

# Testosterone, 17 $\beta$ -estradiol and pubertal growth

Akademisk avhandling

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Av

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Avhandlingen baseras på följande delarbeten:

- I. **Albin AK**, Niklasson A, Westgren U, Norjavaara E.  
Estradiol and pubertal growth in girls.  
Horm Res Paediatr. 2012;78(4):218-25.
- II. **Albin AK**, Norjavaara E.  
Pubertal growth and serum testosterone and estradiol levels in boys.  
Horm Res Paediatr. 2013;80(2):100-10.
- III. **Albin AK**, Ankarberg-Lindgren C, Nilsson S, Niklasson A, Norjavaara E, Albertsson-Wikland K;  
Growth and serum testosterone during puberty in growth-hormone-treated short boys without growth hormone deficiency.  
In manuscript
- IV. **Albin AK**, Ankarberg-Lindgren C, Tuvemo T, Jonsson B, Albertsson-Wikland K, Ritzén EM; on behalf of the study group.  
Does growth hormone treatment influence pubertal development in short children?  
Horm Res Paediatr. 2011;76(4):262-72.



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## ABSTRACT

**Background and aims:** It is well established that the interaction of sex steroids with the growth hormone (GH)/ insulin-like growth factor 1 (IGF-1) axis is of major importance in children for normal pubertal growth. However, detailed understanding is still lacking. The overall aims of this thesis were to study the association between testosterone, estradiol and pubertal growth in healthy girls (Paper I), in boys (Paper II), and in GH-treated short boys without deficient GH secretion (Paper III), and to study the impact of GH treatment on pubertal development (Paper IV).

**Patients and Methods:** In the first two papers, 35+37 profiles of 24-hour serum 17 $\beta$ -estradiol and 41 profiles of serum testosterone were analyzed in relation to pubertal height velocity in 27 girls and 26 boys. The children were referred to the endocrine unit for short or tall stature, or were recruited as healthy volunteers at the Göteborg Pediatric Growth Research Center. The short children without deficient GH secretion in Paper III and IV were enrolled in a randomized, controlled, multicenter dose-response study performed in Sweden and were randomized into three groups: untreated controls, GH 33  $\mu$ g/kg/day, or GH 67  $\mu$ g/kg/day. Paper III studied 65 boys and Paper IV studied 124 children (33 girls). Serum testosterone was measured by a modified radioimmunoassay (RIA), detection limit 0.03 nmol/L. Serum 17 $\beta$ -estradiol was determined using an ultrasensitive extraction RIA, detection limit 4 pmol/L. To calculate height velocity, a sixth-degree polynomial was fitted to each child's individual height measurements and its derivatives were used to estimate height velocity with accelerations and decelerations.

**Results:** Using a dose-response model, the EC<sub>50</sub> for serum estradiol and testosterone was calculated as the concentration at a 50% gain in height velocity from prepuberty up to peak height velocity (PHV) in puberty. The EC<sub>50</sub> for estradiol in Paper I and II was 20 pmol/L (95% confidence interval 13–31) for girls and 6.5 pmol/L (3.2–13) for boys. The EC<sub>50</sub> for testosterone in boys was 3.1 nmol/L (2.4–4.2). Serum estradiol levels >51 pmol/L were found in girls close to PHV. In boys close to PHV, serum levels of estradiol and testosterone were >9 pmol/L and >10 nmol/L, respectively. GH-treated boys in Paper III showed lower testosterone levels in relation to pubertal height velocity in a GH dose-dependent manner compared to untreated controls. However, it was apparent that the calculated PHV did not accurately represent pubertal PHV, as this calculation could not discriminate pubertal PHV from catch-up growth stimulated by the GH treatment. Boys with longer duration from GH start to PHV or from puberty onset to PHV, where most of the catch-up growth finished before pubertal growth started, had similar EC<sub>50</sub> values to the untreated boys. GH treatment in the boys and girls in Paper IV had no effect on age at onset of puberty or final maturation compared to controls. GH-treated boys had significantly greater maximum mean testicular volumes without differences in testosterone levels, and GH-treated girls showed a significantly longer pubertal duration compared to their controls.

**Conclusions:** Serum estradiol levels seen in early puberty in girls and serum testosterone in early transition to midpuberty in boys are associated with accelerated height velocity. There was no indication of negative impact of GH treatment on pubertal onset or progression in short children without deficient GH secretion.

**Keywords:** Testosterone, estrogen, pubertal growth, growth hormone treatment

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