



**Section 1 - Studies indicating that supplementation with growth hormone (GH) results in decreased body fat, increased lean muscle, decreased heart disease and an increase in quality of life.**

1. *"The overall deterioration of the body that comes with growing old is not inevitable... We now realize that some aspects of it can be prevented or reversed. Effects of 10-20 years of aging on lean body mass and adipose tissue reversed in 6 months with testosterone and hgh."*

Daniel Rudman, M.D. "Effects of Growth Hormone in Men over 60 Years Old," New England Journal of Medicine. New England Journal of Medicine. 1990 Jul 5;323(1):1-6.

2. Life with low growth hormone (GH) is poor both in quantity and quality.

*"GH peaks at puberty and begins to decrease at 21."*

*"At age 60 most adults have total 24-hour secretion rates indistinguishable from those of hypopituitary patients with organic lesions in the pituitary gland."*

Almost all adults 40 years of age or older have a growth hormone (IGF-1) deficiency.

Savine R. Growth hormone replacement for the somatopause. Horm Res 2000;53 Suppl 3:37-41 Savine R. et al.

3. GH decreased body fat in men and women by 14% and increased lean muscle in both men and women. Synergistic with testosterone (decreased body fat 17-18%). GH resulted in substantial increase in aerobic capacity, decreased total and LDL (bad) cholesterol, improved cholesterol coronary risk ratio and lowered PSA levels.

Mark Blackman of Johns Hopkins University and National Institute on Aging.

4. *"The fall in GH secretion seen with aging coincides with changes in body composition and lipid metabolism that are similar to those seen in adults with GH deficiency."*

- Growth hormone has positive effects of GH on lean body mass, central fat, low-density lipoprotein cholesterol and aerobic capacity.

Savine R. Is the Somatopause an indication for growth hormone replacement? J Endocrinol Invest 1999;22(5 Suppl):142-9.

5. Low IGF-1 (measurement of low growth hormone) in older women results in poor muscle strength, slow walking speed and 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.

6. Aging and adult growth hormone deficiency both have:

- Increased Cardiovascular morbidity and mortality
- Decreased muscle mass and bone mass
- Total and visceral fat increased
- LDL (bad cholesterol) increased

With GH supplementation body composition changes:

- Reduction in total and visceral fat and increase in lean body mass
- Improvement in cardiovascular function and lipids
- Reverse atherosclerotic changes in carotids
- Quality of life improves
- Bone mineral density increases

Johannsson et al. Growth Hormone and IGF Research 2000, Supplement B 25-30.

7. GH deficiency results in abnormal body fat and distribution and insulin resistance. hGH replacement results in increased lean body mass, decreased abdominal fat by up to 50% and increased insulin sensitivity (prevents diabetes).

Christiansen, J. Effects of GH upon body composition.. Growth Hormone in Adults, 1996, Cambridge University Press.

8. GH secretion is impaired in obesity.

- GH decreases adiposity
- Inhibits lipoprotein lipase
- Enhances lipolysis
- Improves dyslipidemia

Nam SY et al. Growth Hormone and Adipocyte Function in Obesity. Horm Res 2000 Jul;53 Suppl S1:87-97.

9. Middle age men with low GH and abdominal obesity: Nine months of hGH treatment (9.5 microg/kg/day):

- Decreased fat, abdominal visceral 18% and subcutaneous 6%
- Improved insulin sensitivity (prevents diabetes)
- 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 lipo protein metabolism and reduces diastolic BP. J Clin Endocrinol Metab 1997;82:727-734.

10. Five years hGH replacement:

Significant increase in:

- lean body mass
- Bone mineral density
- HDL-C (good cholesterol)

Significant decrease in:

- Total cholesterol,
- LDL-C (bad cholesterol)
- Triglycerides

- Hemoglobin A1C (lower glucose levels and diabetes preventative)
- “5 year GH substitution is safe and well tolerated.”

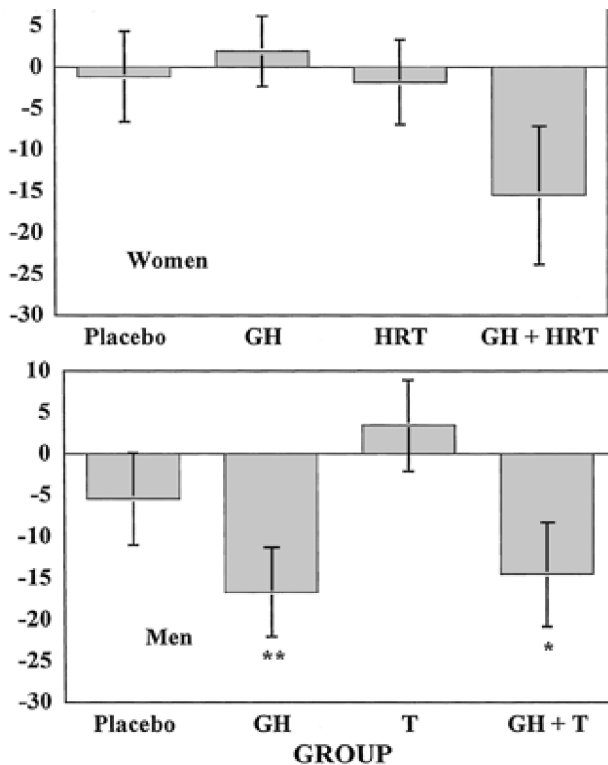
Gotherstrom G et al. A prospective study of 5 years of GH replacement therapy in GH-deficient adults: sustained effects on body composition, bone mass, and metabolic indices. J Clin Endocrinol Metab 2001 Oct;86(10):4657-65

10. GH +/- sex steroids and subcutaneous and visceral fat with testosterone and HRT

T=Testosterone Enanthate 100 mg q 2 weeks

GH = 20 micrograms/kg 3 x a week

Significantly decreased body fat in growth hormone and growth hormone and HRT verses placebo



Munzer T, Harman SM, Hees P, Shapiro E, Christmas C, Bellantoni MF, Stevens TE, O'Connor KG, Pabst KM, St Clair C, Sorkin JD, Blackman MR. 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.

11. GH deficiency results in impaired physical performance. Growth hormone replacement increases exercise capacity.

Johansson, J. Psychosocial and CNS effects. Growth Hormone in Adults 1996, Cambridge University Press  
 Juul, A. Adult GH deficiency and effects of GH treatment on muscle strength, cardiac function and exercise performance. GH in adults, Cambridge University Press, 1996, p 254-241

12. GH deficiency results in chronic fatigue and depression.

GH Replacement results in:

- Increased 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.

## Section 2 - Growth Hormone and the Brain

1. Adult nerve cells are targets of IGF-1.

IGF-1 increases dendritic formation of cortical neurons (improved mental function).

Riddle D. Role of IGF -1 in cortical dendritic growth Journal of GH and IGF Research Oct 99  
 Caro, E et al Body to brain signaling mediated by circulating IFG-1. Journal of GH and IGF Research Oct 99.

2. IGF-1 reverses age-related D2 (Dopamine) receptor deficits and improve age related impairment in learning and memory.

Thornton et al. Journal of GH and IGF Research Oct 99.

3. IGF-1 correlated with cognitive function in men average age 69. GH deficiency correlates with poor emotional and psychosocial functioning.

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

4. GH increases connexin-43 (improves mental function).

- In cerebral cortex
- In hypothalamus
- IGF-1 does not increase connexin-43
- Connexin-43 forms gap junctions that mediate intercellular communication and improved mental function
- Increased neuronal communication

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

5. GH exerts profound effects on CNS and improves:

- Cognitive capabilities
- Memory
- Alertness
- Motivation, Work Capacity
- GH receptors present in the brain
- Hypothalamus, choroid plexus, hippocampus
- GH crosses BBB

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.

6. IGF-I exerts cytoprotection against A beta-amyloid induced neuronal cell death (prevents Alzheimer's disease).

Takako Niikura 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-



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### Section 3 - Growth Hormone and Bone

#### 1. GH deficiency causes reduced bone density

Growth hormone replacement reverses osteoporosis.

Logobardi, J Endocrinol Invest, May 1999.

#### 2. Bone density significantly improved with hGH therapy.

- Increases formation and strength of cortical bone
- Synergistic effect with exercise
- Lower growth hormone levels are found in patients with bone fractures

Growth Hormone and Mild Exercise in Combination Markedly Enhance Cortical Bone Formation and Strength in Old Rats. Oxlund H et al Endocrinology, April 1998, p. 1899-1904 Vol. 139, No 4.

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.

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.

#### 3. Effect of GH on body composition and bone turnover in women with osteoporosis.

- Increase in handgrip strength
- Decrease in waist/hip ratio
- Increased bone formation
- Decreased osteoporosis

Sugimoto T et al. Effect of recombinant human growth hormone in elderly osteoporotic women. Clin Endocrinol (Oxf) 1999 Dec;51(6):715-724.

#### 4. Growth hormone replacement in men (18 month study)

- Increase bone density and lean body mass
- Body fat decreased
- Low incidence of side effects

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.

#### 5. 42 month study

- Increases of bone mineral density in spine and femoral neck
- Patients with osteopenia (low bone mass) were reduced by 50%
- Better results in males and younger
- "GH deficient patients with osteoporosis or osteopenia should be considered candidates for GH replacement"

Valimaki MJ et al Effects 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.

### Section 4 - Growth Hormone and the Heart

#### 1. GH Deficiency associated with increased cardiovascular (CV) deaths.

GH Replacement results in:

- Increased CV function
- Improves lipid profile
- Reverses arteriosclerosis
- 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.

#### 2. Growth hormone and atherosclerosis:

HGH normalized intima media thickness (IMT) of carotid arteries in 3 months and improvement continued during 18 months of study.

- IMT negatively correlated with IGF-1
- Direct effect on arterial wall via Nitric oxide

Pfeifer M et al. Growth Hormone (GH) Treatment Reverses Early atherosclerotic Changes in GH-Deficient Adults J Clin Endocrinol Metab 84: 453-457, 1999.

Borson-Chazot 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.

#### 3. Growth hormone improves cardiac performance.

- Increases contractility and cardiac output
- Improves cardiac function in dilated cardiomyopathy

Fazio et al. A preliminary study of GH in the treatment of dilated cardiomyopathy. NEJM 1996;334:809-814.

Isgaard J et al. GH improves cardiac function in rats with experimental MI. Eur J Clin Invest 1997;27:517-525.

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.

#### 4. Growth hormone treatment in heart failure patient increased ejection fraction 13% to 28% (doubled heart function). Heart medications were able to be discontinued.

Bocchi EA et al. Growth hormone for optimization of refractory heart failure treatment. Arq Bras Cardiol 1999 Oct;73(4):391-8.

#### 5. Cardiac performance impaired in GH deficiency

- Reduction of LV mass
- Reduction of ejection fraction
- Reversed after GH replacement

Colao A et al. Impaired cardiac performance in elderly patients with growth hormone deficiency J Clin Endocrinol Metab 1999 Nov;84(11):3950-5.

#### 6. GH decreases coronary inflammation and prevents heart attacks.

- GH deficient adults have increased cardiovascular mortality
- Inflammatory markers are predictive of cardiovascular events
- C-Reactive Protein increased in GH deficiency

With GH Replacement therapy:

- C-Reactive protein decreased
- Visceral and subcutaneous fat decreased
- Lipoprotein(a) decreased



Sesnilo 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.

#### 7. IGF-1 and the heart:

- Improves cardiac contractility, cardiac output, stroke volume, ejection fraction
- Improves cardiac function after myocardial infarction by stimulating contractility and promoting tissue remodeling
- Facilitates glucose metabolism, lowers insulin levels, increases insulin sensitivity, and improves the lipid profile

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.

#### 8. GH Increases coronary blood flow and capillary density.

- Decline in GH leads to decline in tissue growth, maintenance and repair in older animals (and humans)
- Deterioration of cardiovascular function contributes to decline of physical function and quality of life
- Decreased coronary flow and capillary density with aging reversed by GH

Khan AS et al. Growth hormone increases regional coronary blood flow and capillary density in aged rats. *J Gerontol A Biol Sci Med Sci* 2001 Aug;56(8):B364-71.

### Section 5 - Growth Hormone and Immune System

#### 1. Connection between neuroendocrine and immune and 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

Clark R. The somatogenic hormones and insulin-like growth factor-1: stimulators of lymphopoiesis and immune function. *Endocr Rev*. 1997 Apr;18(2):157-7.

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.

### Section 6 - Growth Hormone and Crohn's Disease

#### 1. Significant improvement in patients treated with hGH.

Slonim AE et al. A preliminary study of growth hormone therapy for Crohn's disease. *N Engl J Med* 2000 Jun 1;342(22):1633-7

### Section 7 - GH and Chronic Fatigue and Fibromyalgia (See CFIDS and Fibromyalgia page)

- HGH deficiency mimics fibromyalgia
- Low GH secretion, IGF-1 and IGFBP3 in fibromyalgia
- Rx with HGH or GHRH produced increases in IGF-1 and IGFBP3
- Can be significant improvement in symptoms with hGH replacement

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Leal-Cerro et al. The Growth Hormone (GH)-Releasing Hormone - GH -Insulin-like Growth Factor-1 Axis in Patients with Fibromyalgia Syndrome *J Clin Endocrinol Metab* 84: 3378-3381, 1999

#### 2. Growth hormone deficiency more common in fibromyalgia patients. Supplementation with HGH can result in improvement in symptoms

Bennett RM, *Z Rheumatol* 1998;57 Suppl 2:72-6.

#### 3. Growth hormone supplementation results in significant improvement in symptoms.

*"Women with fibromyalgia and low IGF-1 levels experienced an improvement in their overall symptomatology and number of tender points after 9 months of daily growth hormone therapy. This suggests that a secondary growth hormone deficiency may be responsible for some of the symptoms of fibromyalgia."*

Bennett RM; Clark SC; Walczyk J. *Am J Med* 1998 Mar;104(3):227-31.

#### Other references

1. Al-Shoumer, K.A.S., et al., "Effect of Four Years' Treatment with Biosynthetic human Growth Hormone (GH) on Body Composition in GH-Deficient Hypopituitary Adults." *European Journal of Endocrinology*. 135:559-67,1996.

2. Terry, L. Cass, Halter, J.B., "Aging of the Endocrine System." *Principles of Geriatric Medicine and Gerontology*, Eds. Hazard, et al., McGraw Hill, 1995.

3. Oriander, PR., Nader, S., *Endocrinology*. "Youthful hormones." *Lancet*. 348 Suppl. 2:sII6, 1996.

4. Amato, G., et al., "Low Doses Recombinant Human Growth Hormone Normalizes Bone Metabolism and Cortical Bone Density and Improves Trabecular Bone Density in Growth Hormone Deficient Adults Without Causing Adverse Effects." *Clinical Endocrinology*. 45:37-32,1996.

5. Johannsson, G., et al., "Two years of Growth Hormone (GH) Treatment Increases Bone Mineral Content and Density in Hypopituitary Patients with Adult Onset GH Deficiency." *Journal of Clinical Endocrinology & Metabolism*, 81:2865-73, 1996.

6. Bengtsson, B.A., et al., "Cardiovascular Effects of GH". *Journal of Endocrinology*. 152:1-3, 1997.

