

childhood SBP. **Methods:** Brachial SBP was measured for 75 children aged 3-6 years from the Manchester BabyGRO Study, using a Tensiomed<sup>®</sup> Arteriograph with a child-sized cuff. SBP quartiles were generated. Participants were born to mothers who had attended a specialised clinic, following identification of higher FGR risk based on abnormal maternal serology (pregnancy associated plasma protein-A,  $\beta$ -human chorionic gonadotrophin,  $\alpha$ -fetoprotein, Inhibin-A). Antenatal ultrasound data at 23 weeks gestation were obtained. Uterine artery Doppler (UtAD) notching was assigned a rank (0=absent, 1=unilateral, 2=bilateral). Random forest (RF) is a machine learning approach that generates many independent, uncorrelated decision trees based on multiple variables. This was used to determine the relative importance of antenatal variables in prediction of upper quartile of childhood SBP. Variables included in the model were maternal body mass index (BMI), parity, ethnicity (black/white/asian/mixed), maternal SBP and diastolic BP (DBP), maternal serology relating to FGR risk, UtAD pulsatility index, resistance index and notching rank (all measures of uteroplacental blood flow resistance), placental size measurements, 23 week estimated fetal weight (EFW) centile,  $\Delta$ 23w EFW-birthweight centile and birthweight SDS. A receiver operating characteristic (ROC) curve was generated, providing an area under the curve (AUC). A variable of importance (VIP) score was calculated for each marker that was significant in the model. All analyses were conducted in R (version 3.6). **Results:** RF analysis demonstrated antenatal markers relating to FGR risk predict the upper quartile of childhood SBP with an AUC 0.97. The top five ranked variables were maternal DBP (VIP score 14.0), birthweight SDS (11.5), parity (9.9), notching rank (9.5) and  $\Delta$ 23w EFW-birthweight centile (9.1). **Conclusion:** Maternal and antenatal markers, as well as birthweight SDS are linked with the upper quartile of SBP at 3-6 years. Antenatal markers were within the top five ranked and could help identify those babies at risk of higher SBP in childhood.

## Pediatric Endocrinology

### PEDIATRIC ENDOCRINOLOGY: ADRENAL, THYROID, AND GENETIC DISORDERS

#### *Are Current Normal Values of 11DOC Useful for Diagnosis of Non Classical Congenital Adrenal Hyperplasia Due to 11 $\beta$ -Hydroxylase Deficiency?*

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**Background:** A non-classic form of 11 $\beta$ -hydroxylase deficiency (NC 11 $\beta$ -OHD) has been reported to cause mild androgen excess, with a clinical presentation of precocious puberty, menstrual cycle abnormalities, or hirsutism during adolescence. Since genetic diagnosis of NC 11 $\beta$ OHD is yet not routinely available, the current gold standard for biochemical diagnosis is elevated 11 DOC levels after corticotropin stimulation test (ACTHstimT). However, there are no clear hormone level cutoffs. One of the accepted references for basal and stimulated levels for the pediatric

population was published in 1991 by Lashansky et al<sup>1</sup>. **Aim:** To determine the correlation between 11DOC levels measured during ACTHstimT, clinical symptoms attributed to NC11 $\beta$ OHD and androgen levels at presentation, and long-term follow-up among children and adolescents with hyperandrogenism. **Methods:** a retrospective study including all patients who underwent ACTHstimT between 2007/2015, in one center, during which 11 DOC levels were routinely measured as part of the test. Clinical data was collected from the patients' medical files and, by telephone calls for complete long-term follow-up. 11DOC levels before and after ACTHstimT were categorized as elevated according to both pre-defined cut-offs; greater than 1.5 times the 95th percentile according to Lashansky<sup>1</sup> normal level for sex and age, and greater than 1.5 times the upper limit of the normal level of the commercial kit. **Results:** Data were complete at presentation for 136 patients, 92 females, and for long for 98 patients, 68 females, mean follow up duration of 3.1 years (1.37,5.09). There was no statistically significant difference in the number of cases with elevated 11DOC according to both cut-offs, among patients with precocious and early puberty, premature adrenarche nor acne. Higher baseline and stimulated 11 DOC levels were demonstrated in females who presented with mild hirsutism and regular menses. Long term data demonstrated no statistically significant difference in the number of cases with elevated 11DOC levels among patients with compromised final adult height, PCOS or hyperandrogenism. There was negative correlation between stimulated 11 DOC levels and basal levels of testosterone, androstenedione and DHEAS levels. **Conclusions:** This report demonstrates that the current interpretation of 11DOC levels, basal and ACTHstimulated in children, according to 1.5 times the highest range, of both, the Lashansky<sup>1</sup> acceptable norms for children, and some of the laboratory's kit, are not clinically applicable.<sup>1</sup>Lashansky G, Saenger P, Fishman K, Gautier T, Mayes D, Berg G and Reiter E. Normative data for adrenal steroidogenesis in a healthy pediatric population: Age- and sex-related changes after adrenocorticotropin stimulation. *J. Clin. Endocrinol. Metab.* 1991; 73(3): 674-686.

## Pediatric Endocrinology

### PEDIATRIC ENDOCRINOLOGY: ADRENAL, THYROID, AND GENETIC DISORDERS

#### *Associations of Size at Birth and Metabolic Syndrome Antecedents With Serum Spexin Levels in Prepubertal Children*

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**Background:** Spexin is a novel peptide implicated in food intake and obesity. The primary aim of this study was to analyze whether serum spexin levels, along with total leptin and active ghrelin levels were different in prepubertal children born small for gestational age(SGA)

and appropriate for gestational (AGA). Secondary aims were to analyze whether serum spexin, leptin and active ghrelin levels correlated with metabolic syndrome (MS) antecedents according to the Dietary and lifestyle-induced health effects in children and infants (IDEFICS) study. **Subjects and Methods:** We conducted a cross-sectional study on prepubertal SGA- (median: 5.6 yr) and 50 prepubertal AGA-born children (median: 5.9 yr). Anthropometric data, homeostasis model assessment of insulin resistance (HOMA-IR), plasma lipids, serum spexin, total leptin and active ghrelin levels were analyzed. Associations of serum spexin levels with MS antecedents according to the IDEFICS study were investigated. **Results:** Children born SGA had higher body mass index and waist circumference than AGA-born peers ( $p < 0.05$ ). Serum total leptin levels were higher in SGA-born children than in AGA-born peers ( $p < 0.05$ ). Plasma active ghrelin and spexin levels were not different between the subgroups ( $p > 0.05$ ). Children born SGA had higher MS risk scores than AGA-born peers ( $p < 0.05$ ). Small for gestational age-born children had higher plasma glucose, insulin and HOMA-IR than AGA-born peers ( $p < 0.05$ ). In children born SGA, the number of subjects with excess adiposity ( $N_{SGA} = 18$  (43.9%) and  $N_{AGA} = 7$  (14%),  $p = 0.016$ ) and insulin resistance ( $N_{SGA} = 14$  (34%) and  $N_{AGA} = 6$  (12%),  $p = 0.035$ ) was higher than in AGA-born peers. There was no significant difference in frequency of dyslipidemia between the subgroups ( $p = 0.19$ ). The frequency of children with more than one MS antecedent was higher in SGA-born children than in AGA-born peers (Chi-Square  $p < 0.01$ ). Metabolic syndrome risk score according to IDEFICS was higher in SGA born children than in AGA-born peers ( $2.2 \pm 1.8$  vs  $1.1 \pm 1.8$ ;  $p = 0.008$ ). Serum spexin levels were lower in children with MS antecedents than those without MS antecedents in both AGA- and SGA-born children [Serum spexin levels in AGA-born children with and without MS antecedents:  $48.5$  pg/mL (25-75% IQR:  $19.8$ - $93.8$  pg/mL) and  $143$  pg/mL (25-75% IQR:  $104$ - $211$  pg/mL),  $p < 0.001$ ; respectively, serum spexin levels in SGA-born children with and without MS antecedents:  $31.0$  pg/mL (25-75% IQR:  $16.5$ - $47.0$  pg/mL) and  $79.5$  pg/mL (25-75% IQR:  $49.5$ - $274.8$  pg/mL),  $p = 0.0016$ ; respectively]. In the whole study group, the most important factor associated with excess adiposity was history of being born SGA (Odds Ratio =  $91.3$  [95% CI:  $2.2$ - $374$ ;  $p = 0.017$ ]). **Conclusions:** Serum spexin levels were not different in SGA- and AGA-born children. Serum spexin levels were reduced in children with MS antecedents independent of size at birth.

## Pediatric Endocrinology

### PEDIATRIC ENDOCRINOLOGY: ADRENAL, THYROID, AND GENETIC DISORDERS

#### *Brain Tumours Involving the Areas of the Circadian System Result in Disturbances in Melatonin Secretion, Fatigue and Poor Quality of Life*

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**Background:** Sleep disturbances, circadian abnormalities and poor health are often reported in children with brain tumours. The objective of this study was to examine circadian function, sleep pattern, fatigue and mental health in these children. We hypothesized that children with tumours involving the areas of the circadian system have altered melatonin secretion.

**Design:** Cross-sectional study.

**Methods:** 309 children diagnosed with a tumour in the brain or cervical medulla and aged  $\leq 18$  years were identified, 174 met the inclusion criteria, and 68 consented to participate. They were divided according to their tumour location into 1) location involving the areas of the circadian system, i.e. diencephalon, pineal gland, brain stem and cervical medulla and 2) other areas. Sleep-wake patterns were assessed by two weeks of sleep diary recordings and actigraphy in 66 and 61 children, respectively. Diurnal saliva-melatonin levels were measured in 51 children. Sleep quality, fatigue and mental health were assessed in 65 children by Children's Sleep Habits Questionnaire, Strengths and Difficulties Questionnaire and Pediatric Quality of Life Inventory, Multidimensional Fatigue Scale and Generic Core Scale.

**Results:** All children had normal sleep-wake patterns without significant between-group differences. The children with tumours involving the areas of the circadian system had lower melatonin peak levels ( $p = 0.03$ ) and a tendency of lower levels at 00 h and 04 h (all  $p = 0.06$ ). Three patterns of diurnal melatonin profiles were observed: Normal, low peak and phase-shifted peak. In comparison of the two patient groups, more children with tumours involving the areas of the circadian system had melatonin profiles with low peak values (29% vs 13%) and one had phase-shifted peak (3% vs 0%), although not significant. These children were more affected by mental problems ( $p < 0.01$ ), more cognitively fatigued ( $p = 0.03$ ) and had poorer quality of life ( $p = 0.01$ ) than children with tumours located elsewhere.

**Conclusion:** Children with tumours affecting the areas of the circadian system including the diencephalon, pineal gland, brain stem and cervical medulla have altered melatonin secretion, are fatigued, have poor mental health and poor quality of life. Circadian disturbances may adversely affect health and have negative psychological impact.

## Pediatric Endocrinology

### PEDIATRIC ENDOCRINOLOGY: ADRENAL, THYROID, AND GENETIC DISORDERS

#### *Clinical Features and Remission Rate of Pediatric Graves' Hyperthyroidism Treated With Antithyroid Drug*

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**Introduction:** Pediatric Graves' hyperthyroidism needs long-term therapy and there is no specific guideline.