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# SEX STEROID SECRETION DURING CHILDHOOD IN MALES

- with focus on prematurity, birth size, and growth  
patterns

Akademisk avhandling

Som för avläggande av medicine doktorexamen vid Sahlgrenska akademien,  
Göteborgs universitet kommer att offentligen försvaras i föreläsningssal Tallen,  
Drottning Silvias barnsjukhus, den 12 november 2021, klockan 09.00

av Kjersti Kvernebo Sunnergren

Fakultetsopponent:

Professor Anders Juul

Afdeling for Vækst og Reproduktion,

Rigshospitalet og Institut for Klinisk Medicin, SUND, Københavns Universitet

## Avhandlingen baseras på följande delarbeten

- I. Kvernebo-Sunnergren K\*, Ankarberg-Lindgren C\*, Åkesson K, Andersson MX, Samuelsson L, Lovmar L, Dahlgren J. Hyperestrogenism affects adult height outcome in growth hormone treated boys with Silver-Russell syndrome. *Frontiers in Endocrinology* 2018; 9:780
- II. Kvernebo Sunnergren K, Ankarberg-Lindgren C, Dahlgren J. Adrenal and gonadal activity, androgen concentrations, and adult height outcomes in boys with Silver-Russell Syndrome. *Frontiers in Endocrinology* 2019; 10:829
- III. Kvernebo Sunnergren K, Karlsson AK, Allvin K, Nilsson S, Ankarberg-Lindgren C, Dahlgren J. Adrenal androgen trajectories are established during childhood in preterm boys. *Acta Paediatrica* 2021; 00:1–8. *Online ahead of print*
- IV. Kvernebo Sunnergren K, Dahlgren J, Karlsson AK, Nilsson S, Allvin K, Ankarberg-Lindgren C. Estrogen and testosterone concentrations during childhood are inversely associated with birth weight in preterm boys. *Submitted manuscript*

\* Shared first authorship

**SAHLGRENSKA AKADEMIN  
INSTITUTIONEN FÖR KLINISKA VETENSKAPER**



# SEX STEROID SECRETION DURING CHILDHOOD IN MALES

## -with focus on prematurity, birth size, and growth patterns

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### Abstract

**Aim:** The overall aim of the thesis was to evaluate sex steroid secretion patterns during childhood in boys and to study how sex steroid concentrations relate to gestational age, birth weight, growth patterns, and adult height outcome.

**Patients and Methods:** In paper I, 11 growth hormone-treated boys with Silver–Russell syndrome (SRS) who had reached adult height were included. In paper II, two further patients were added. Data on birth characteristics and growth at 6, 8, 10, 12, 14, and 16 years of age were collected retrospectively. Blood samples taken at the same ages, were analyzed for sex steroid concentrations. Two groups were defined and compared, those who reached an unexpected short adult height (non-responders) and those with an expected adult height (responders). Correlations between sex steroid concentrations and adult height were assessed. In papers III and IV, 58 boys born at gestational age 32+0 to 36+6 were followed prospectively. Growth data and sex steroid concentrations were analyzed at 5, 6, 7, 8, and 10 years of age, and correlations between sex steroid concentrations and both birth characteristics and growth patterns were assessed. Mass-spectrometry-based methods were used for sex steroid analysis in all four papers.

**Results:** Paper I showed that non-responders had higher estradiol ( $E_2$ ) at 10–14 years of age and less pubertal height gain compared to responders.  $E_2$  at 10 years of age correlated strongly and negatively with adult height. In paper II, non-responders had higher adrenal androgens from 10–12 years and higher gonadal androgens from 10–14 years of age, compared to responders. There were strong negative correlations between dehydroepiandrosterone-sulfate (DHEAS) (8–12 years), testosterone (10–14 years), and dihydrotestosterone (DHT) (10 and 12 years of age), and adult height. In paper III, DHEAS and androstenedione ( $A_4$ ), correlated with weight at 7–10 years and DHEAS with waist-to-height ratio (WHtR) at 7 and 10 years of age; longitudinal analysis also showed significant associations between weight and WHtR and DHEAS and  $A_4$ . The trajectories of adrenal androgens were established at 5 years of age. Paper IV showed negative correlations between both testosterone at 8 and 10 years and  $E_2$  at 10 years of age and birth weight, both in grams and standard deviation score.

**Conclusions:** Birth weight was inversely associated with concentrations of testosterone from 8 to 10 years and  $E_2$  at 10 years of age in preterm boys. Childhood adrenal androgen concentrations were associated with body weight and WHtR but not with birth weight and adrenal androgen trajectories were established at 5 years of age. In boys with SRS, non-responders had higher concentrations of sex steroids from 10 to 14 years of age. Prepubertal and pubertal sex steroid concentrations correlated inversely with adult height and higher levels of adrenal androgens and earlier increase in gonadal androgens and  $E_2$  were associated with shorter adult height. The results of this thesis suggest that there is a relationship between birth weight, childhood sex steroid secretion patterns and growth patterns both in boys with SRS and in preterm boys without SRS.

**Keywords:** Androgens, birth weight, body height, body weight, child, estrogens, male, mass spectrometry, premature birth, Silver–Russell syndrome.

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