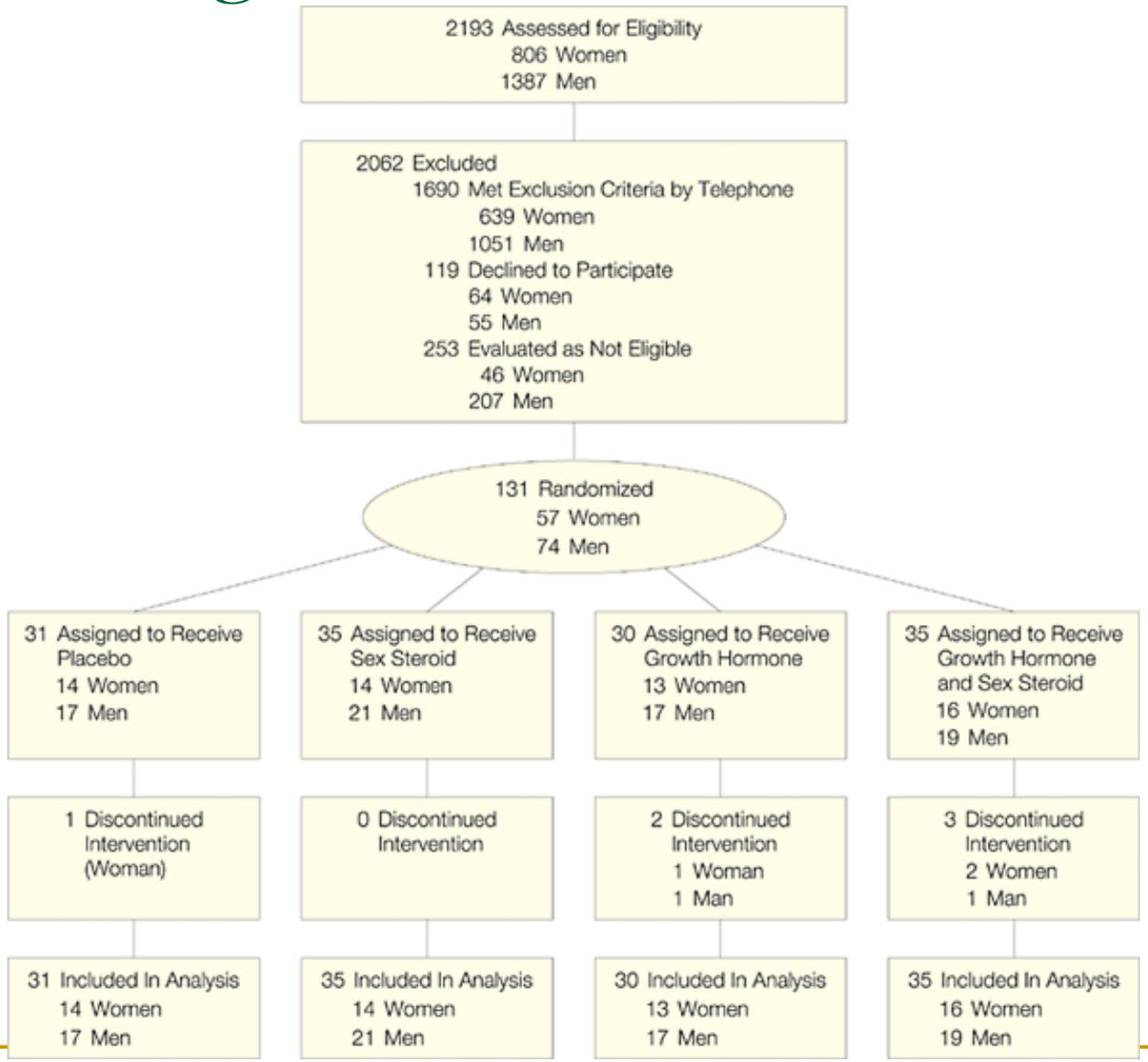
Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

"Syringe of Youth?" Not so fast

- Participants were randomized into on of 4 groups:
  - Placebo alone (sex steroid and HGH)
  - Sex steroid + HGH placebo
  - HGH + sex steroid placebo
  - HGH + sex steroid
- Transdermal estradiol (100 µg/d) + oral medroxyprogesterone acetate (10 mg/d) during last 10 days of each 28-day menstrual cycle
- Testosterone enanthate IM biweekly (100 mg)
- GH (30 µg/kg reduced to 20 µg/kg) SubCut 3x/wk

Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

Study Design



Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

Table 1. Baseline Characteristics by Treatment Group*

	Women					Men				
	Placebo (n = 14)	HRT (n = 14)	GH (n = 13)	GH + HRT (n = 16)	All (n = 57)	Placebo (n = 17)	Testosterone (n = 21)	GH (n = 17)	GH + Testosterone (n = 19)	All (n = 74)
Age, y	72 (1.3)	71 (0.9)	70 (1.1)	71 (1.3)	71 (0.6)	70 (1.1)	70 (0.7)	71 (1.3)	73 (1.4)	72 (0.6)
Weight, kg	67.1 (2.1)	65.5 (2.7)	66.1 (2.3)	60.6 (2.5)	65.1 (2.0)	86.8 (2.4)	78.9 (2.3)	83.2 (2.0)	80.9 (2.0)	82.3 (1.1)
Body mass index†	26.1 (0.7)	25.5 (0.7)	26.3 (0.9)	24.4 (1.0)	25.5 (0.8)	27.2 (0.4)	26.6 (0.7)	27.4 (0.6)	27.1 (0.7)	27.0 (0.3)
IGF-I, ng/mL	110 (12)	122 (13)	105 (10)	136 (15)	115 (6)	131 (8)	132 (8)	146 (10)	117 (10)	133 (6)
Testosterone, ng/dL‡						392 (23)	409 (20)	421 (14)	375 (23)	398 (9)

*All data are presented as mean (SE). HRT indicates hormone replacement therapy; GH, growth hormone; and IGF-I, insulinlike growth factor I. Values were significantly different ($P<.001$) between women and men for weight, body mass index, and IGF-I.

†Body mass index is calculated as the weight in kilograms divided by the square of height in meters.

‡To convert testosterone to nmol/L, multiply values by 0.0347. Estradiol levels are not reported for women because the assay's sensitivity (20 pg/mL) was higher than serum estradiol levels in many women.

“Syringe of Youth?” Not so fast

- The main outcomes measured included:
  - Lean body mass (DXA)
  - Fat mass (DXA)
  - Muscle strength (1-RM)
  - Maximum oxygen uptake (VO2 max) (graded treadmill; modified Bruce protocol)
  - Side effects (examined weekly)
- Outcomes (except side effects) measured at 26 weeks

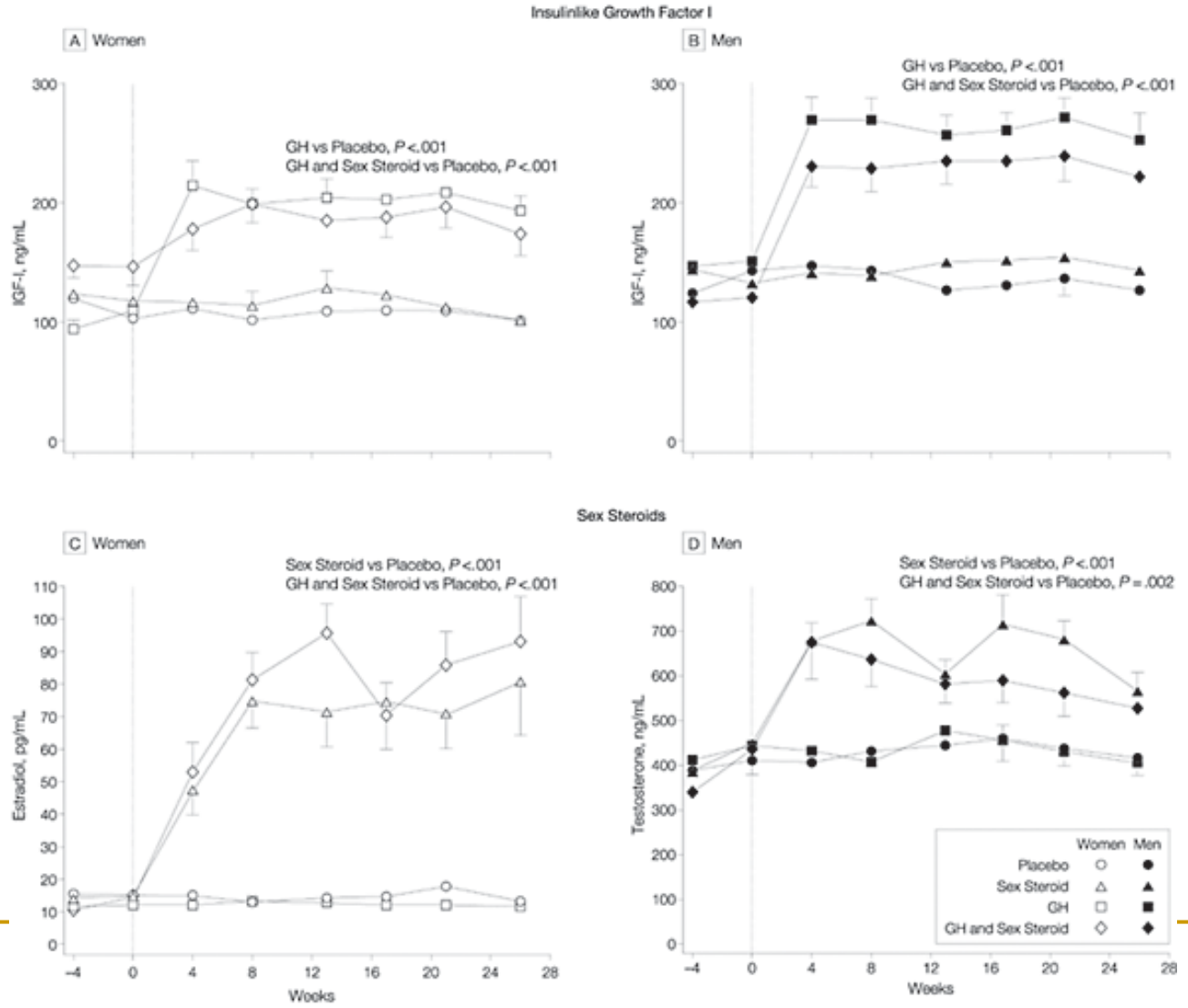
Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

“Syringe of Youth?” Not so fast

- Authors found with both sex steroid and HGH, estradiol, testosterone and IGF-1 levels all increased significantly
- Investigators found that HGH with or without sex steroids in healthy, aged men and women increased lean body mass and decreased fat mass

Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

Effects of 26 Weeks of Hormone or Placebo Administration



Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

Effects of HGH and Sex Steroid on Body Composition

Table 2. Effects of Treatments on Lean Body Mass and Fat Mass as Demonstrated by DXA*

	Women				Men			
	Placebo (n = 14)	HRT (n = 14)	GH (n = 13)	GH + HRT (n = 16)	Placebo (n = 17)	Testosterone (n = 21)	GH (n = 17)	GH + Testosterone (n = 19)
Total lean body mass, kg								
Baseline	35.7 (1.0)	36.7 (1.1)	36.8 (1.0)	35.8 (0.8)	57.0 (1.6)	51.5 (1.0)	54.4 (1.2)	52.7 (0.8)
26 Weeks	36.1 (1.1)	37.9 (1.0)	37.8 (0.9)	37.9 (0.8)	57.0 (1.4)	53.0 (1.1)	57.5 (1.3)	57.1 (1.0)
Change	0.4	1.2	1.0	2.1	0.1	1.4	3.1	4.3
P value for change vs placebo		.09	.001	<.001		.06	<.001	<.001
Total body fat mass, kg								
Baseline	28.4 (1.2)	25.7 (1.7)	27.8 (1.5)	22.6 (1.7)	25.0 (1.1)	23.3 (1.7)	24.4 (1.4)	23.9 (1.6)
26 Weeks	28.1 (1.3)	25.1 (1.4)	25.3 (1.4)	20.8 (1.6)	25.0 (1.3)	22.2 (1.7)	21.1 (1.4)	19.0 (1.3)
Change	−0.02	−0.59	−2.44	−2.10	0.1	−1.2	−3.2	−4.8
P value for change vs placebo		.69	.001	.006		.12	<.001	<.001

*DXA indicates dual-energy absorptiometry; HRT, hormone replacement therapy; and GH, growth hormone. All mass values are reported as mean (SE). Baseline and week 26 data are crude values; change and *P* values are adjusted for age and initial value using the method of Dunnett.[29]

Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

Effects of HGH and Sex Steroid on Total Body Strength

Table 3. Effects of Hormone Administration on Total Body Strength*

	Women				Men			
	Placebo (n = 13)	HRT (n = 13)	GH (n = 12)	GH + HRT (n = 13)	Placebo (n = 16)	Testosterone (n = 19)	GH (n = 15)	GH + Testosterone (n = 18)
Baseline	108.0 (7.5)	111.8 (4.5)	107.1 (5.3)	101.6 (4.7)	209.8 (6.8)	189.5 (6.8)	202.4 (9.9)	198.5 (8.3)
26 Weeks	104.9 (6.6)	115.9 (4.8)	109.2 (5.7)	105.4 (5.6)	212.8 (7.0)	197.0 (6.2)	212.5 (11.7)	211.6 (7.9)
Change	−3.1	4.2	2.3	3.6	3.5	6.2	10.3	13.5
P value vs placebo		.09	.29	.14		.86	.28	.05

*Strength, reported as mean (SE), was measured in kilograms on 1-repetition maximum testing. HRT indicates hormone replacement therapy; GH, growth hormone. Baseline and week 26 data are crude values; change and *P* values are adjusted for age and initial value using the method of Dunnett.[29]

(6.8%)

Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

Effects of HGH and Sex Steroid on Maximal Oxygen Capacity

Table 4. Effects of Hormone Treatments on Maximal Oxygen Capacity ($\dot{V}O_2$max) by Graded Treadmill Exercise Testing*

	Women				Men			
	Placebo (n = 14)	HRT (n = 14)	GH (n = 12)	GH + HRT (n = 16)	Placebo (n = 17)	Testosterone (n = 21)	GH (n = 17)	GH + Testosterone (n = 18)
Baseline	21.4 (1.2)	22.9 (1.0)	23.1 (1.7)	21.7 (0.8)	28.1 (1.4)	26.5 (0.6)	28.2 (1.2)	26.9 (1.4)
26 Weeks	21.1 (0.9)	22.3 (0.9)	24.4 (1.6)	23.2 (0.7)	26.8 (1.4)	26.4 (0.9)	28.4 (1.4)	29.0 (1.4)
Change	−0.4	−0.4	1.4	1.3	−1.2	−0.4	0.3	2.3
P value vs placebo		>.99	.07	.06		.49	.11	<.001

*$\dot{V}O_2$max is reported as mean (SE) milliliters per minute per kilogram of body weight. HRT indicates hormone replacement therapy; GH, growth hormone. Baseline and week 26 data are crude values; change and *P* values are adjusted for age and initial value using the method of Dunnett.[29]

Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

Common Adverse Effects of HGH and Sex Steroid Supplementation

Table 5. Common Adverse Effects During 26 Weeks of Treatment*

	Women						Men						
	Placebo (n = 14), No. (%)	HRT (n = 14)		GH (n = 13)		GH + HRT (n = 16)		Placebo (n = 17), No. (%)	Testosterone (n = 21)		GH (n = 17)		GH + Testosterone (n = 19)	
		No. (%)	*P* Value	No. (%)	*P* Value	No. (%)	*P* Value		No. (%)	*P* Value	No. (%)	*P* Value	No. (%)	*P* Value
Edema	0	4 (29)	.10	5 (39)	.02	6 (38)	.02	2 (12)	2 (10)	>.99	5 (30)	.40	4 (21)	.66
Carpal tunnel symptoms	1 (7)	3 (21)	.60	5 (38)	.08	4 (25)	.34	0	2 (10)	.49	4 (24)	.10	6 (32)	.02
Arthralgias	1 (7)	1 (7)	>.99	6 (46)	.06	5 (31)	.18	0	2 (10)	.49	7 (41)	.007	0	>.99
Mastodynia	0	6 (43)	.02	0	>.99	7 (44)	.007							
Gynecomastia								0	0	>.99	2 (12)	.49	2 (11)	.49
Headaches	0	1 (7)	>.99	3 (23)	.10	3 (19)	.23	0	1 (5)	>.99	0	>.99	0	>.99

*HRT indicates hormone replacement therapy; GH, growth hormone. *P* values (vs placebo) were calculated with the Fisher exact test.

Blackman et al. Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men. JAMA 2002; 288:2282-92

Common Adverse Effects of HGH and Sex Steroid Supplementation

Table 6. Rates of Fasting Glucose Intolerance and Diabetes by Treatment Group*

	Women				Men			
Glucose Classification†	Placebo	HRT	GH	GH + HRT	Placebo	Testosterone	GH‡	GH + Testosterone‡
Normal (<110 mg/dL)								
Baseline	14	14	13	16	17	18	17	19
Follow-up	12	12	11	14	14	17	8	10
Impaired (110-126 mg/dL)								
Baseline	0	0	0	0	0	3	0	0
Follow-up	2	2	2	2	3	3	* 7	6
Diabetes (>126 mg/dL)								
Baseline	0	0	0	0	0	0	0	0
Follow-up	0	0	0	0	0	1	* 2	3

*All values were measured at 4-week intervals. HRT indicates hormone replacement therapy; GH, growth hormone.
†Glucose classification defined by American Diabetes Association criteria.[27] To convert glucose to mmol/L, multiply values by 0.0555. Impaired glucose tolerance and diabetes were defined as ≥2 measurements meeting the criteria.
‡For diabetes, combined GH and GH+testosterone groups vs combined placebo and testosterone groups, $P = .06$; for diabetes or impaired fasting glucose, combined GH and GH+testosterone groups vs combined placebo and testosterone groups, $P = .006$.

***Returned to normal 2-6 weeks off HGH**

“Syringe of Youth?” Not so fast

- In 2007, a metanalysis review of RCTs looking at the effects of GH in the elderly was published in the Annals of Internal Medicine which corroborated the findings of Blackman et al
- After reviewing 31 journal articles describing 18 unique study populations (220 participants), authors found that GH supplementation resulted in a 2.1 kg decrease in fat mass ($P<0.001$) and 2.1 kg increase in lean body mass ($P<0.001$)

“Syringe of Youth?” Not so fast

- The “small” benefits in body composition were counterbalanced by significant adverse side effects:
  - Soft tissue edema (50%; range 23-89%)
  - Arthralgias (21%; range 0-50%)
  - Carpal tunnel syndrome (19%; range 0-50%)
  - Impaired fasting glucose, glucose intolerance or frank diabetes (22%; 6-53%)

Outline

- Objectives
- Introduction/Background
- HGH replacement in GH deficiency
- HGH in the elderly
- HGH in athletes
- Conclusion

www.bigmusclesbuilding.com/hgh-1

- “Another Shot !!
  Get these results with Human Growth Hormone in the least time.”
- “Hgh increases energy levels in the body and its capacity to get itself recharged also increases with decrease in time required.”

www.silownia.net/steroids/human_growth_hormone

- Active Life: varies by injection method
- Drug Class: GH/IGF-1 Precursor (for injection)
- Average Dose: 2-6 I.U. total daily
- Acne: No
- Water Retention: Rare
- High Blood Pressure: Rare
- Liver Toxic: No
- Aromatization: No
- Comments: High Anabolic/No androgenic effects

http://www.hghblen.com/hghigf1-2.htm

- Only $449.90 for case of 12 bottles (year supply)
- Apparently extracted from “young deer antler cartilage”

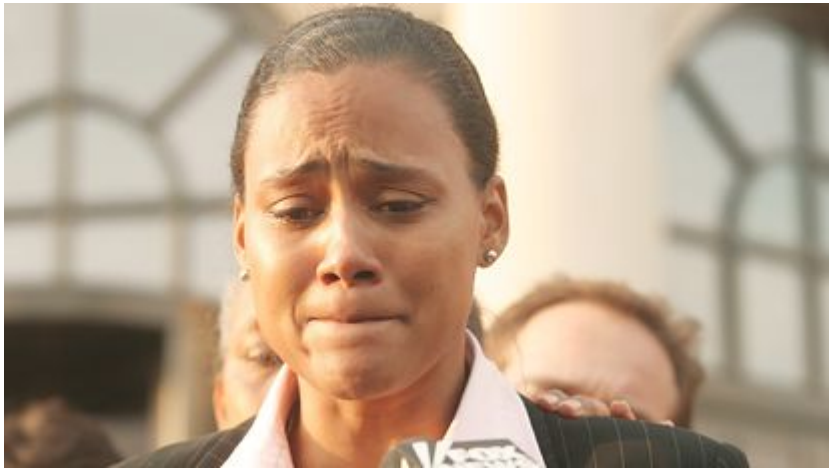
www.hghreview.net

- Benefits of Human Growth Hormone Products
  - Increased Energy Levels
  - Improved Bone Density
  - Enhanced Vigor and Stamina
  - Gains in Lean Muscle Mass
  - Loss of Body Fat
  - Improved Sexual Performance
  - Decreased Risk of Illness
  - Deeper More Restful Sleep
  - Better Feeling of Overall Health and Wellness

Sad Day

- Rodney Harrison (suspended 4 games)

Fall From Grace



- Marion Jones reports to a Texas prison Friday March 7, 2008

Growth Hormone and Athletic Performance

- Paucity of research examining effects of HGH supplementation in healthy athletes
- Acromegaly results in persistent suprphysiological GH serum levels
- Acromegalics have increased muscle mass but not increased muscle strength or endurance
- Suffer from arthralgias, arthritis, carpal tunnel syndrome, HTN and DM

Growth Hormone and Athletic Performance

- Only one randomized, double-blinded, placebo-controlled study of HGH on muscle power in trained athletes prior to 2002
- 22 adult male power athletes (age 23.4 +/- 0.5 yrs) from a sports club training 8-14 hrs weekly for at least 6 months were analyzed (6 week trial)
- 3 of 11 subjects withdrew 2/2 side effects (edema, arthralgias)

Growth Hormone and Athletic Performance

- HGH administered estimated to be 2-3x less than doses professional athletes use
- Urine tested to screen for concomitant anabolic steroid use
- Special care taken to ensure blinding and adherence
- Results showed significant increase in strength of the biceps and quadriceps in BOTH groups (training alone works)

Growth Hormone and Athletic Performance

- In 2005, researchers in Sweden published a double-blinded, placebo-controlled RCT studying effects of HGH in young athletic men AND women
- 30 non-professional athletes were recruited from a local community
- No participants suffered from comorbid conditions
- All women tested negative for pregnancy

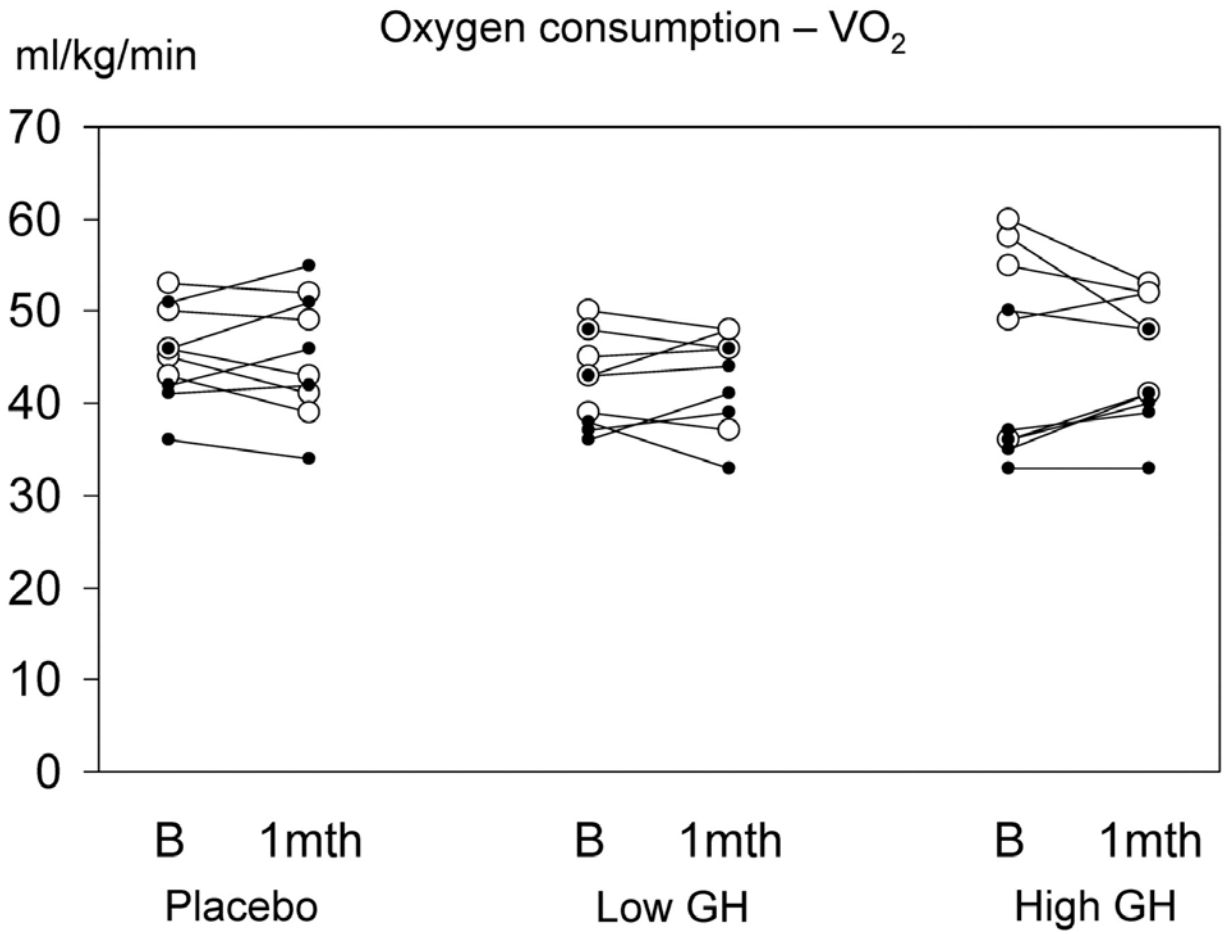
Growth Hormone and Athletic Performance

- After baseline H+P, participants were randomized in an even gender distribution to one of 3 groups:
  - Placebo (n=10)
  - Low dose GH (0.033 mg/kg/d) (n=10)
  - High dose GH (0.067 mg/kg/d) (n=10)
- Treated for 28 days after which time power output and oxygen uptake on bicycle exercise were measured

Growth Hormone and Athletic Performance

- Despite a significant elevation in serum IGF-1 ($P<0.001$), there was no effect on maximum oxygen uptake
  - Placebo 45.2 +/- 1.6 to 45.2 +/- 2.1 ml/kg/min
  - Low dose GH 42.8 +/- 1.6 to 42.8 +/- 1.6 ml/kg/min
  - High dose GH 44.8 +/- 3.4 to 44.8 +/- 2.2 ml/kg/min

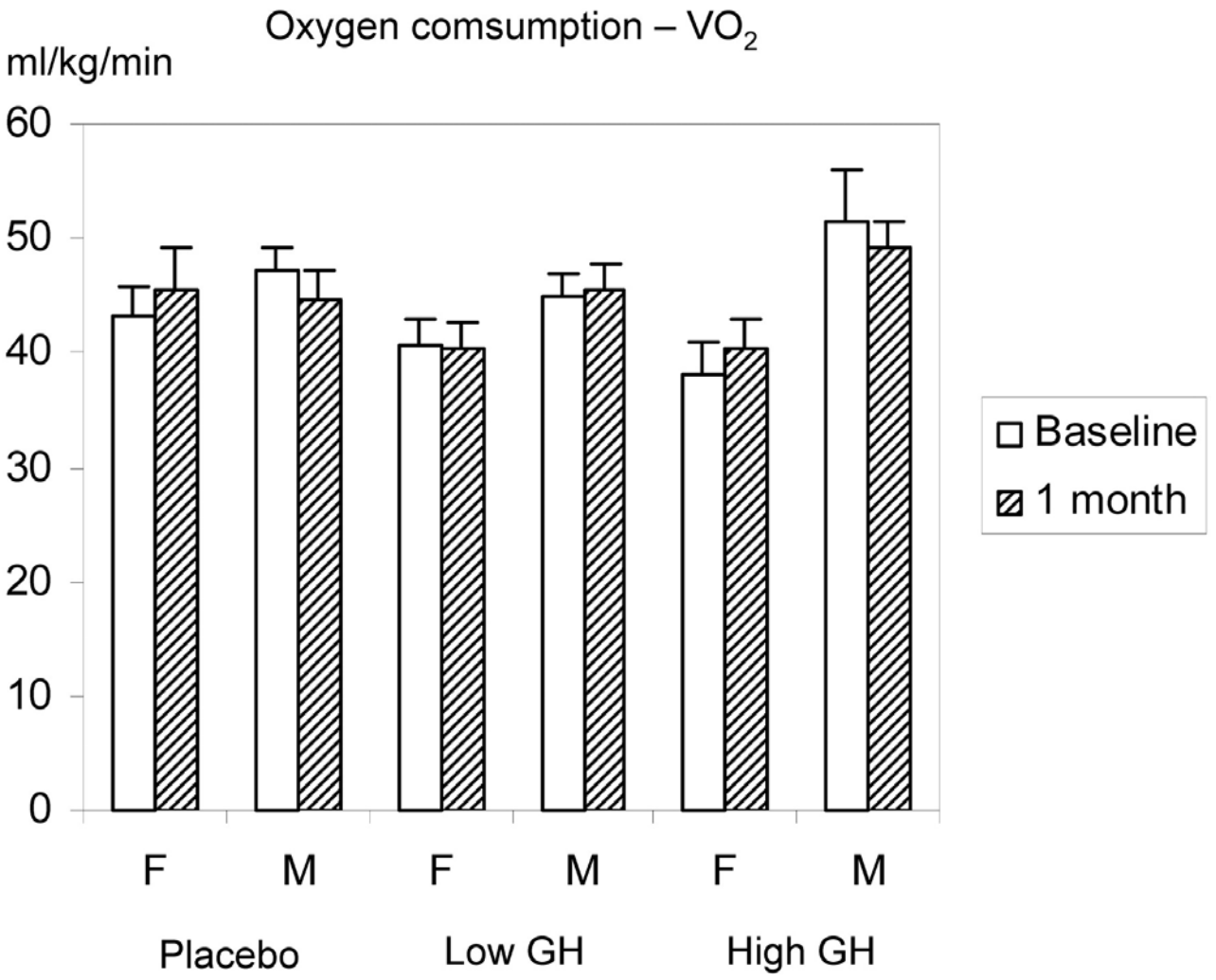
VO2 max at baseline (B) and after 28 days of treatment



Berggren, A. et al. J Clin Endocrinol Metab 2005;90:3268-3273

The Journal of Clinical Endocrinology & Metabolism

Average oxygen consumption (+/-SE) in the 3 study groups



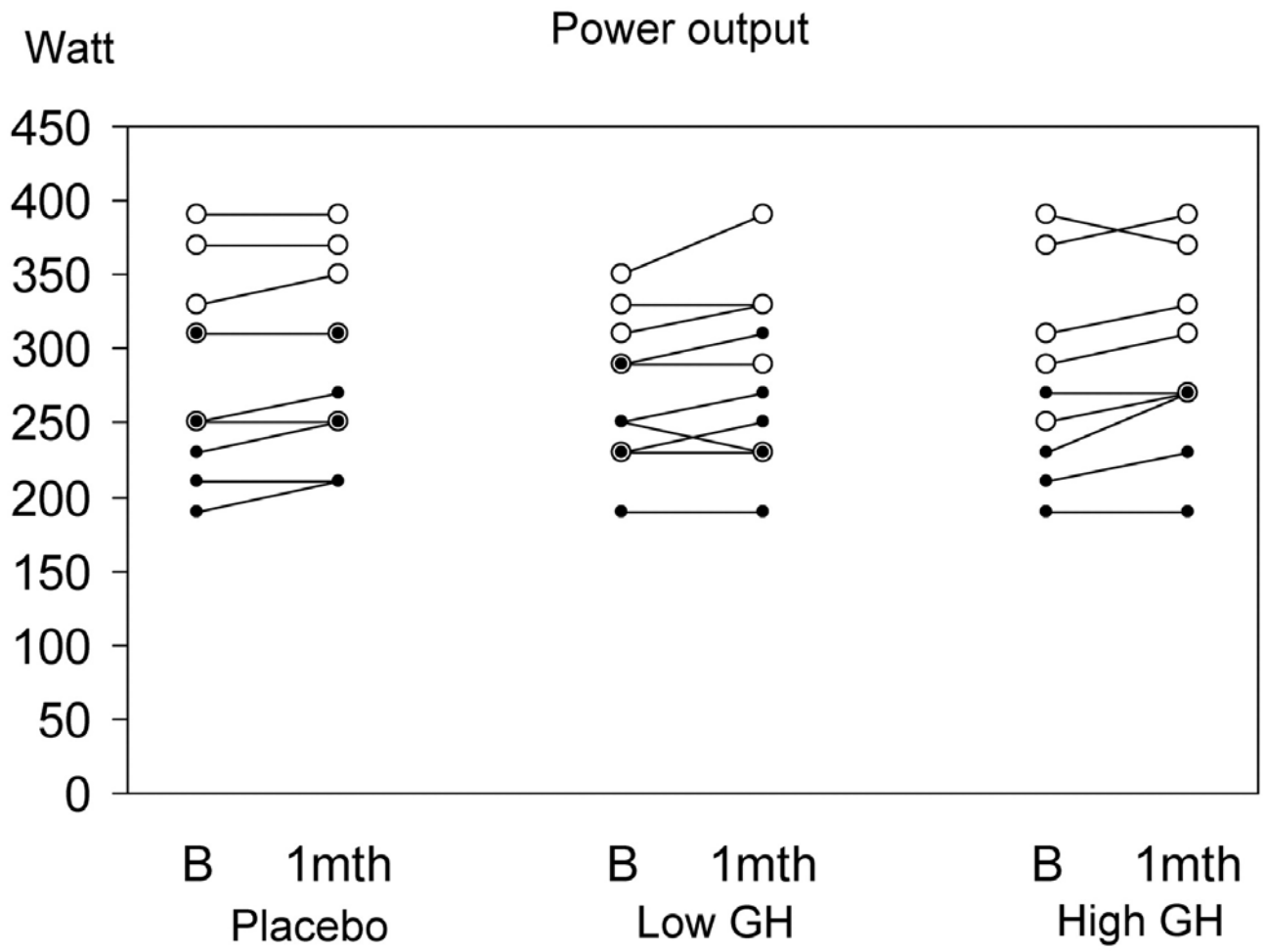
Berggren, A. et al. J Clin Endocrinol Metab 2005;90:3268-3273

The Journal of Clinical Endocrinology & Metabolism

Growth Hormone and Athletic Performance

- Despite a significant elevation in serum IGF-1 ($P<0.001$), there was no effect on maximum achieved power output during exercise

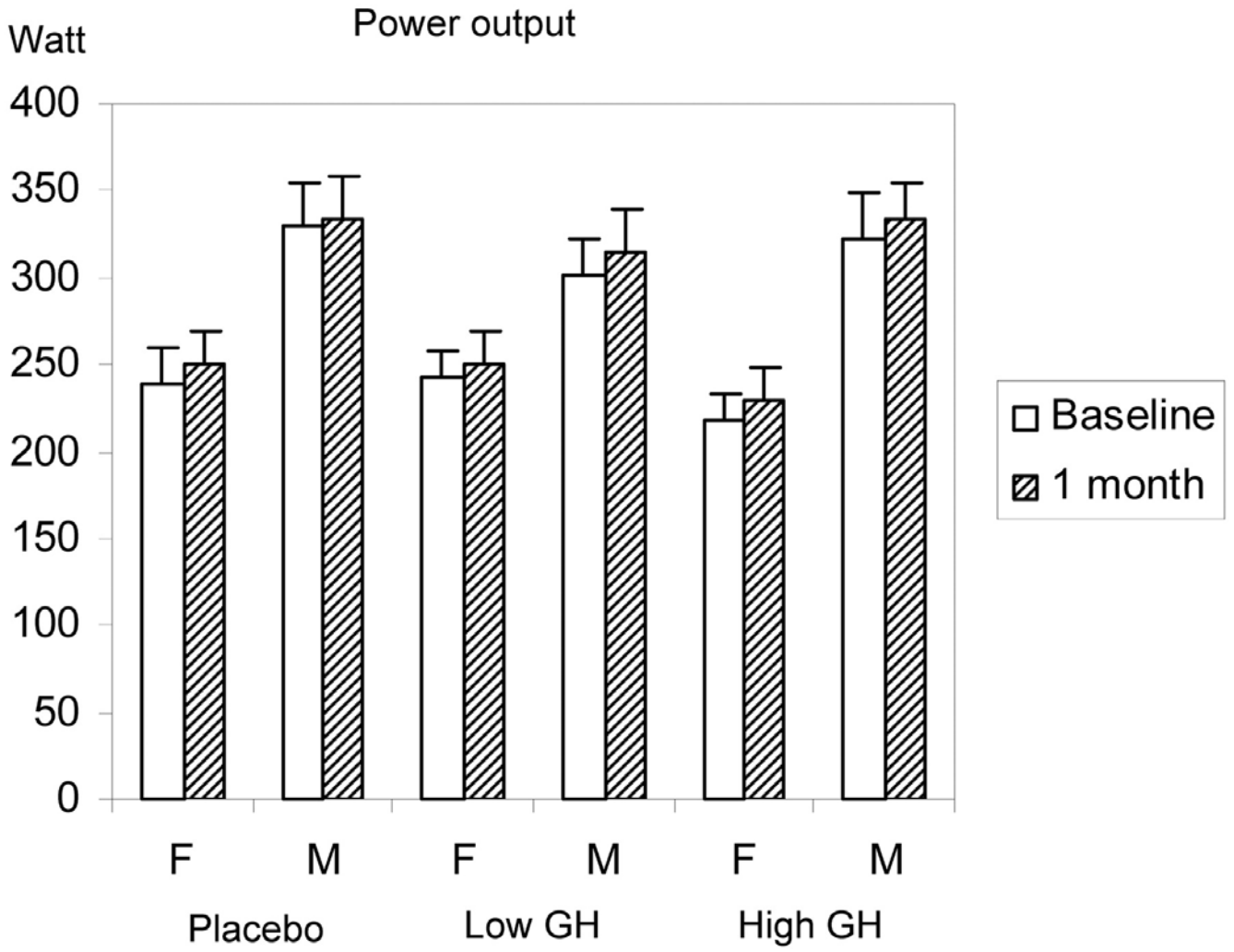
Maximum power output at baseline (B) and after 28 d of treatment in the placebo group and in the low dose GH group (0.033 mg/kg/d) and the high dose GH group (0.067 mg/kg/d)



Berggren, A. et al. J Clin Endocrinol Metab 2005;90:3268-3273

The Journal of Clinical Endocrinology & Metabolism

Average maximum power output ({+/-}SE) in the 3 study groups



Berggren, A. et al. J Clin Endocrinol Metab 2005;90:3268-3273

The Journal of Clinical Endocrinology & Metabolism

Growth Hormone and Athletic Performance

- Authors did find a significant increase in weight for both low-dose GH (72.5 +/- 13.7 to 74.0 +/- 14.8 kg) and high-dose GH (67.2 +/- 10.5 to 69.0 +/- 10.9 kg) with P=0.0279
- Ascribed to fluid retention (increase ECW) rather than in increase in muscle mass

Outline

- Objectives
- Introduction/Background
- HGH replacement in GH deficiency
- HGH in the elderly
- HGH in athletes
- Conclusion

Conclusions

- rHGH is an expensive medication that has benefit in patients with GHD
- Risk-Benefit ratio high for GH-depleted elderly
- No proven benefit in athletes who risk their reputation and legacy
- Primary care practitioners should take care to counsel against HGH abuse in their adolescent and young adult patients as well as their elderly patients
- HGH distribution and use as an anti-aging therapy or PED remains illegal in the U.S. and has not been approved by the USFDA

Has the HGH hype carried over into Residency?

- Can you become a stronger, more efficient resident?
- Can you recover from 30 hour shifts faster?
- Anecdotal evidence exists…

Has the HGH hype carried over into Residency?

Has the HGH hype carried over into Residency?

Before

Thank You

Go Red Sox (obligatory)!!