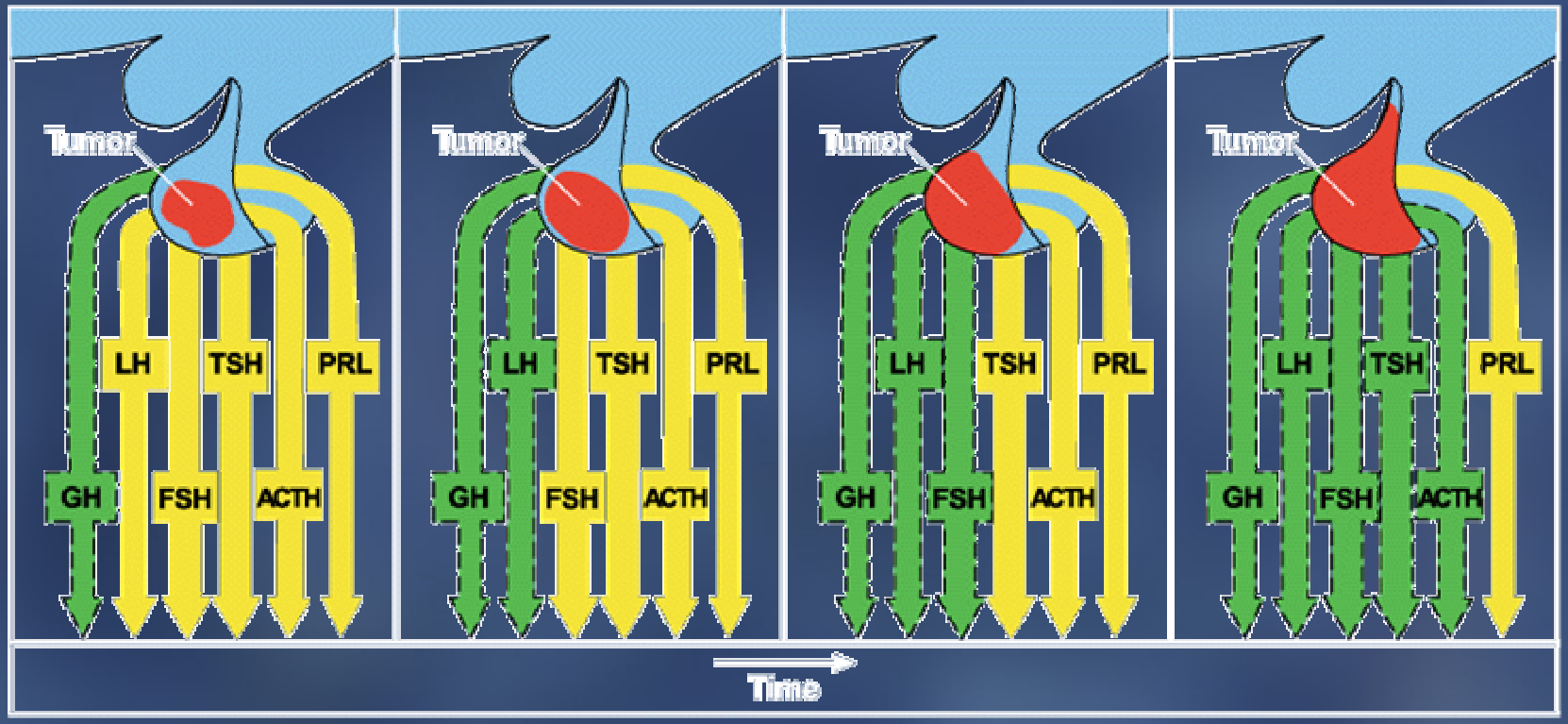
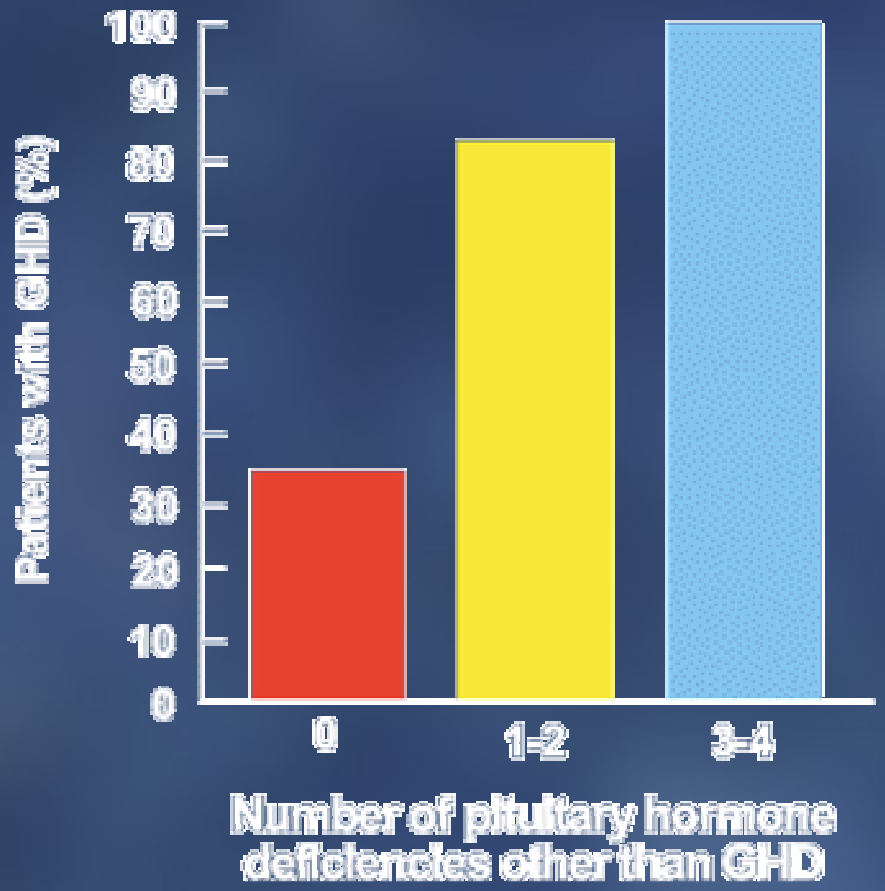
GH Replacement Therapy in Growth Hormone Deficient Adults

Sequence of hormone loss in hypopituitarism depending on location of a benign tumor



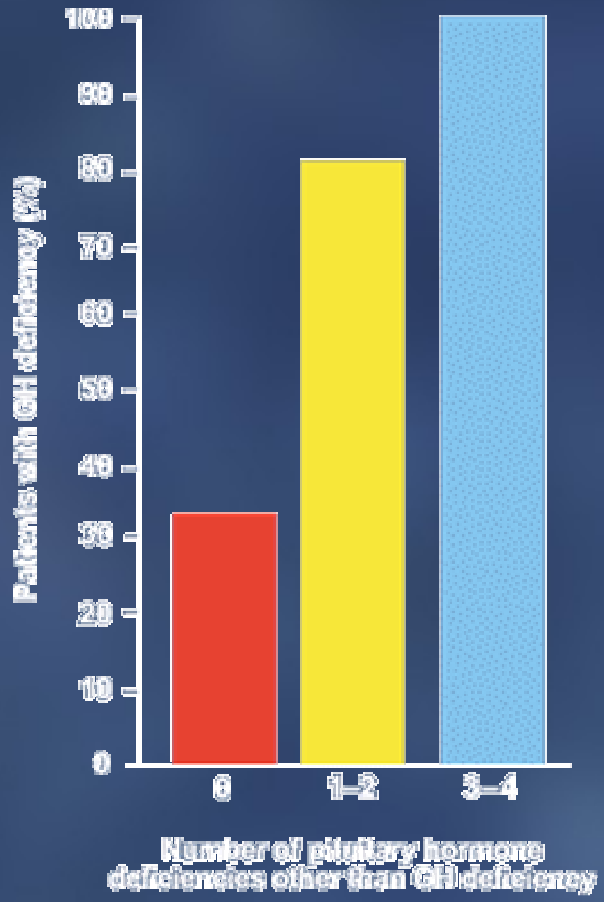
Besser GM, Cudworth AG, eds. Clinical endocrinology: an illustrated text. London: Gower Medical Publishing, 1987

Patients with other pituitary hormone deficiencies are more likely to be GH deficient



Sönksen PH et al. In: Adashi EY, Thorner MO, eds. *The somatotrophic axis of the reproductive process in health and disease.* New York: Springer-Verlag, 1995

GH deficiency is related to the extent of hypopituitarism and other hormone deficiencies

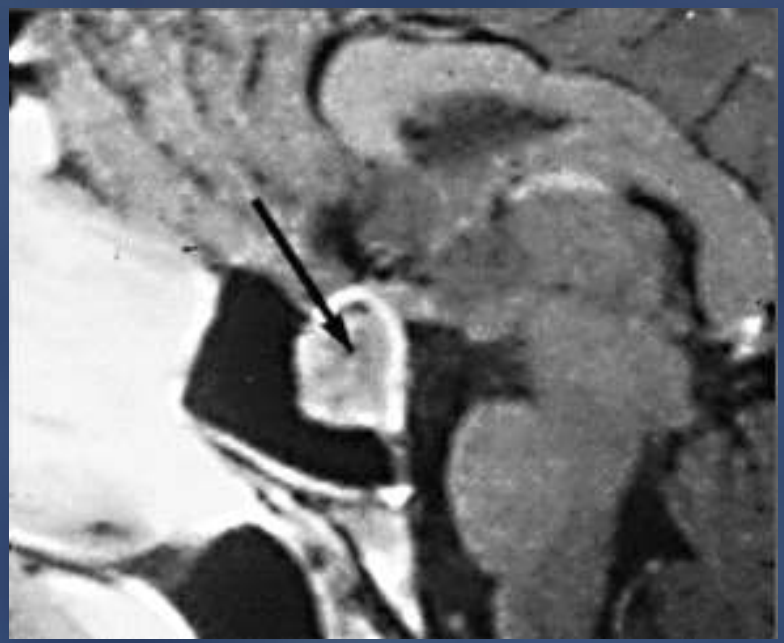


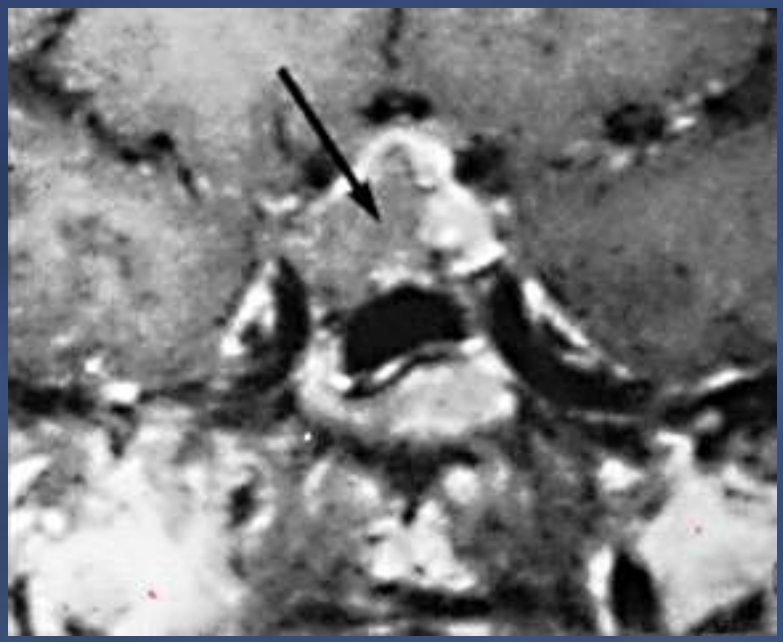
Sönksen PH et al. In: Adashi EY, Thorner MO, eds. *The somatotrophic axis of the reproductive process in health and disease.* New York: Springer-Verlag, 1995

Causes of pituitary insufficiency in 333 patients

Cause	Number of patients
Idiopathic (unknown)	53
Pituitary adenoma	223
Craniopharyngioma	34
Meningioma	7
Cholesteatoma	2
Pinealoma	1
Dysgerminoma	1
Myxogerminoma	1
Chordoma	1
Astrocytoma	1
Arachnoidal cyst	1
Benign cyst teratoma	1
Undifferentiated tumor	7

MRI scans of pituitary adenoma





Characteristic clinical features of growth hormone deficiency in adults

- Increased fat mass
- Reduced lean body mass
- Decreased extracellular water (dry, thin skin)
- Low bone density
- Impaired cardiac function
- Poor physical performance
- Impaired psychological well-being

Symptoms and signs of GH deficiency in adults

Symptoms

Decreased psychological well-being
- Reduced energy and vitality
- Poor general health
- Impaired self-control
- Disturbed emotional reaction
- Lack of positive well-being
- Depressed mood
- Increased anxiety
- Increased social isolation

Increased abdominal adiposity

Reduced strength and physical endurance

Thin, dry skin

Signs

Truncal obesity

Increased waist:hip ratio

Thin, dry skin

Abnormal body composition
- Decreased lean body mass
- Increased body fat
- Reduced extracellular water

Decreased psychological well-being

Reduced exercise performance

Abnormal cardiac structure and function

Cardiovascular risk factors
- Hyperlipidemia
- Decreased fibrinolysis
- Increased atherosclerosis

Decreased bone density

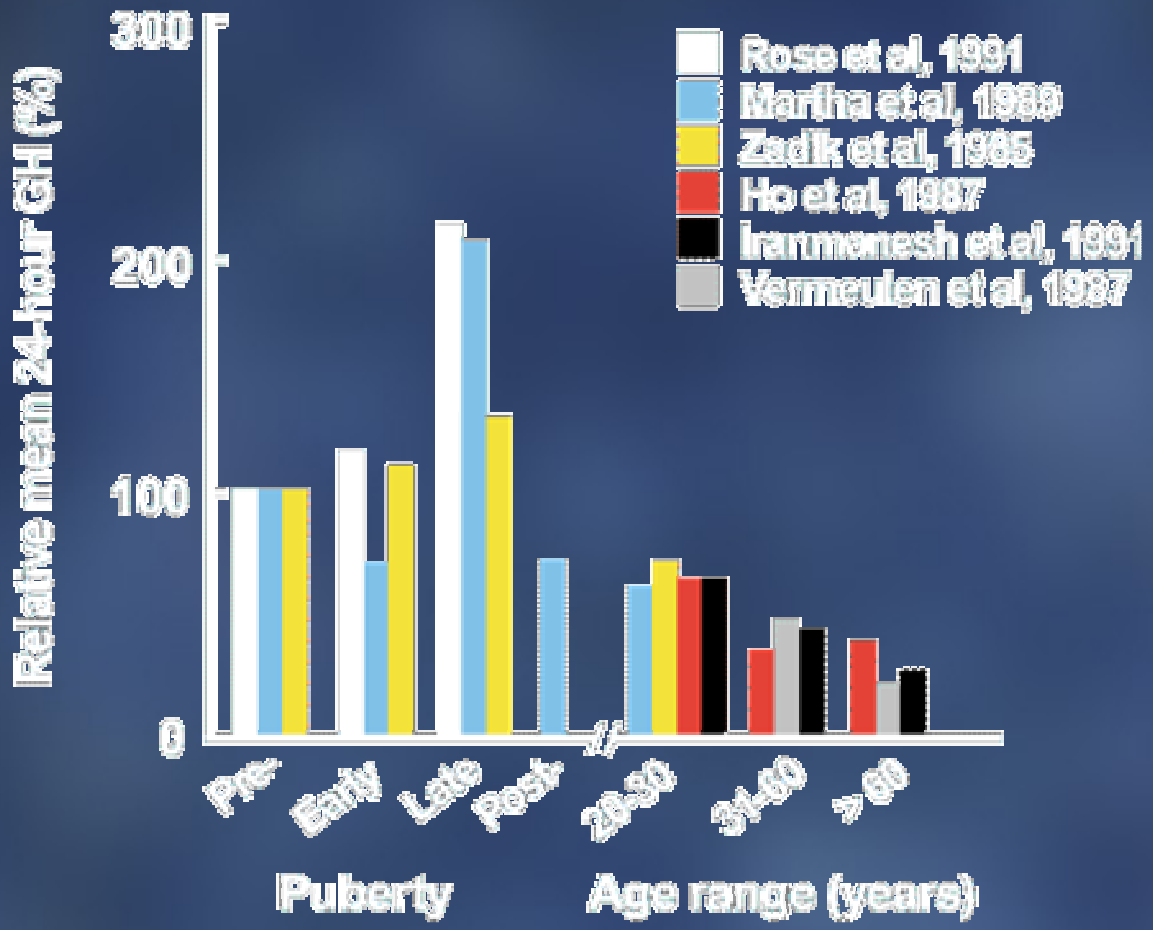
Disturbed renal function
- Reduced glomerular filtration rate
- Reduced renal plasma flow

Lowered basal metabolic rate

Increased insulin resistance

Modified from Cuneo et al. *Clin Endocrinol* 1992; 37: 387-97

GH secretion varies throughout life



Ho KY, Hoffman DM. In: Laron Z, Butenandt O, eds. *Growth hormone replacement therapy in adults – pros and cons.* Tel Aviv/London: Freund Publishing House, 1993: 5-16

Actions of growth hormone

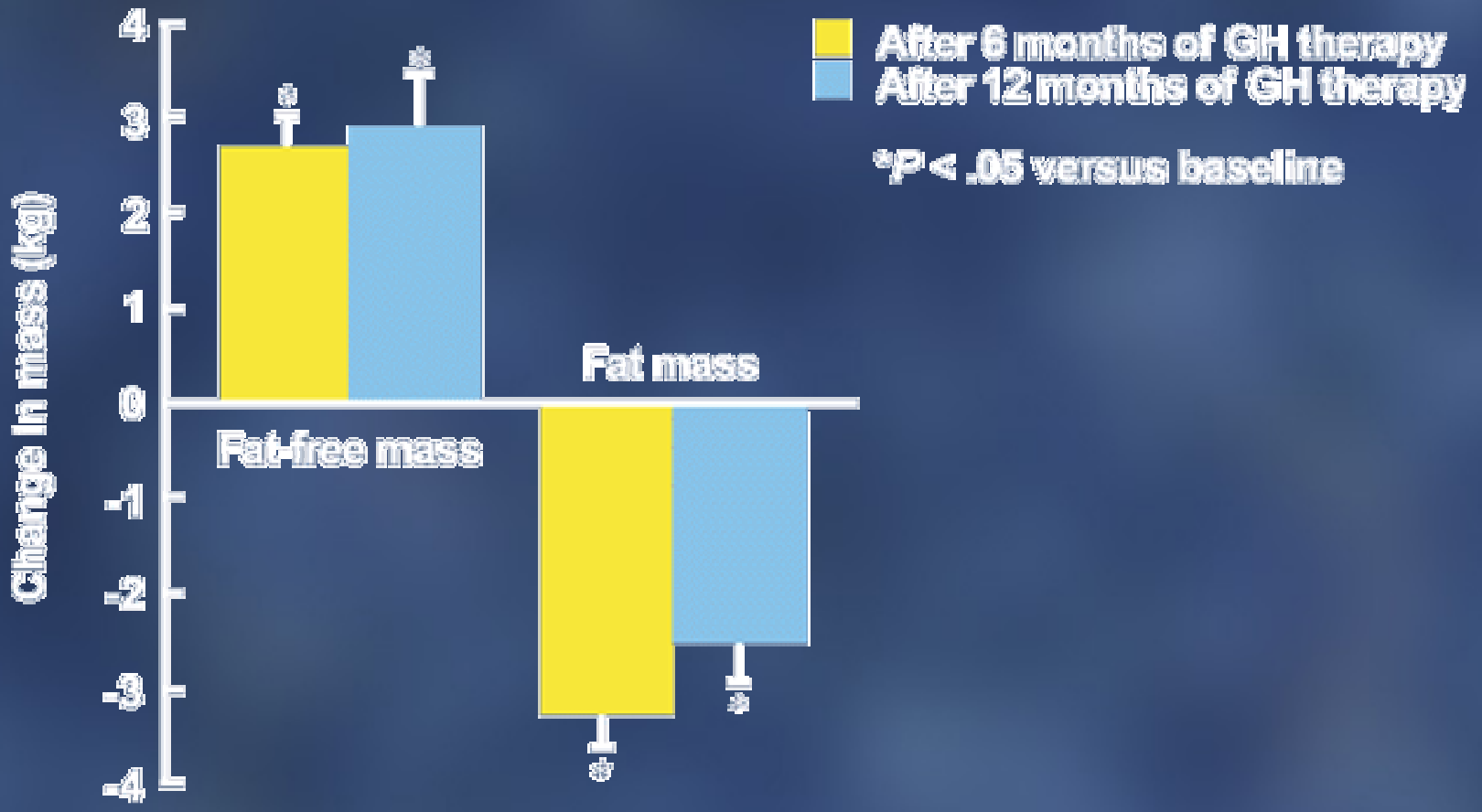
Anabolic action (muscle building)

Lipolytic action

Stimulation of bone and cartilage growth

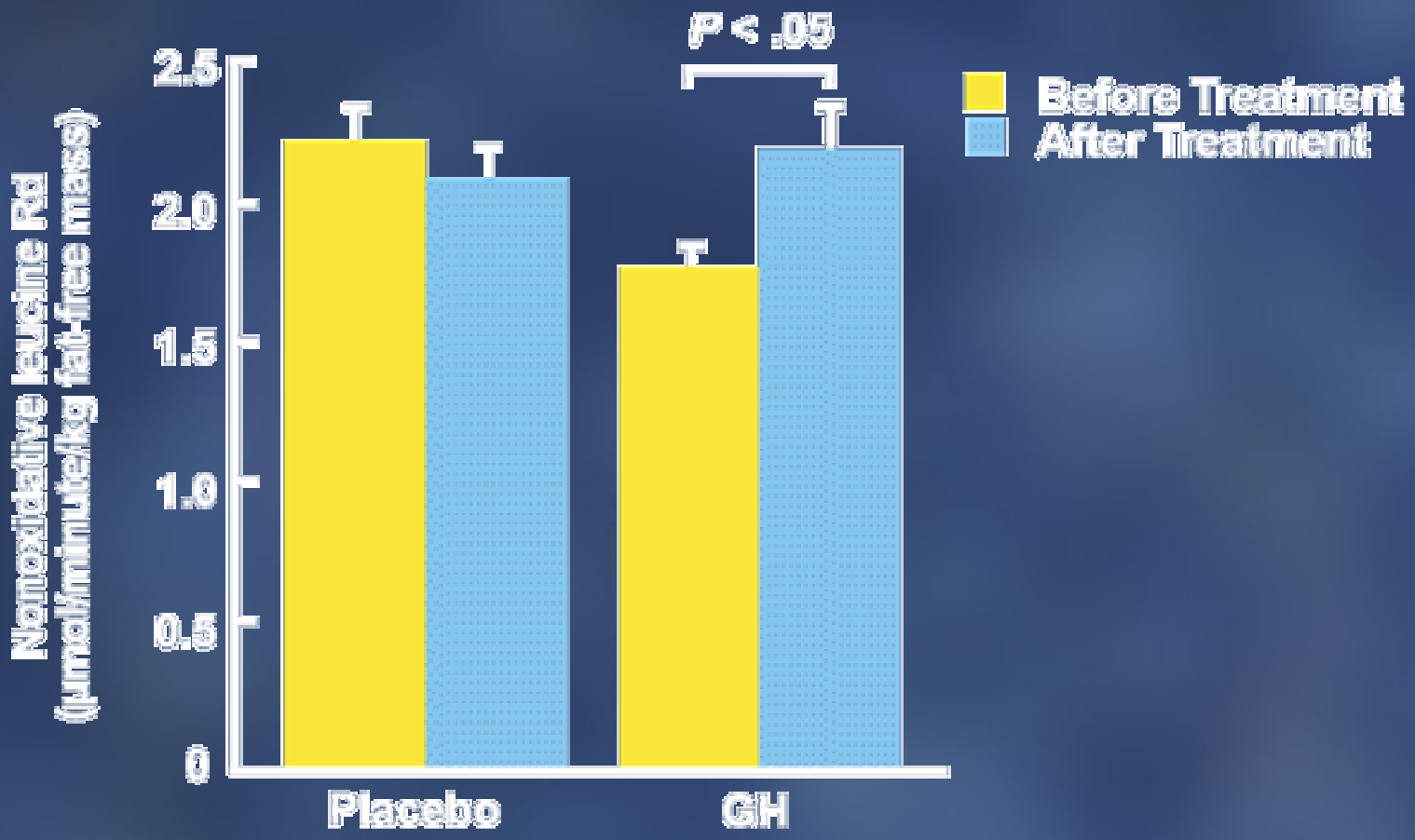
CNS action

GH replacement therapy has beneficial effects on body composition



Mårdh G et al. *Endocrinol Metab* 1994; 1 (Suppl A): 43-9

GH replacement therapy increases protein and muscle synthesis



Russell-Jones DL et al. *Acta Endocrinol* 1993; 128 (Suppl 2): 44-7

Actions of growth hormone

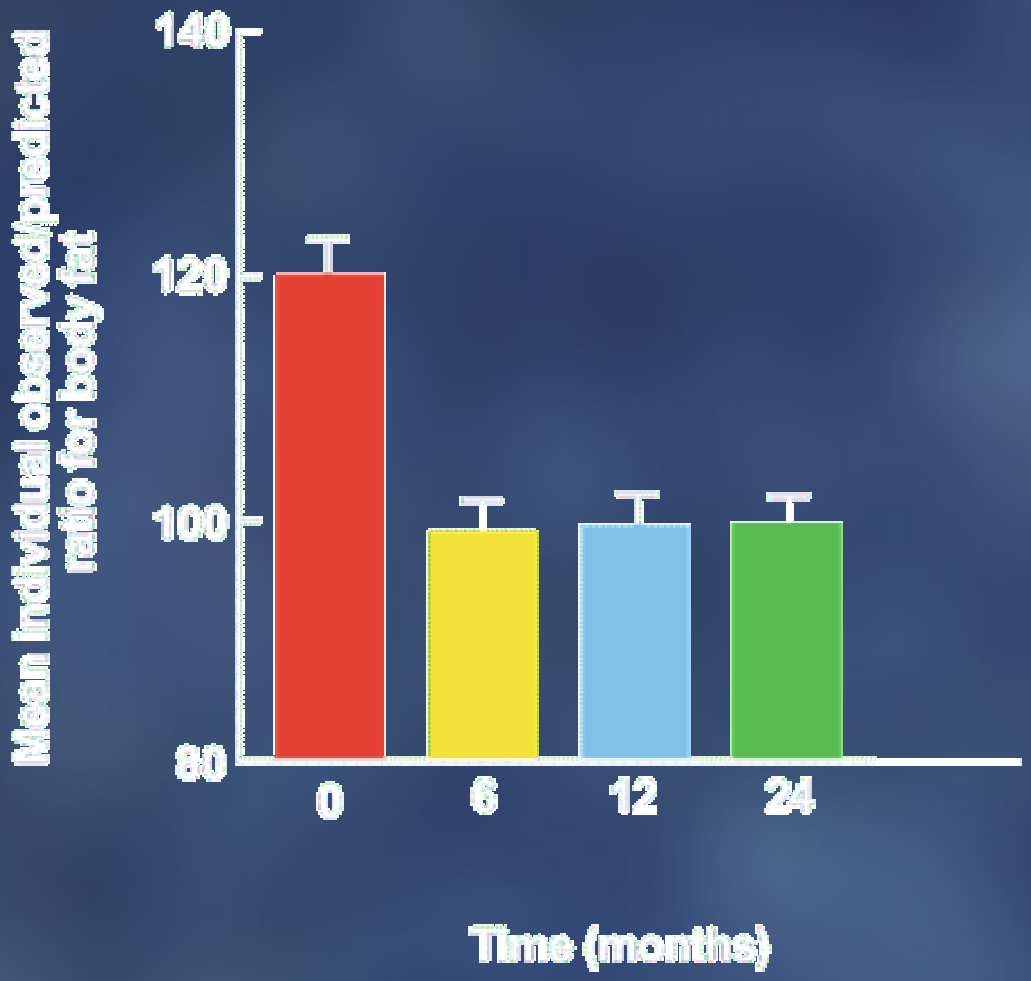
Anabolic action

Lipolytic action (fat burning)

Stimulation of bone and cartilage growth

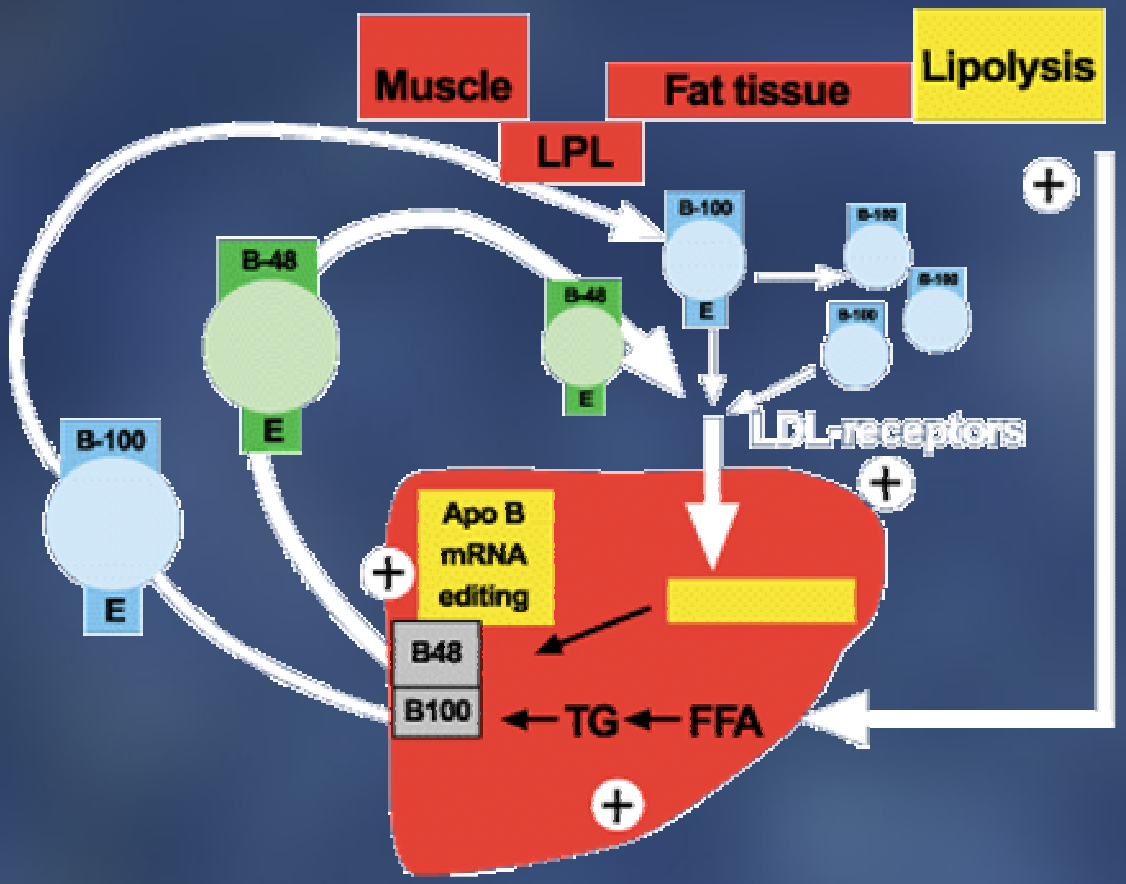
CNS action

Two years of GH replacement therapy reduces body fat



Johannsson G et al. *Endocrinol Metab* 1996: 3 (Suppl A): 3-12

The role of GH in fat metabolism



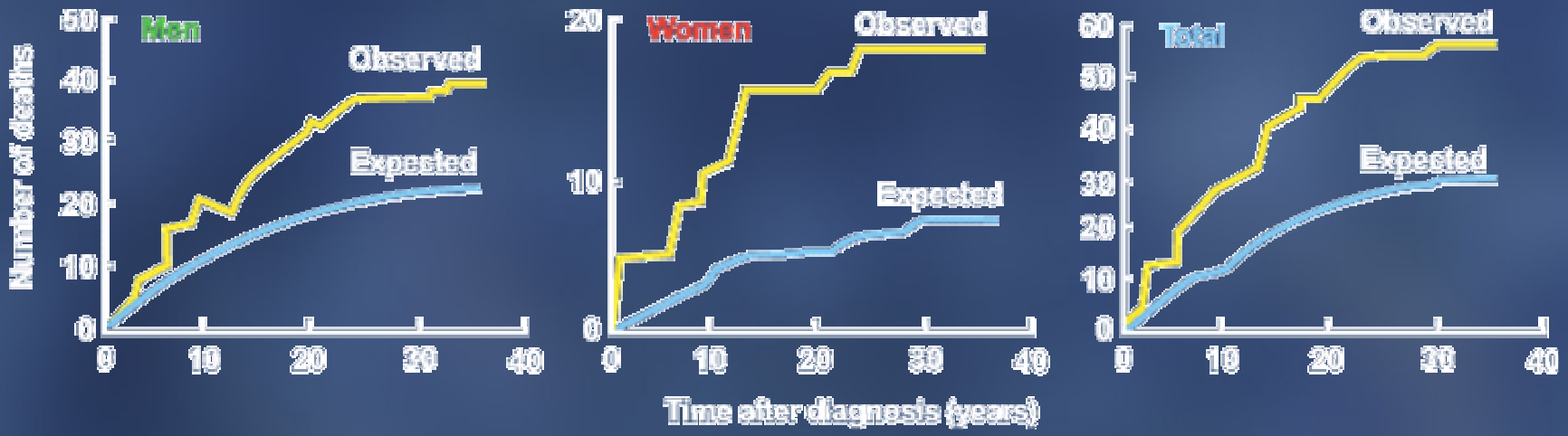
With kind permission of Professor B Angelin

GH has net beneficial effect on lipid metabolism (reducing excess fats)

		0 months	12 months	24 months
Cholesterol	P	234 (59)	233 (48)	232 (44)
(mg/dL)	V	269 (56)	231 (60)***	226 (50)***
LDL Cholesterol	P	167 (56)	168 (49)	159 (45)
(mg/dL)	V	191 (51)	160 (59)**	151 (52)***
TC/HDL-C	P	5.9 (1.9)	5.8 (1.5)	5.3 (2.2)
	V	7.6 (3.3)	5.6 (2.0)**	5.4 (1.7)**
LDL-C/HDL-C	P	4.3 (1.7)	4.1 (1.4)	3.7 (2.0)
	V	5.2 (2.1)	3.9 (1.8)**	3.6 (1.5)**
Lp (a)	P	9.5 (0.4 – 44.8)	8.4 (0.6 – 54.0)	11.8++ (1.2 – 89.1)
	V	6.7 (0.5 – 87.4)	9.0 (0.7 – 181.0)	10.6 (1.05 – 162.0)

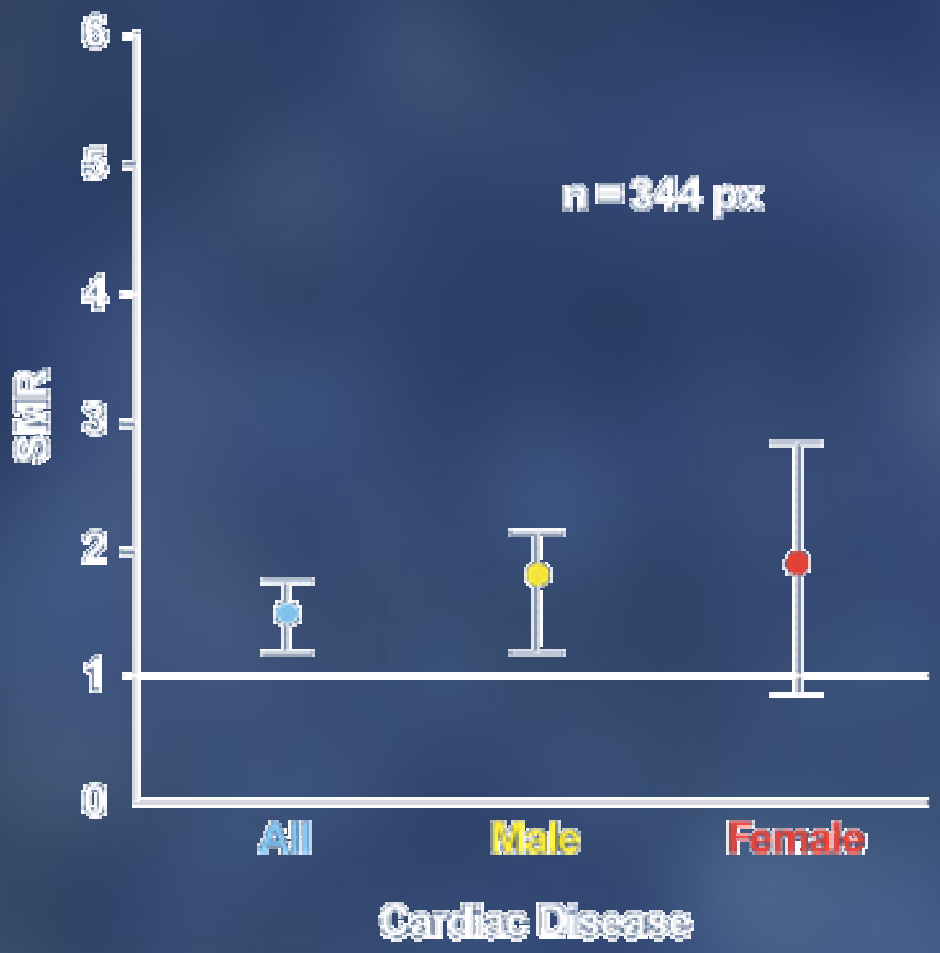
Table 2, Nolte, p 137.

Cardiovascular death is higher in patients with GH deficiency



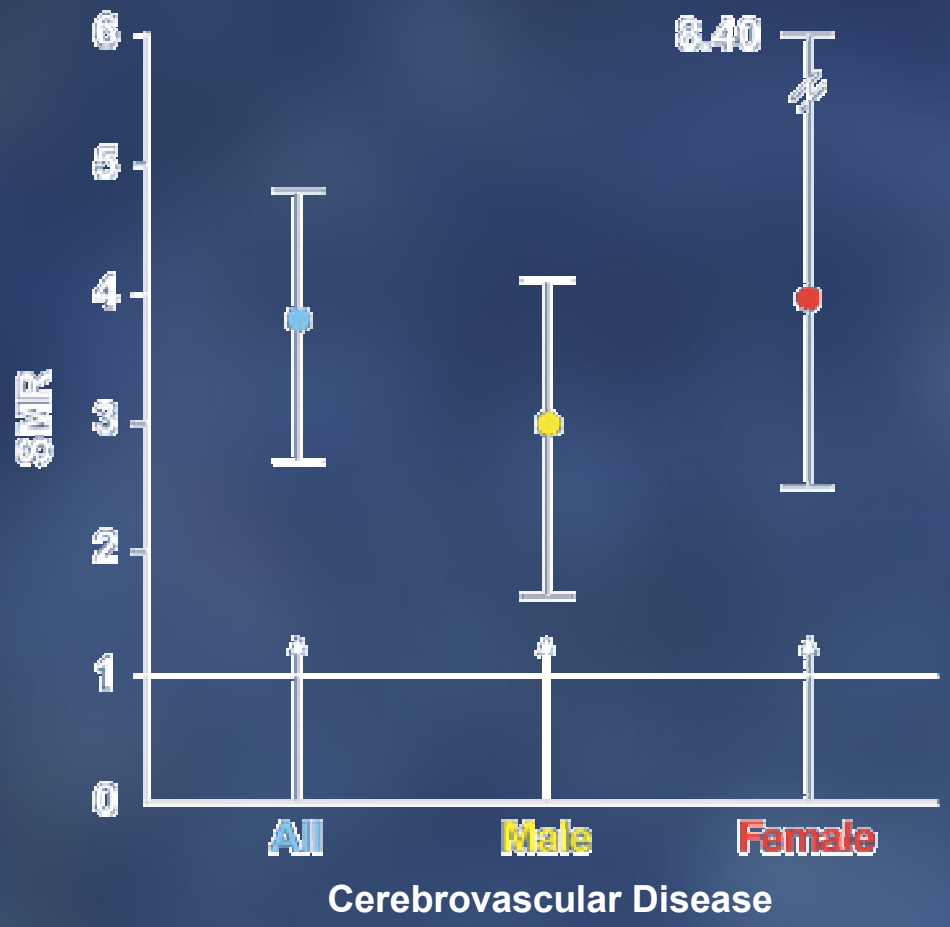
Rosèn and Bengtsson. *Lancet* 1990; 336: 285-8; 77: 1671-6

Cardiovascular death is higher in GH Deficiency



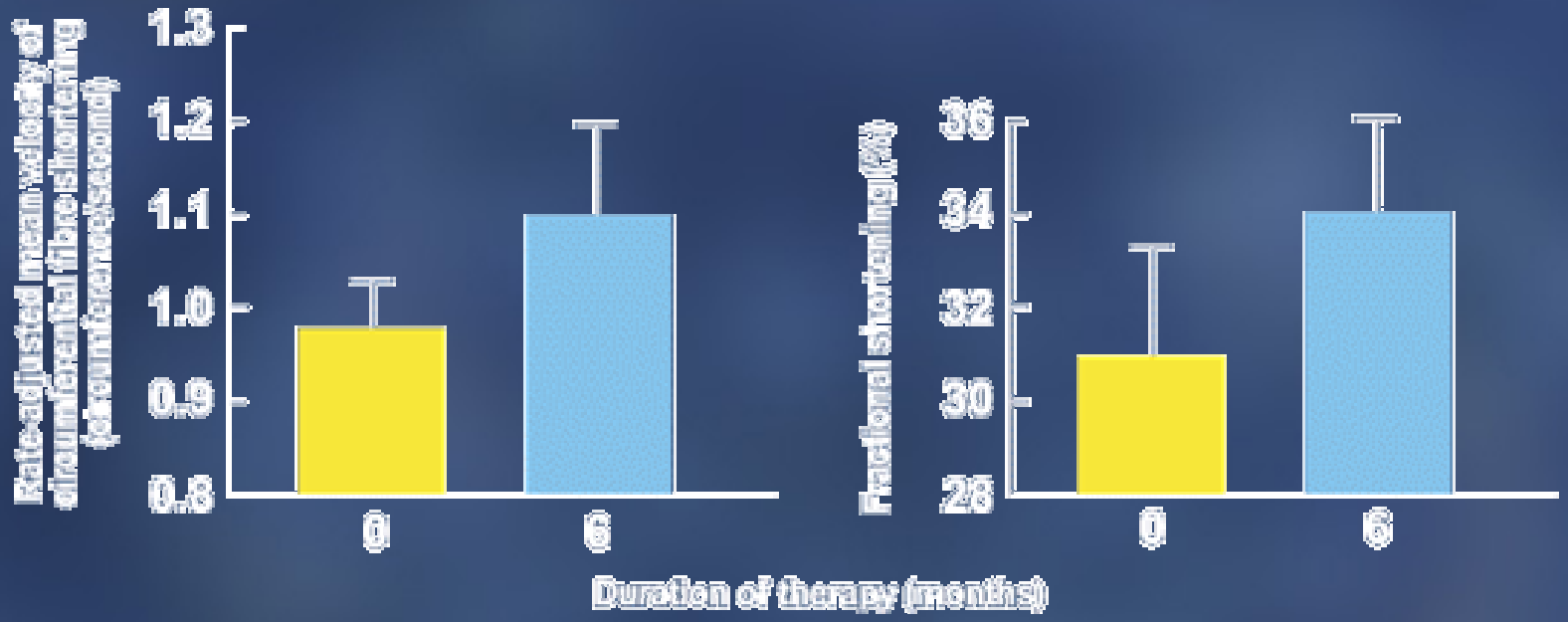
Bülow B et al. The effects of 10 years of recombinant human growth hormone (GH) in adult GH-deficient patients. *J Clin Endocrinol Metab*. 1997; 46: 75-81.

Cerebrovascular disease is higher



Bülow B et al. The effects of 10 years of recombinant human growth hormone (GH) in adult GH-deficient patients. *J Clin Endocrinol Metab*. 1997; 46: 75-81.

Myocardial contractility (heart pumping) is improved after GH therapy



Amato et al. *J Clin Endocrinol Metab* 1993; 77: 1671-6

Actions of growth hormone

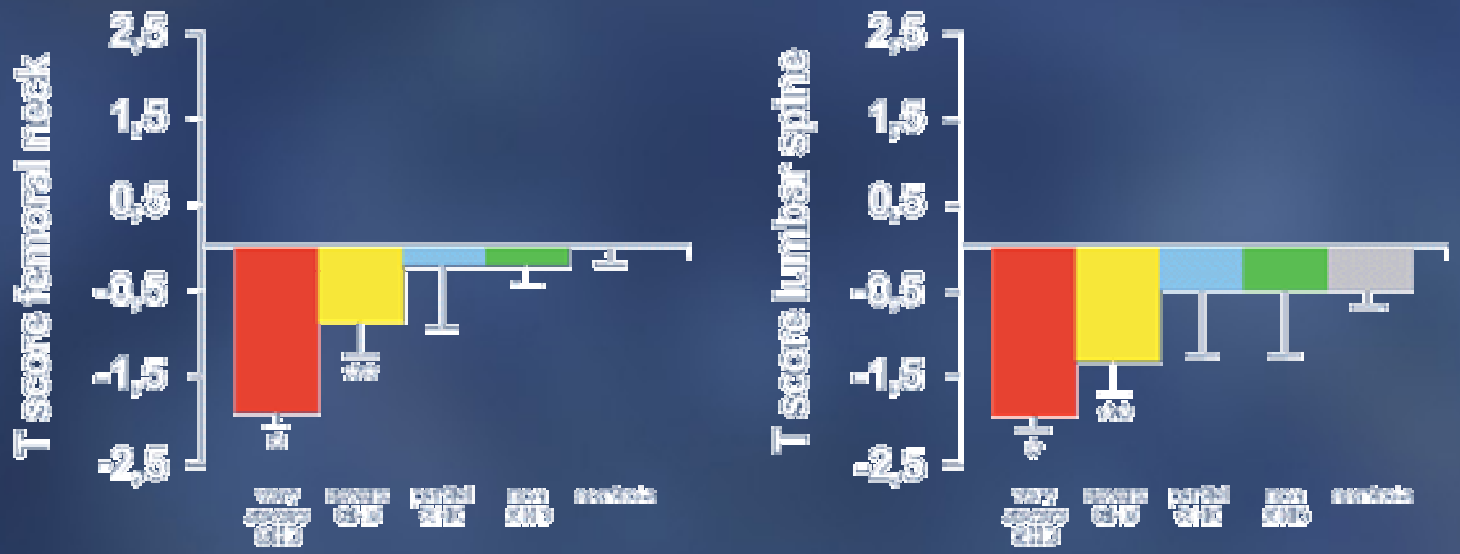
Anabolic action

Lipolytic action

Stimulation of bone and cartilage growth

CNS action

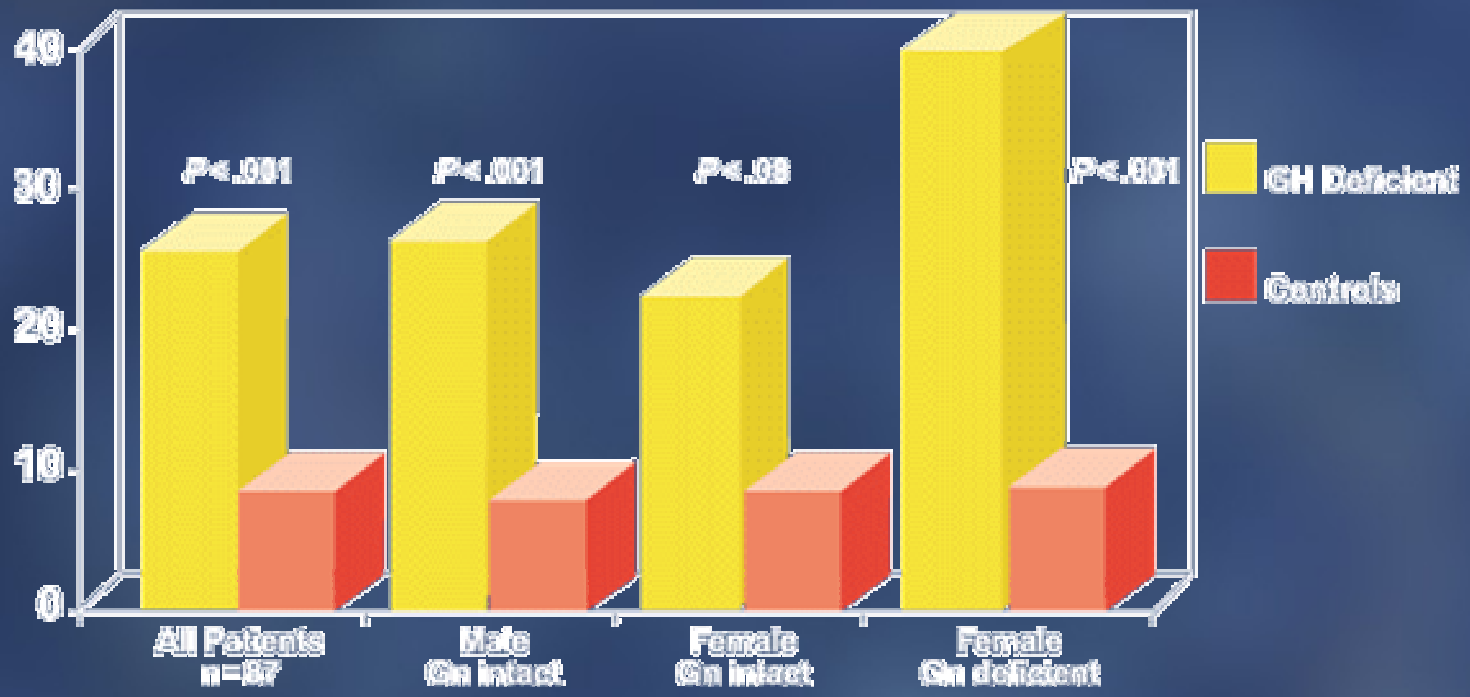
Bone mineral density and strength decreases in GH Deficiency



Colao A et al. *JCEM* 84:1919, 1999

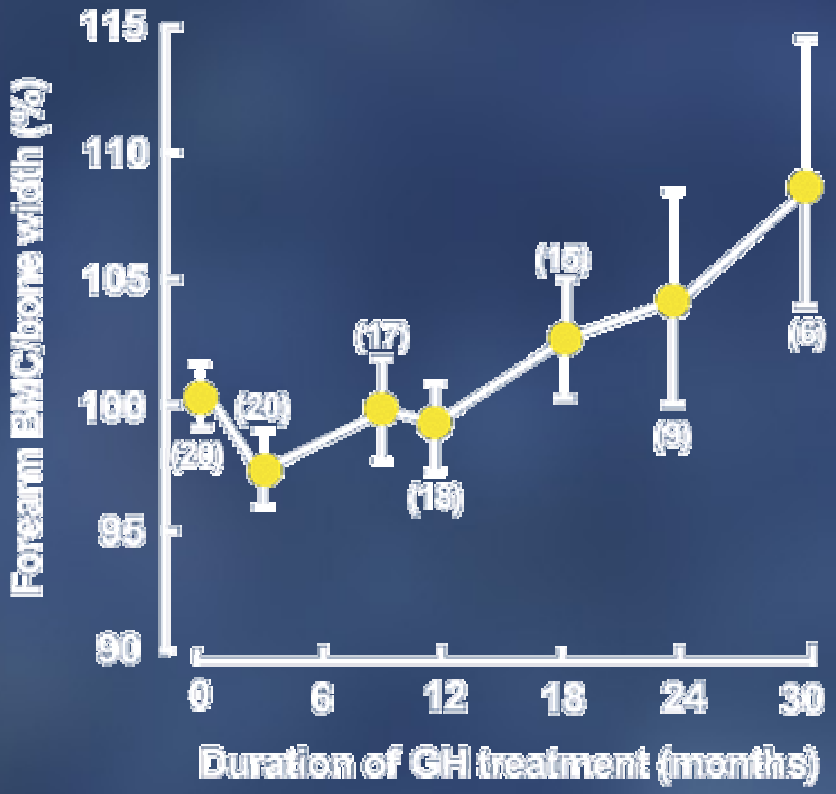
Fig. 1. Lumbar spine BMD *(right panel)* and femoral neck BMD *(left panel)* evaluated as *t* scores in the five groups of subjects divided on the basis of the GH response to ARG+GHRH test: very severe GHD, GH peak below 3 µg/L; severe GHD, GH peak between 3. 1-9 µg/L; partial GHD, peak between 9.1-16.5 ug/L; non-GHD, GH peak above 16.5 µg/L; and controls, GH peak above 16.5 µg/L. *, *P* < .001, group 1 vs. groups 3-5. **, *P* < .05, group 2 vs. groups 1 and 5.

Fractures increase with GH Deficiency



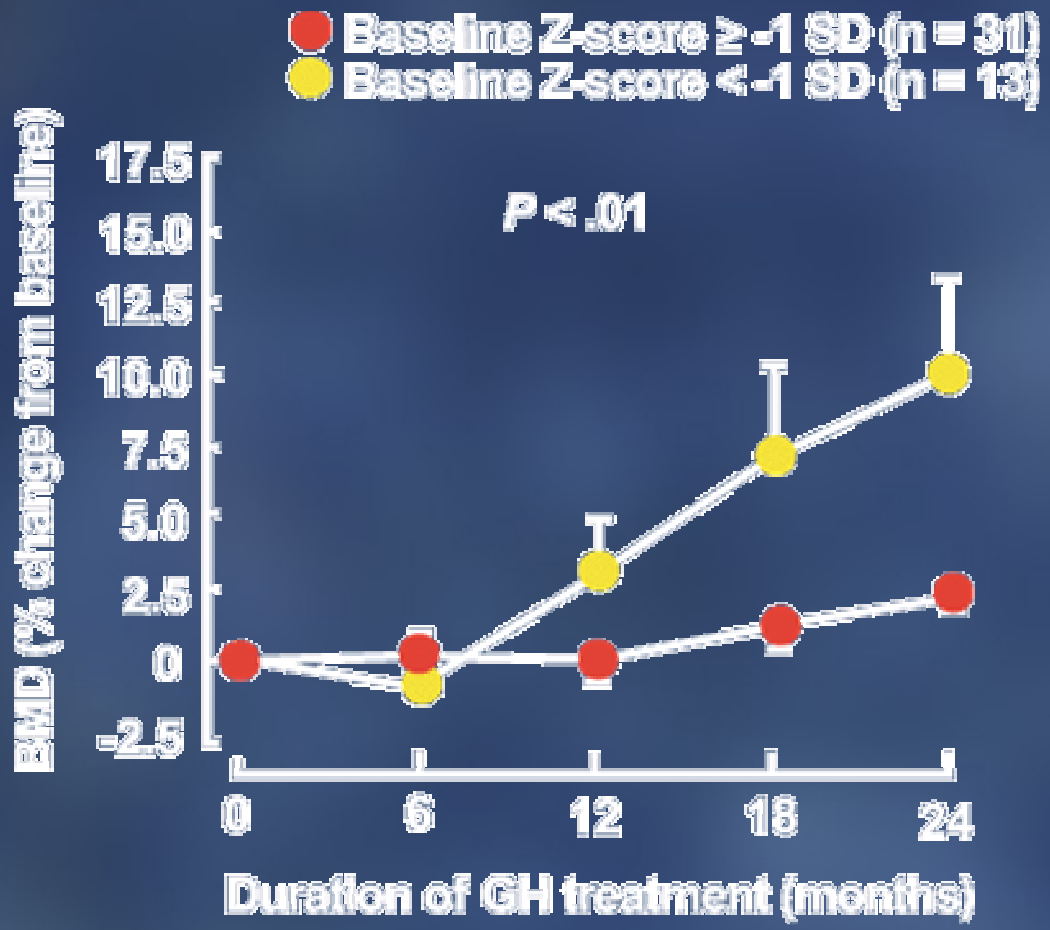
Rosèn et al, *Eur J Endocrinol* 1997

Long-term GH replacement therapy increases forearm Bone Density

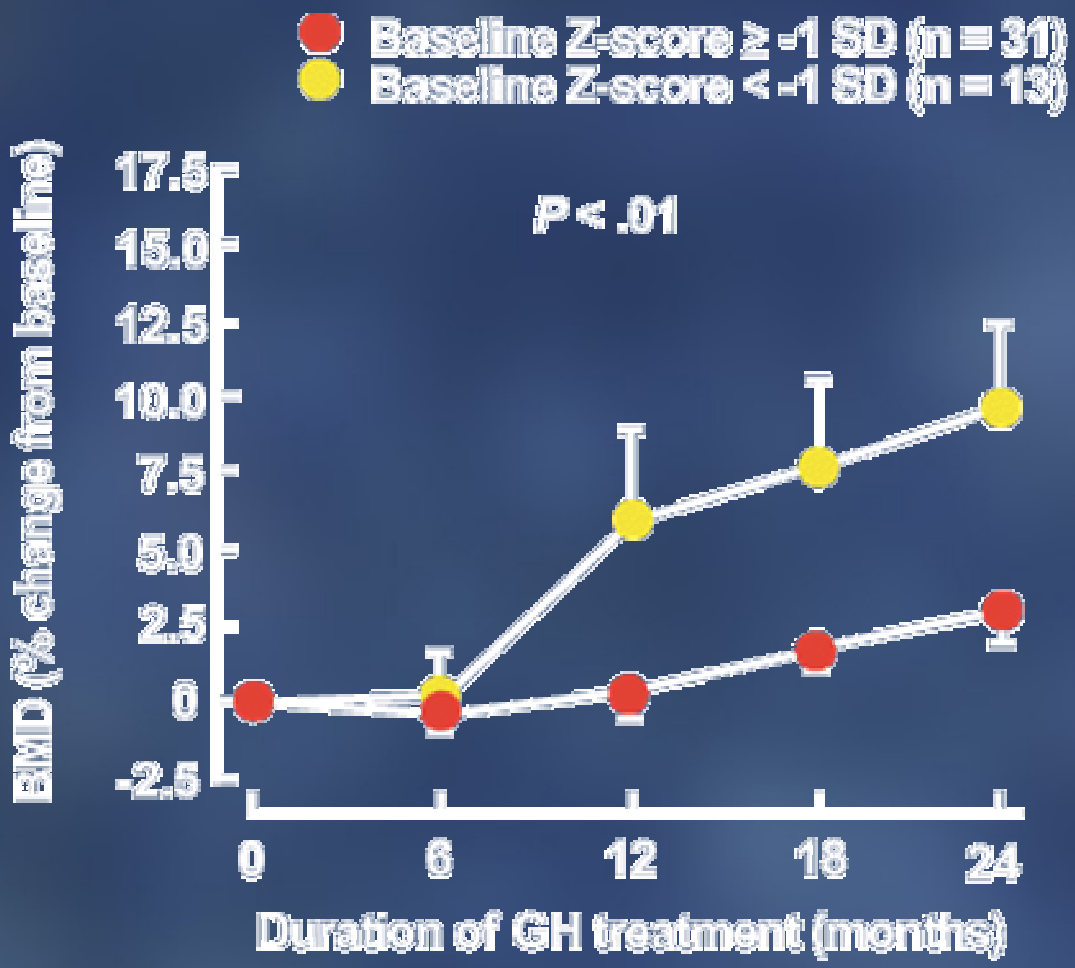


Vandeweghe M et al. *Clin Endocrinol* (Oxf) 1993; 39: 409-15

Two years of GH replacement therapy increases Bone Density in the lumbar spine (L2-L4)



Two years of GH replacement therapy increases Bone Density in the femoral neck



Actions of growth hormone

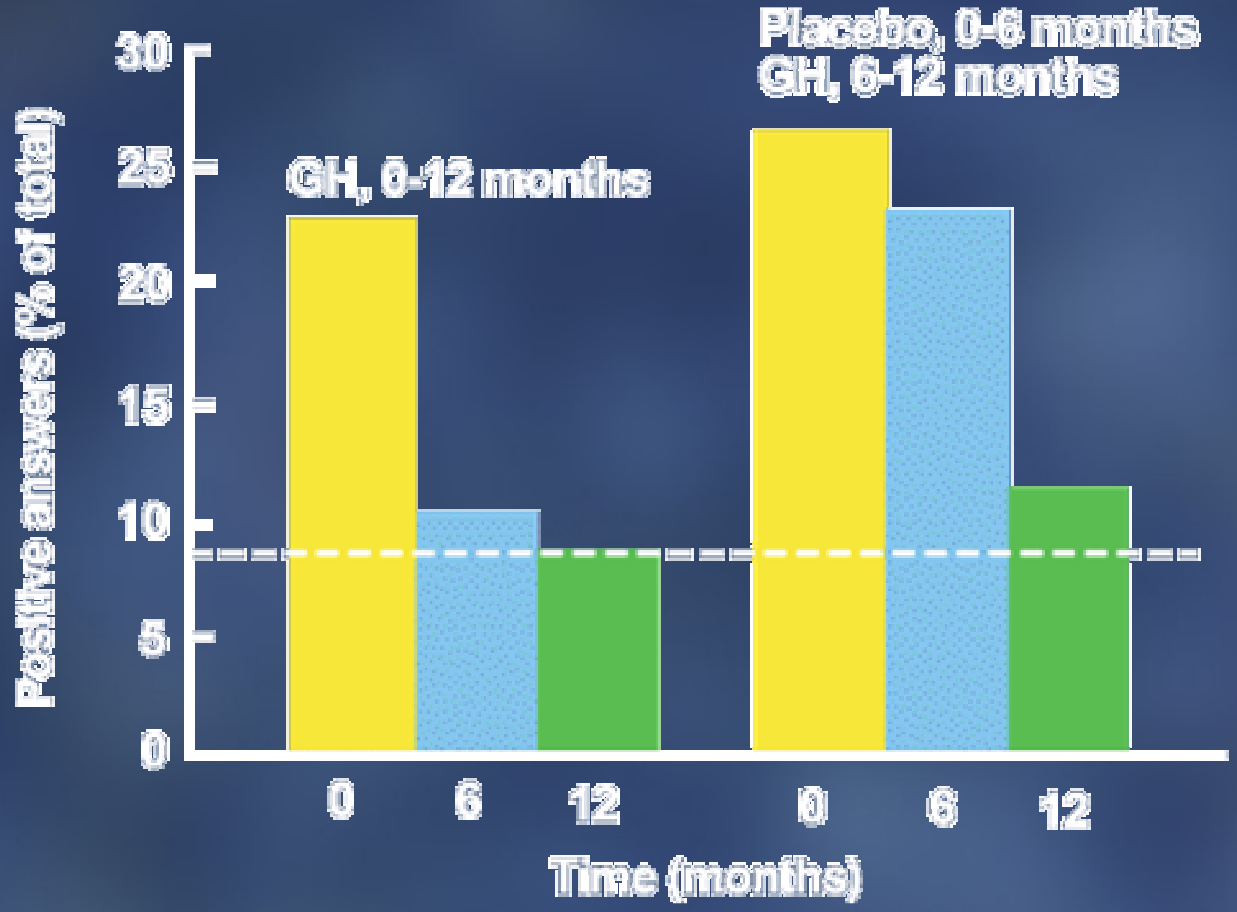
Anabolic action

Lipolytic action

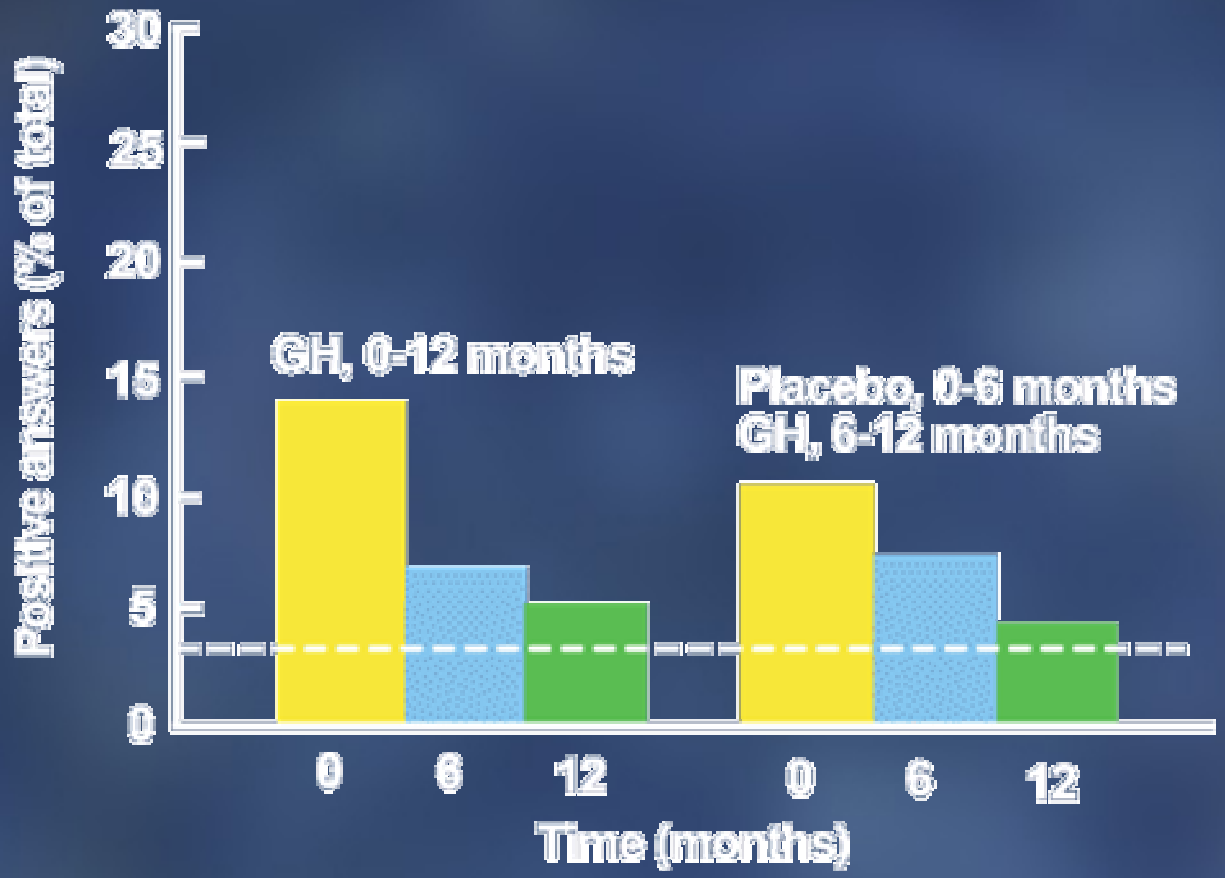
Stimulation of bone and cartilage growth

CNS action (Nervous System Rebuilding)

GH replacement therapy improves energy based on the Nottingham Health Profile



GH replacement therapy improves social isolation scores of the Nottingham Health Profile



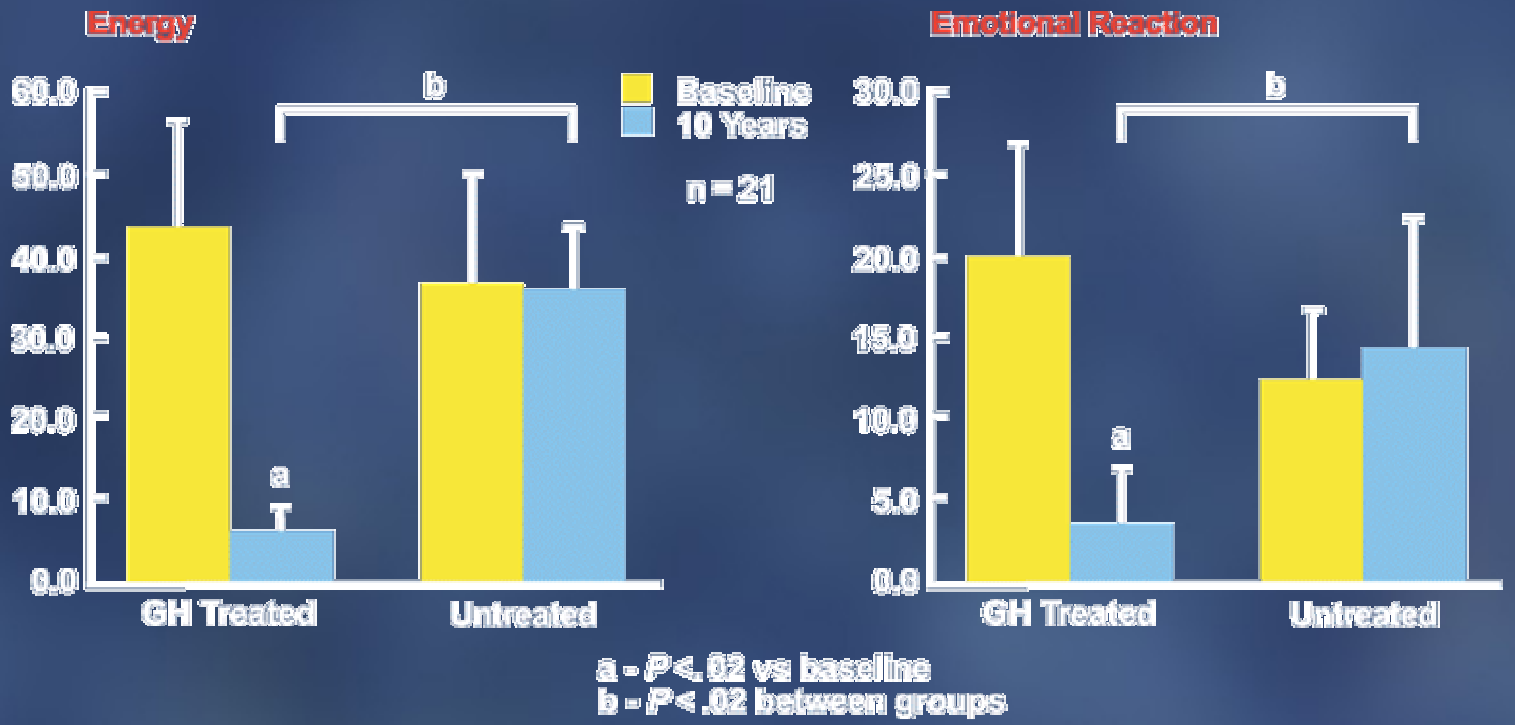
Mårdh G et al. *Endocrinol Metab* 1994; 1 (Suppl A): 43-9

The dose of GH used for replacement therapy must be tailored to the needs of the patient

Treatment should start with a low dose, which should be increased gradually until symptoms abate and IGF-I levels are normalized

Energy level and emotions are better based on the Nottingham Health Profile

- NHP revealed improvements in overall score
- Improved energy levels and emotional score in GH treated 10-year group vs. untreated



Gibney J et al. The effects of 10 years of recombinant human growth hormone (GH) in adult GH-deficient patients. *J Clin Endocrinol Metab*. 1999; 84: 2596-2602.

GH Deficiency causes more body fat

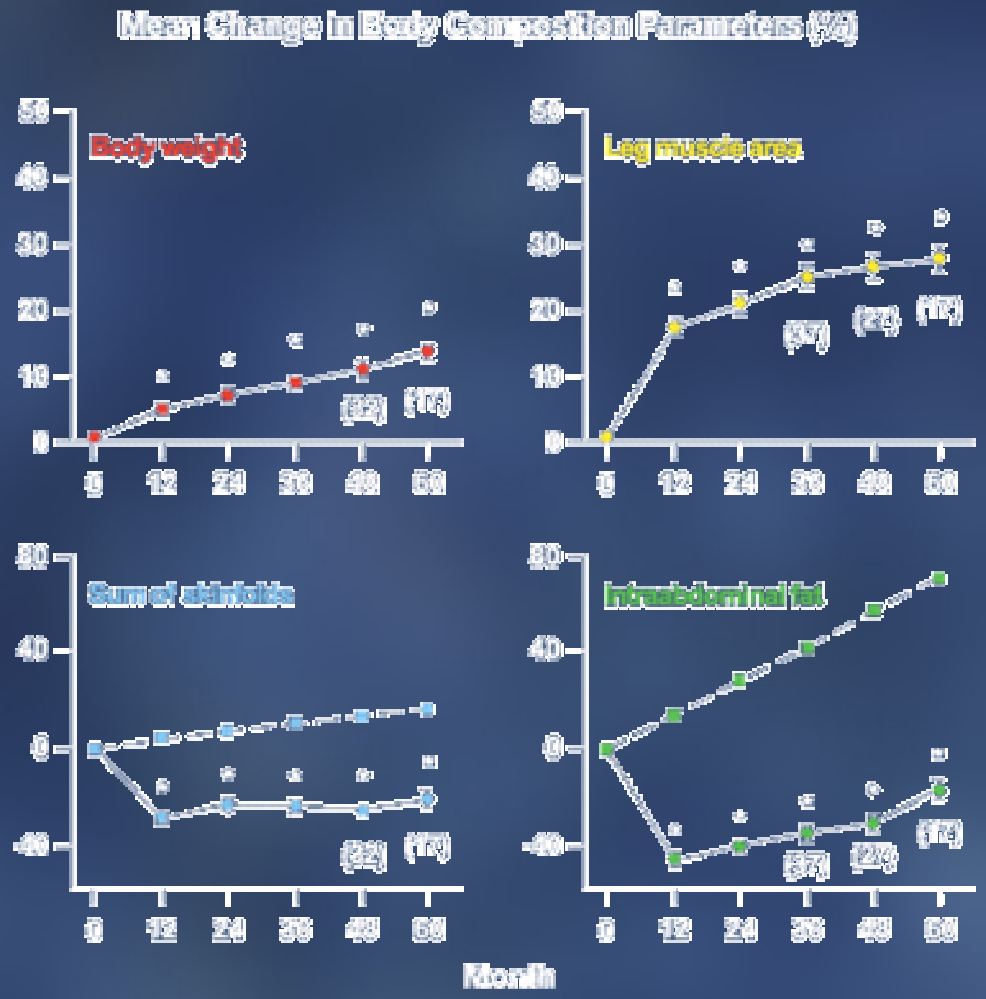


Fig. 1. Mean (±SE) measured (•) and expected (■) changes in body composition parameters from baseline values in men with GHD receiving GH for 5 yr. Data are shown for body weight, leg muscle area (measured by computed tomographic scanning), sum of skinfolds (measured at seven sites with a Harpenden skinfold caliper), and intraabdominal fat (measured by computed tomographic scanning). n = 38 unless stated otherwise. *, $P < .001$ for comparison of changes from baseline.

Ter Maaten et al.

Long-term GH replacement increases bone density

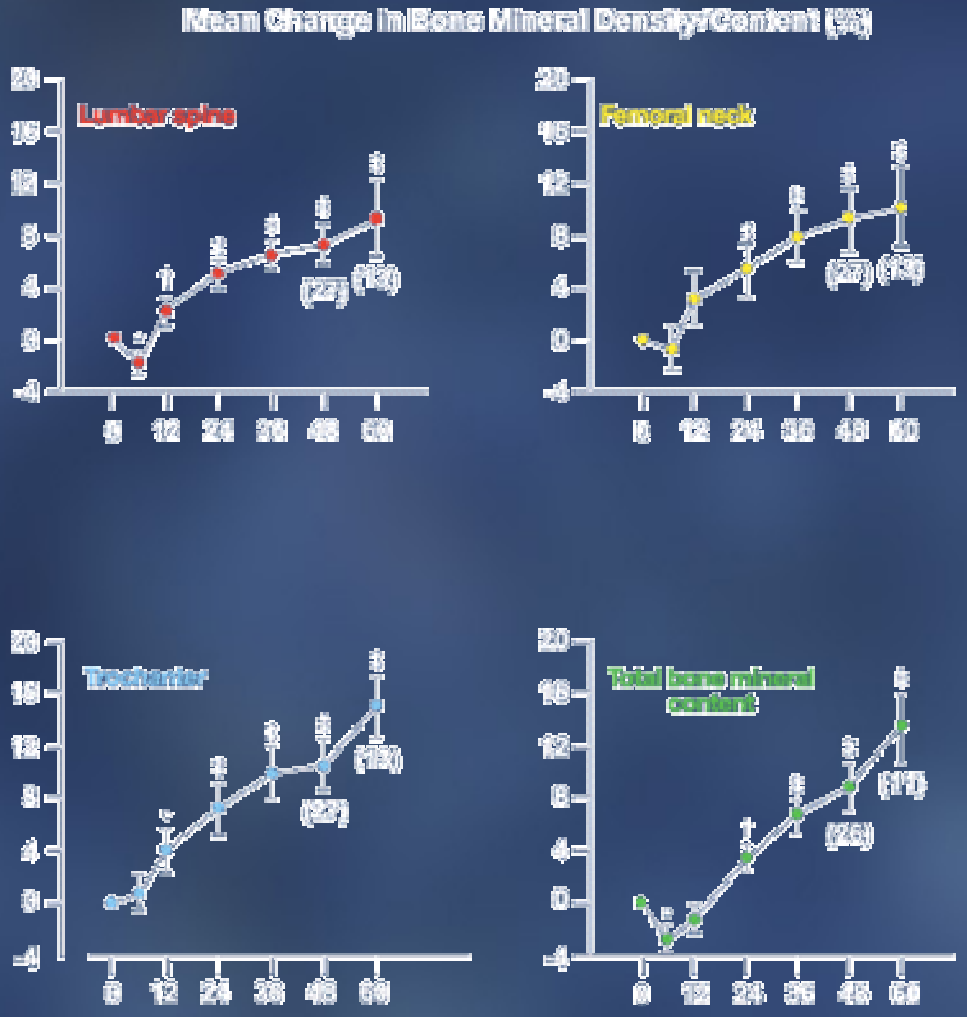


Fig. 2. Mean (±SE) changes in BMD/bone mineral content from baseline values in men with GHD receiving GH for 5 yr. Data are shown for BMD of the spine, femoral neck, and trochanter and for total bone mineral content (measured by dual energy x-ray absorptiometry). n = 38 unless stated otherwise. *, $P < .05$; †, $P < .01$; ‡, $P < .001$ (for comparison of changes from baseline).

How It Feels to be GH Deficient!