

## Pediatric Endocrinology

### PEDIATRIC PUBERTY, TRANSGENDER HEALTH, AND GENERAL ENDOCRINE

#### *Age of Critically Ill Children at Time of Exposure to Early Parenteral Nutrition Determines Its Impact on Long-Term Physical and Cognitive Development*

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#### SUN-072

##### Background

The PEPaNIC RCT, which investigated critically ill children admitted to the pediatric intensive care unit, showed that early administration of parenteral nutrition (early PN) as compared with withholding PN for 1 week (late PN) negatively affected 6 neurocognitive functions assessed 2 years later (1). However, it is theoretically possible that age at time of exposure determines whether early PN has negative or positive impact on long-term physical and cognitive development, possibly resulting in a neutral outcome for the total study population. In this secondary analysis of the PEPaNIC RCT, we investigated whether age at exposure to early PN determined its 2 years developmental impact.

##### Methods

The 786 children who were evaluated 2 years after inclusion in the PEPaNIC RCT for health status, anthropometrics, executive functioning, emotional and behavioral problems, intelligence and visual motor integration were categorized for age at randomization (0–17 years). We defined 4 ±similarly sized age groups based on previously reported timing of cerebral maturation spurts: neonates ≤28 days old (n=121), infants 29 days to <11 months old (n=239), toddlers 11 months to <5 years old (n=223), children 5 years or older (n=203). For each outcome, interaction between the randomized intervention and age at randomization was assessed with a multivariable linear regression analysis adjusted for baseline risk factors. For the outcomes with an interaction  $p \leq 0.15$ , we subsequently compared the adjusted effect of early PN versus late PN within each age group.

##### Results

Interaction between randomization and age group was identified for weight, development of inhibitory control, flexibility, working memory, planning and organization, metacognition, total executive functioning and internalizing and total behavioral problems. In particular among infants 29 days to <11 months old, harm by early PN was observed for several neurocognitive functions [inhibitory control ( $p=0.008$ ), flexibility ( $p=0.02$ ), working memory ( $p=0.009$ ), planning and organization ( $p=0.004$ ), metacognition ( $p=0.008$ ), total executive functioning ( $p=0.004$ ), internalizing ( $p=0.005$ ) and total behavioral problems ( $p=0.01$ )]. Among toddlers 11 months to <5 years old, neurocognitive harm by early PN was only observed for inhibitory control ( $p=0.003$ ) and total executive functioning ( $p=0.02$ ). In neonates ≤28 days old, early PN did not affect neurocognitive development whereas it increased weight ( $p=0.03$ ) but not height. Among children 5 years or older,

early PN only appeared to affect development of planning and organization in a positive manner ( $p=0.03$ ).

##### Conclusion

Critically ill children who were exposed to early PN at an age between 29 days and 11 months were found to be most vulnerable for neurocognitive developmental harm evoked by early administration of PN, as assessed 2 years later.

1 Verstraete et al. Lancet Respir Med 2018

## Neuroendocrinology and Pituitary

### PITUITARY TUMORS II

#### *Acromegaly Comorbidity Costs, Quality of Life, and Mortality: Lifetime Comparisons for Controlled Acromegaly, Uncontrolled Acromegaly, and the General US Population*

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#### MON-306

Acromegaly is a rare, chronic disorder characterized by hypersecretion of growth hormone (GH) that stimulates the production of insulin-like growth factor 1 (IGF-1). In addition to the physical manifestations, such as acral soft-tissue enlargement and maxillofacial changes, patients may develop a number of comorbidities, often prior to diagnosis. The goal of acromegaly treatment is to achieve biochemical control (normalization of GH and IGF-1 levels), which may resolve or prevent worsening of comorbid conditions. The objective of this study was to quantify the economic burden of comorbidities associated with acromegaly, including diabetes, hypertension, colon cancer, sleep apnea, and hypopituitarism. Comparisons were made between patients with acromegaly and biochemical control, patients with acromegaly without biochemical control, and the general population. Literature was reviewed to identify the prevalence of comorbidities among the groups, as well as the influence of each comorbidity on healthcare costs, quality of life, and mortality. Inputs from the literature were synthesized using a decision-analytic cohort model with a starting age of 55 years old and 55% female and extrapolated over a lifetime. Acromegaly-associated morbidity and mortality were not modeled due to possible double counting between acromegaly and other comorbidities. The average comorbidity count measure (range from 0 to 5) was a sum across all 5 comorbidity prevalence rates for all those living in the cohort per year of survival. Comorbidity prevalence was higher among acromegalic patients vs the general population for all comorbidities. Within acromegaly, uncontrolled disorder was associated with a higher prevalence of diabetes, hypertension, and sleep apnea. Lifetime discounted comorbidity costs were ~\$121,000, ~\$313,000, and ~\$406,000 in the general population, acromegaly controlled, and acromegaly uncontrolled populations, respectively. Lifetime discounted life years were 17.6, 16.9, and 16.7 in the general population, acromegaly controlled, and acromegaly uncontrolled populations, respectively. Lifetime discounted quality-adjusted life years were 14.6, 11.7, and 10.4 in in the general population, acromegaly

controlled, and acromegaly uncontrolled populations, respectively. Lifetime discounted average comorbidity count was 0.8, 1.9, and 2.4 in each group, respectively. Compared with controlled acromegaly, uncontrolled disorder resulted in \$93,000 additional comorbidity-related costs, 1.3 fewer years of perfect health, and 0.5 more comorbidities across the remaining lifespan. This simulation model suggests achieving biochemical control seems to be associated with improvements in cost, quality of life, and mortality. A multimodal treatment strategy including biochemical control and management of comorbidities is necessary to promote optimal patient outcomes.

## Pediatric Endocrinology

### PEDIATRIC ENDOCRINE CASE REPORTS I

#### *Auto-Destruction of the Thyroid and Coexisting Glutamic Acid Decarboxylase Mediated Neurological Disease in an Adolescent: An Unusual Presentation of Autoimmunity*

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#### SAT-066

**BACKGROUND:** Autoimmune thyroiditis (AT) is a common cause of acquired hypothyroidism in children characterized by lymphocytic thyroid infiltration. Sometimes gradual thyroid failure occurs due to apoptosis of thyroid cells. It may occur via apoptotic cytokines, ligands and receptors, including T regulatory cells, tumor necrosis factors etc. AT can coexist with other organ specific autoimmune conditions. Rarely neurological autoimmunity due to glutamic acid decarboxylase (GAD) antigen may be associated with AT. In fact, up to 70% of patients with GAD 65 neuropathy may have other autoimmune disease (AT, type 1 diabetes, pernicious anemia). We present a case of AT that led to total destruction of the thyroid gland with coexisting neurological autoimmunity.

**CLINICAL CASE:** A 7 yr old male presented with tiredness, heat intolerance and weight loss for 4 months, unsteady gait with frequent falls for 2 weeks. Exam showed tachycardia, firm thyromegaly and difficulty with tandem walking without other cerebellar signs. Labs showed undetectable TSH, elevated FT3, FT4 with positive thyroid antibodies, and negative for viral serology. MRI brain was normal and neurological symptoms resolved within few weeks. Thyroid ultrasound (TUS) showed hypervascularity and heterogeneity with right lobe volume (RLV) 2.8 cc, left lobe volume (LLV) 2.3cc with 0.9cm nodule. Thyroid scan showed increased uptake (52% and 61% at 4, 24 hrs). He required methimazole for 2.2 yrs. Five months later, at age 9.6 yrs he was hypothyroid and was started on Levothyroxine(LT4). TUS showed RLV 4.6cc, LLV 2.5cc and solid left nodule 1.2cm. FNA was consistent with AT. At age 14.4 yrs, TUS showed near complete involution of RL and isthmus with LLV 4.9cc and 0.6cm nodule and thyroid scan was negative for uptake. Repeat FNA reconfirmed AT. Due to progressive atrophic thyroiditis

he had hyperthyrotropinemia with euthyroxinemia (TSH range 12–165, Normal FT4 1.15–1.73) requiring increasing dose of LT4 over nearly 7.6 yrs.

At 14.8 yrs, he developed focal epilepsy treated with Levetiracetam and new-onset left fourth cranial nerve palsy. Autoimmune workup revealed extremely elevated GAD 65 antibodies in serum and cerebral spinal fluid, 1703 and 14.2 nmol/L respectively ( $N < 0.02$ ), confirming a diagnosis of GAD-65 central nervous system disease. He is currently receiving monthly IVIG.

At 15.3 yrs, complete atrophy of RL with involuting LLV 2.4cc was noted. He remains euthyroid and seizure free on anti-epileptics with recovering cranial nerve palsy.

#### CONCLUSION:

This is an unusual and extreme form of atrophic thyroiditis leading to near total destruction of thyroid gland related to apoptosis with autoimmunity. GAD-65 CNS autoimmunity is important to be considered in children with AT presenting with seizures or focal neurological signs. Continued vigilance and follow up for the development of other autoimmune conditions is warranted.

## Bone and Mineral Metabolism

### BONE AND MINERAL CASE REPORTS I

#### *A Novel Mutation in the Calcium-Sensing Receptor Gene Presenting in a Kindred as Autosomal Dominant Familial Hypocalciuric Hypercalcemia*

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#### SAT-351

A Novel Mutation in the Calcium-Sensing Receptor Gene Presenting in a Kindred as Autosomal Dominant Familial Hypocalciuric Hypercalcemia

**Rationale:** Familial hypocalciuric hypercalcemia (FHH) is a benign cause of hypercalcemia. The majority of cases result from an inactivating mutation in the calcium-sensing receptor (CaSR). While affected patients are usually asymptomatic and require no treatment, this condition may go unrecognized and inappropriate parathyroidectomy for presumed primary hyperparathyroidism could be performed. Over 130 mutations in the CaSR gene have been reported and novel variants continue to emerge.

**Methods:** The initial patient was a 49 year-old female who presented with mild hypercalcemia, elevated PTH and undetectable urine calcium. She reported several of her family members had elevated calcium levels. Given high clinical suspicion for FHH genetic analysis was performed.

**Results:** Sequencing of the CaSR gene revealed a point mutation at c.1744T>A which resulted in p.Cys582Ser in exon 7. This cystine residue is highly conserved and predictive algorithms suggest this variant is likely disruptive leading to heterozygous loss of function in the CaSR. The patient's 26 year-old daughter was tested and found to have the same mutation.

**Conclusion:** We report the identification of a novel heterozygous mutation in the CaSR gene manifesting as FHH in a family of Iraqi decent. Additional family members are currently undergoing genetic analysis which will be included at the time of presentation.