

## ENDObytes

A monthly summary and commentary of recent topical publications in Paediatric Endocrinology from Professor Wayne Cutfield and Associate Professor Paul Hofman of The Liggins Institute, University of Auckland, Auckland, New Zealand.

### **Hydrocortisone dosing during puberty in patients with classical congenital adrenal hyperplasia: an evidence based recommendation.**

Bonfig W, Pozza SBD, Schmidt H, Pagel P, Knorr D, Schwartz HP. J Clin Endocrinol Metab 2009; 94; 3882-8.

#### **Summary**

In 92 adolescents with congenital adrenal hyperplasia (CAH) total pubertal growth was reduced and the risk of short adult stature increased from 30 to 60% in those receiving higher doses of hydrocortisone doses of  $>17$  mg/m<sup>2</sup>/day. In an audit of a large CAH clinic population all children received hydrocortisone administered three times each day. Hydrocortisone dose adjustment was made based upon linear growth, skeletal maturity (bone age, goal within 1 year of chronological age) and early morning serum 17 hydroxyprogesterone (17OHP, goal  $<18$  mg/l). None of the children received GnRH analogues nor aromatase inhibitors to delay puberty. Final height was determined by age  $>18$  yrs, epiphyseal fusion on X-Ray and a height velocity  $<2$  cm/yr. Mean final height was  $159\pm 5.3$  cm in females and  $170.2\pm 6.2$  cm in males. There was no difference between the final heights of salt losing and simple virilising forms of CAH. During puberty the mean hydrocortisone dose was  $17.2$  mg/m<sup>2</sup>/day in females and  $17.9$  mg/m<sup>2</sup>/day in males. Total pubertal growth in the simple virilisers versus salt wasters was  $13.2$  versus  $13.7$  cm in girls and  $16.2$  and  $17.7$  cm in boys respectively (NS). The positive predictive value for short stature with increasing hydrocortisone dose has a curvilinear relationship with increasing risk of short stature at a dose of  $>10$  mg/m<sup>2</sup>/day. The risk of short stature (height  $<-2$  SD) increases from 30% with a hydrocortisone dose  $<17$  mg/m<sup>2</sup>/day to 40-60% with a dose of  $>17$  mg/m<sup>2</sup>/day.

#### **Commentary**

*Although the final heights of these patients are better than those published 10 years ago there were still an appreciable number with short adult heights. The hydrocortisone doses used were higher (mean  $17$  mg/m<sup>2</sup>/day) than used in most clinics during childhood and certainly during puberty. The total pubertal growth achieved was only about 60% of that achieved in normal males (26-28 cm) and females (23-25 cm) accounting for 10 cm of lost pubertal height in both sexes. There is growing recognition that pubertal growth is the most vulnerable phase of childhood growth to over-zealous glucocorticoid treatment in CAH. In our clinic the hydrocortisone dose is lowered to approximately  $10$  mg/m<sup>2</sup>/day during puberty with higher 17OHP values accepted whilst attempting to avoid virilisation in girls.*

### **Prevalence and trends of metabolic syndrome among Korean adolescents: from the Koreana NHANES Survey, 1998-2005mpact study.**

Park MJ, Boston BA, Oh M, Jee SH. J Pediatr 2009; 155; 529-34.

#### **Summary**

Supported by an educational donation from Pfizer New Zealand, manufacturers of Genotropin® (somatropin). Refer to [www.medsafe.govt.nz](http://www.medsafe.govt.nz) for further information.

The opinions in this publication are not necessarily those of the sponsor.

In Korean youth the prevalence of the metabolic Syndrome (MetS) has declined between 1998 and 2005 (2.2 to 1.8%) despite an increase in obesity prevalence (an increase of 6.5% in boys and 2.4% in girls) over that period. A total of 4,164 adolescents aged 10 to 19 years participated in the study. Cross sectional assessment occurred at three time points 1998, 2001 and 2005. BMI was used to define overweight as 85-94<sup>th</sup> percentile and obesity >95<sup>th</sup> percentile. Paediatric MetS was defined according to the IDF criteria. All subjects had a waist circumference  $\geq 90^{\text{th}}$  percentile for Korean children. Two or more of the following were required: fasting triglycerides >1.7 mmol/l, fasting glucose >5.6 mmol/l, blood pressure  $\geq 130$  mm Hg systolic,  $\geq 85$  mm Hg diastolic and/or HDL cholesterol <1.29 nmol/l. There was a family history of hypertension in 12.8% and diabetes mellitus in 8.9%. The prevalence of obesity in females increased from 5.2% in 1998 to 9.7% in 2001 and then decreased to 7.6% in 2005. In males the obesity prevalence progressively increased from 5.9% in 1998 to 11.6% in 2001 and 12.4% in 2005. Conversely the incidence of the MetS in the sexes combined slightly decreased over the same three time periods from 2.2% to 3.6% to 1.8%. Predictably the prevalence of the MetS was greatest in obese adolescents (26.1% in males and 14.7% in females). The commonest manifestation of the MetS was hyperglycaemia (22.7%) and hypertension the least common (7.7%).

#### **Commentary**

*Over the past 20 years we have seen an obesity epidemic in childhood with escalating rates of obesity. Paediatric endocrinologists have predicted that this will lead to an epidemic of type 2 diabetes and the metabolic syndrome amongst adolescents. Early reports from Japan supported this notion with parallel increases in obesity and type 2 diabetes prevalence. However recent studies are not reporting increasing prevalence rates of type 2 diabetes in adolescents. Interestingly, this study reports increasing rates of physical activity between 2001 and 2005 suggesting that exercise may reduce the rate of the MetS prior to a change in obesity prevalence. Worldwide it appears that the increase in type 2 diabetes cases are seen in specific ethnic groups such as Pacific Islanders, Indians and American Blacks and not in Caucasian or other Asian populations. The explanation of the vulnerability of these ethnicities to diabetes is not clear.*

#### **Kisspeptin serum levels in girls with central precocious puberty.**

De Vries L, Shtauf B, Phillip M, Gat-Yablonski G. Clin Endocrinol 2009; 71: 524-8.

#### **Summary**

Serum kisspeptin levels were found to be higher in 31 girls with central precocious puberty (CPP) compared to 14 age matched prepubertal control girls. Precocious puberty was defined as breast bud development <8 yrs of age, progressive breast development, and growth acceleration or bone age acceleration. A GnRH stimulated peak LH >5.0 IU/l was used to confirm but not diagnose (CPP). A commercial radioimmunoassay was used to measure serum kisspeptin. Kisspeptin levels were higher in CPP girls (15.4  $\pm$  10.7 pmol/l) than in control girls (8.4  $\pm$  1.0 pmol/l, p<0.02). There was no correlation between peak LH and kisspeptin level.

#### **Commentary**

*The distinction between CPP and premature thelarche (PT) can be challenging with no single gold standard diagnostic test. Although a GnRH stimulation test is invariably used it has high specificity but low sensitivity for the diagnosis of CPP. Thus the diagnosis is based upon a cluster of parameters that include GnRH testing, thelarche progression,*

Supported by an educational donation from Pfizer New Zealand, manufacturers of Genotropin<sup>®</sup> (somatropin). Refer to [www.medsafe.govt.nz](http://www.medsafe.govt.nz) for further information.

The opinions in this publication are not necessarily those of the sponsor.

*height acceleration and bone age acceleration. Hypothalamic kisspeptin stimulates the GPR54 receptor that activates GnRH secretion. Thus it is reasonable to hypothesise that centrally produced kisspeptin may cross the blood brain barrier and be present in the peripheral circulation. Whilst this hypothesis appears to have been borne out, the overlap between serum kisspeptin in CPP and control girls is too large for serum kisspeptin to be used as a diagnostic tool for CPP. There are several possible reasons as to why kisspeptin is poorly discriminatory in the diagnosis of CPP. Firstly serum levels may not accurately reflect CSF kisspeptin levels. Secondly, the time of the day may influence kisspeptin levels. Thirdly CPP may not always be due to activation through kisspeptin and may include direct activation of GPR54. Lastly it may not be a very precise assay. Clearly further studies are needed to evaluate whether serum kisspeptin has any value in the diagnosis of CPP.*