

beats/minute;  $P = .05$ ). The nondippers also presented greater end-systolic diameter (28.7 vs 25.9 mm;  $P = .001$ ) and left-ventricular end-diastolic diameter (47.8 vs 45.1 mm;  $P = .040$ ) and greater LVMI (90.2 vs 78.3 g/m<sup>2</sup>;  $P = .044$ ) compared with the dippers. During stepwise multiple regression, the most important factors affecting LVMI were mean HR (day) ( $b = -0.40$ ;  $P = .001$ ), high-frequency variable of heart rate variability ( $b = 0.38$ ;  $P = .016$ ), and hemoglobin A1c: ( $b = 0.67$ ;  $P = .001$ ).

**CONCLUSIONS:** A group of normotensive diabetic adolescents with abnormal nocturnal BP reduction and impaired heart rate variation also had impaired left-ventricular function. Our findings suggest that an altered diurnal BP profile, as a result of autonomic dysfunction, may contribute to the development of left-ventricular hypertrophy in patients with type 1 diabetes mellitus.

### **ADIPONECTIN AND PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR $\gamma$ EXPRESSION IN SUBCUTANEOUS AND OMENTAL ADIPOSE TISSUE IN CHILDREN**

**Submitted by Xiaonan Li**

Xiaonan Li, Susanne Lindquist, Gertrud Angsten, Torbjorn Myrnas, Jun Yi, Ronghua Chen, Stenlund Hans, Tommy Olsson, Olle Hernell

**INTRODUCTION:** Adiponectin is an adipocyte-specific protein with insulin-sensitizing properties. Peroxisome proliferator-activated receptor  $\gamma$  (PPAR $\gamma$ ) may be involved in its gene transcription.

**OBJECTIVE:** The aim of this study was to compare the expression levels of the genes that encode adiponectin and PPAR $\gamma$  in subcutaneous and omental adipose tissue in children in relation to age and anthropometric variables.

**METHODS:** Paired biopsies (from subcutaneous and omental adipose tissue) were obtained from 53 children (age: 0.2–14.0 years; BMI: 12.5–25.8 kg/m<sup>2</sup>). Messenger RNA (mRNA) levels of adiponectin and PPAR $\gamma$  were measured by using reverse-transcription and quantitative real-time polymerase chain reaction.

**RESULTS:** Adiponectin mRNA levels in adipose tissue were positively associated with PPAR $\gamma$  mRNA levels in children (subcutaneous adipose:  $r = 0.73$ ,  $P < .001$ ; omental adipose:  $r = 0.78$ ,  $P < .001$ ). In overweight children, the median adiponectin mRNA level was lower in omental adipose tissue (odds ratio: 0.51 [95% confidence interval: 0.1–2.17]) compared with subcutaneous adipose tissue (odds ratio: 1.29 [95% confidence interval: 0.16–5.08]) ( $P = .032$ ) but not in normal-weight children ( $P = .54$ ), and the difference remained significant after adjustment for age ( $P = .045$ ).

**CONCLUSIONS:** The close association between adiponectin and PPAR $\gamma$  expression supports the hypothesis

that PPAR $\gamma$  is involved in adiponectin gene regulation. The fact that adiponectin expression was decreased in omental adipose tissue relative to subcutaneous adipose tissue in overweight children suggests that a risk of insulin resistance may be present in childhood, which allows such resistance to develop after a relatively short duration of overweight.

### **EFFECT OF BODY WEIGHT ON BONE AGE AND HORMONAL PARAMETERS IN CHILDREN WITH PREMATURE ADRENARCHE**

**Submitted by Asteroula Papathanasiou**

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**OBJECTIVE:** Our goal was to investigate the effect of body weight on bone age (BA) and hormonal features in children with benign premature adrenarche.

**METHODS:** We studied 221 children (175 girls, 46 boys) with premature adrenarche (pubic and/or axillary hair at  $<8$  years of age in girls and  $<9$  years of age in boys) and mean chronological age (CA) at presentation of 7.0 years (girls) and 7.8 years (boys). Anthropometric features and laboratory data (dehydroepiandrosterone sulfate [DHEA-S], 17-hydroxyprogesterone,  $\Delta^4$ -androstenedione [ $\Delta^4$ -A], testosterone, estradiol, insulin-like growth factor I [IGF-I], cholesterol, triglycerides, high- and low-density lipoprotein cholesterol, and BA) were recorded. The population was divided into 3 groups according to BMI: (1) normal weight, (2) overweight (BMI: 85th–95th percentile), and (3) obese (BMI:  $>95$ th percentile). Children with late-onset congenital adrenal hyperplasia were excluded from study.

**RESULTS:** Mean CA of adrenarche was 6.3 years (girls) and 7.1 years (boys). The percentages of overweight and obese children was significantly higher than those reported in the general population of children in Greece. Obese children had significantly more advanced BA compared with overweight and normal-weight children. Higher levels of DHEA-S and  $\Delta^4$ -A were observed in overweight and obese girls compared with normal-weight girls, whereas higher levels of DHEA-S, testosterone, and IGF-I were observed in overweight and obese boys (Table 1). No statistically significant difference was observed between the 3 groups in the levels of 17-hydroxyprogesterone, estradiol, cholesterol, triglycerides, or high- and low-density lipoprotein cholesterol.

TABLE 1. Levels of Adrenal Androgens in Normal-Weight and Obese Children

	Normal Weight Mean (Range)	Overweight Mean (Range)	Obese Mean (Range)	<i>P</i> <sup>a</sup>
Girls				
Testosterone, ng/mL	0.11 (0.06–0.20)	0.14 (0.10–0.21)	0.16 (0.09–0.24)	.112
DHEAS, $\mu$ g/mL	0.71 (0.41–1.10)	0.85 (0.61–1.15)	0.88 (0.57–1.21) <sup>b</sup>	.081
$\Delta^4$ -A, ng/mL	0.4 (0.2–0.8) <sup>b</sup>	0.6 (0.4–1.1) <sup>b</sup>	0.6 (0.4–0.8) <sup>b</sup>	<.05 <sup>b</sup>
IGF-1, ng/mL	199 (140–318)	236 (180–283)	200 (190–266)	.681
Boys				
Testosterone, ng/mL	0.08 (0.04–0.15) <sup>b</sup>	0.17 (0.06–0.26) <sup>b</sup>	0.28 (0.09–0.39) <sup>b</sup>	<.05 <sup>b</sup>
DHEAS, $\mu$ g/mL	0.51 (0.21–0.92)	1.10 (0.82–1.24) <sup>b</sup>	1.12 (0.20–2.12)	.056
$\Delta^4$ -A, ng/mL	0.4 (0.2–0.7)	0.5 (0.3–0.6)	0.6 (0.4–1.0)	.524
IGF-1, ng/mL	200 (89–257) <sup>b</sup>	170 (116–207) <sup>b</sup>	288 (267–369) <sup>b</sup>	<.05 <sup>b</sup>

<sup>a</sup> Kruskal-Wallis test.

<sup>b</sup> Results were significant.

**CONCLUSIONS:** A higher frequency of obesity and advanced BA was observed in children with benign premature adrenarche, with a strong correlation between BA and degree of obesity. Furthermore, obese children were characterized by higher levels of adrenal androgens compared with normal-weight children.

## MANAGEMENT OF DIABETIC KETOACIDOSIS: SUCCESSFUL MANAGEMENT EXPERIENCE OF MORE THAN 32 YEARS

Submitted by Surendra Varma

Surendra Varma, Michael Bourgeois

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**INTRODUCTION:** Diabetic ketoacidosis (DKA) in children and adolescents has a mortality rate of 1% to 2%. The proper management of DKA requires intense monitoring and clear understanding of pathophysiology related to it. Potential complications include cerebral edema, hypokalemia, hypoglycemia, and relapse.

**OBJECTIVE:** Our goal was to describe our long-term experience in the management of diabetic ketoacidosis in children.

**METHODS:** This study comprised a 32-year experience of managing DKA in the pediatric age group. More than 900 episodes of DKA were encountered during this period. The age range of patients was from 9 months to 18 years. These episodes included patients presenting with new-onset type 1 diabetes as well as known patients with recurrent DKA. All patients were managed in a PICU by residents directly supervised by Dr Varma following an established protocol, including careful monitoring and paying particular attention to avoiding complications.

**RESULTS:** In >900 admissions during this period, the mortality rate was 0%, and the incidence of cerebral edema was <0.1%. Hypoglycemia and relapse occurred in <1% of the cases. The only occurrence of severe hypoglycemia (electrocardiographic changes and arrhythmia) was in a patient who was transferred from an outlying hospital after 36 hours of inappropriate treatment.

**CONCLUSIONS:** Our experience demonstrates that children with DKA can be managed successfully with minimal complications by adhering to the following principles:

1. early recognition and rapid transport to an ICU with experienced staff and physicians; and
2. adherence to well-established standards of treatment, including:
  - proper fluid and electrolyte management aimed at avoiding overhydration and extreme levels of electrolytes;
  - cautious correction of acidosis;
  - slow, steady reductions in plasma glucose and avoidance of hypoglycemia;
  - careful monitoring of clinical status (sensorium, state of hydration, vital signs, etc) and laboratory study results; and
  - frequent reassessment of the patient with adjustments and changes in treatment as dictated by the patient's needs.

## Epidemiology

### ASTHMA IN GREEK CHILDREN FROM BIRTH TO 18 YEARS: A LONGITUDINAL STUDY

Submitted by Flora Bacopoulou

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**INTRODUCTION:** The striking worldwide variation in the prevalence of asthma and its divergent changes over time necessitates regional longitudinal studies.

**OBJECTIVE:** We aimed to examine the asthma situation in Greece.

**METHODS:** Data from a longitudinal study of a representative nationwide sample derived from the National Perinatal Survey (11 049 consecutive births in April 1983) were analyzed in an attempt to describe the prevalence and natural course of asthma from birth throughout childhood to adolescence. We followed up with 2133 children (at the ages of 7 and 18 years) by using written questionnaires. The diagnostic labeling of asthma was confirmed by a physician on the basis of a history of wheeze attacks, nocturnal cough, exertional symptoms, and response to treatment.

**RESULTS:** Prevalence rates of current asthma were 7.7% and 4.7% and of lifetime asthma were 19.6% and 26.3% at 7 and 18 years, respectively. More than half (58.2%) of the children with early-onset asthma (onset before the age of 7 years) were free of symptoms at the

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