

## Growth Hormone in Athletes

## Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien vid Göteborgs universitet kommer att offentligen försvaras i Aulan, Sahlgrenska Universitetssjukhuset/Sahlgrenska fredagen den 14 september 2007 kl 09.00

av Christer Ehrnborg Leg. Läkare

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# Avhandlingen baseras på följande delarbeten:

I. Ehrnborg C, Lange KH, Dall R, Christiansen JS, Lundberg PA, Baxter RC, Boroujerdi MA, Bengtsson BA, Healey ML, Pentecost C, Longobardi S, Napoli R, Rosen T; GH-2000 Study Group.

The growth hormone/insulin-like growth factor-I axis hormones and bone markers in elite athletes in response to a maximum exercise test.

J Clin Endocrinol Metab. 2003 Jan;88(1):394-401.

II. Ehrnborg C, Lange KHW, Longobardi S, Healy ML, Dall R, Johansson H, Oden A, Cittadini A, Pentecost C, Christiansen JS, Bengtsson BA, Sonksen P, Rosen T; GH-2000 Study Group.

The GH/IGF-I axis hormones and bone markers in elite athletes. A longitudinal study examining stability over 12 months in- and out-of-competition. *Submitted*.

III. Ehrnborg C, Ellegard L, Bosaeus I, Bengtsson BA, Rosen T.

Supraphysiological growth hormone: less fat, more extracellular fluid but uncertain effects on muscles in healthy, active young adults. *Clin Endocrinol (Oxf).* 2005 Apr;62(4):449-57.

Ciin Endocrinoi (Oxf). 2003 Apr,02(4).449-37.

IV. Berggren A, Ehrnborg C, Rosen T, Ellegard L, Bengtsson BA, Caidahl K. Short-term administration of supraphysiological recombinant human growth hormone (GH) does not increase maximum endurance exercise capacity in healthy, active young men and women with normal GH-insulin-like growth factor I axis.

J Clin Endocrinol Metab. 2005 Jun; 90(6):3268-73.

V. Ehrnborg C, Ohlsson C, Mohan S, Bengtsson BA, Rosen T. Increased serum concentration of IGFBP-4 and IGFBP-5 in healthy adults during one month's treatment with supraphysiological doses of growth hormone. *Growth Horm IGF Res.* 2007 Jun; 17(3):234-41.

## Growth Hormone in Athletes

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#### **Abstract**

Doping with growth hormone (GH) is a well-known problem both among elite athletes and among people training at gyms. It is mainly the anabolic and, to some extent, lipolytic effect of GH that is valued by its users. However, no reliable method to detect GH doping has been available, and the role of GH as an effective doping agent has been discussed.

The aim of this thesis was to investigate markers of the GH/IGF-I axis and specific bone markers in athletes in connection with a maximum exercise test and longitudinally for one year, to validate the use of these markers in a forthcoming doping test for GH. Furthermore, the effects of one month's administration of supraphysiological GH doses on body composition, exercise performance and IGFBP-4 and IGFBP-5 concentrations in well-trained healthy subjects were studied.

The response to a maximum exercise test displayed a fairly uniform pattern, with peak concentrations of markers of the GH/IGF-I axis and bone markers immediately after exercise, followed by a subsequent decrease to baseline levels. The time to peak value for GH was significantly shorter for females compared with males.

Some of the markers show strong evidence of high *inter*- or *intra*-individual variations in resting samples during one year, based on analyses focusing on the right tail of the distribution in relation to a normal distribution. Post-competition values differed from resting values for several of the GH/IGF-I axis and bone markers. Ranges for post competition values and for each marker in each gender at specific time points in connection with a maximum exercise test, are presented.

The administration of supraphysiological doses of growth hormone for one month causes a dramatic increase in IGF-I levels, a reduction in body fat and an increase in the extracellular water volume. However, no significant increase in intracellular water volume was found, indicating limited anabolic effects by the supraphysiological GH doses.

Administration of supraphysiological doses of GH during one month did not improve power output or oxygen uptake in a bicycle exercise test.

Serum levels of IGFBP-4 and IGFBP-5 are increased by supraphysiological GH doses. Some of the effect of GH on IGFBP-4 and IGFBP-5 appears to be IGF-I dependent. However, the results do not support an obvious role for IGFBP-4 and IGFBP-5 as potential markers in a test for detecting GH doping.

In conclusion, this thesis describes different aspects of markers of the GH/IGF-I axis and specific bone markers in connection to rest and exercise, to be used in a forthcoming test for GH doping, in which IGFBP-4 and IGFBP-5 do not seem to have a role. Finally, no obvious anabolic effects on body composition or performance-enhancing effects were seen with supraphysiological GH doses; thus, questioning the role of GH as a potent doping agent.

*Key words:* Growth hormone, IGF-I, bone markers, doping, athletes, maximum exercise test, variability, supraphysiological, body composition, physical performance, IGFBP-4, IGFBP-5.