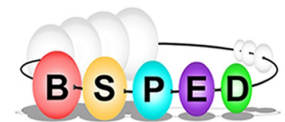


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## 44th Annual Meeting of the British Society for Paediatric Endocrinology and Diabetes 2016

23–25 November 2016, Nottingham, UK

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# CME Training Day

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**CME1**

**GH deficiency vs GH insensitivity**

Helen Storr  
London.

A wide range of disorders must be considered when assessing a child with Short stature (SS). The growth hormone (GH)-IGF-1 axis is essential for normal foetal and childhood growth and defects at many points in the axis will result in growth impairment leading to childhood and adult SS. Severe SS causes physical and psychological disadvantages and the underlying defects may be associated with increased morbidity. Comprehensive investigation of patients with abnormal auxology should lead to a diagnosis, particularly in extreme cases. However, the precise aetiology in many children may remain uncertain. One approach to the assessment of SS is to consider the continuum of GH-IGF-1 axis defects from GH deficiency through to GH insensitivity. The common feature of patients within this continuum is IGF-1 deficiency. The investigation of a child with short stature should follow established protocols. Detailed clinical assessment should include a thorough medical history and physical examination. Auxological evaluation is crucial and will establish the severity of the defect and the need for further investigations. The presence of subnormal height velocity confirms the need for detailed assessment. During the initial evaluation, non-endocrine pathologies should be excluded e.g. dysmorphic syndromes, skeletal dysplasias, small for gestational age and systemic diseases. Disorders of GH action frequently present with short stature in childhood. The growth failure is often clinically significant and may be extreme. Determination of GH secretion is recommended in patients with clinical and auxological features of GH deficiency (GHD) and/or IGF-1 levels below or in the low normal range for age and gender. A peak GH level of < 10 µg/l may be considered supportive of this diagnosis although many centres now use the stricter criteria of < 7.0 µg/l. In patients with normal GH secretion, defects in GH action i.e. GH insensitivity (GHI) should be considered. GHI is characterised by abnormal auxology, normal or elevated GH secretion and IGF-1 deficiency although a wide range of phenotypes and biochemical characteristics are seen. These disorders may result from defects in the GH receptor (GHR) (Laron syndrome) or post-GH receptor (downstream) defects. In its severe form, GHI is associated with dysmorphic and metabolic abnormalities.

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**CME2**

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**CME3**

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**CME5**

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**CME6**

Abstract unavailable.

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**CME7**

**Rare forms of Rickets**

Nick Shaw  
Birmingham.

Rickets is a disorder in which defective mineralisation of the growth plate occurs in growing children. The aetiology is due to deficiency of calcium and/or phosphate with hypophosphataemia being pivotal in the pathogenesis of all forms of rickets. It is convenient to classify rickets as calcipenic or phosphopenic depending on whether there is predominantly a deficiency of calcium or phosphate.

Although nutritional rickets is the most well known and prevalent form of rickets in the world there are a variety of rarer genetically determined causes. Principal amongst these is hypophosphataemic rickets where an understanding of the role of FGF23 has led to identification of several primary forms. The X-linked dominant form is the commonest for which a new treatment option with an FGF23 antibody is emerging. The role of activating somatic mutations in the RAS pathway in causing rickets in epidermal naevus syndromes has recently been recognised.

There are a variety of other secondary causes of hypophosphataemia, most of which are due to renal tubular loss of phosphate eg McCune Albright Syndrome. However dietary phosphate deficiency is also a potential cause with the recent recognition of the role of exclusive elemental formula feeds such as Neocate. Disorders in the Vitamin D metabolism pathway are also important to recognise and distinguish from nutritional rickets as they often occur in the same ethnic groups. These will require long term treatment with a Vitamin D analogue such as Alfacalcidol or Calcitriol rather than Vitamin D as used in nutritional rickets. This talk will provide an overview of rarer causes of rickets and will hopefully lead to early recognition by clinicians.

DOI: 10.1530/endoabs.45.CME7

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**CME8**

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# Main Symposia

## Symposia 1 Fertility

### S1.1

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### S1.2

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Abstract unavailable.

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### S1.3

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Abstract unavailable.

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## Symposia 2

### S2.1

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#### One gene to 100,000 genomes – the evolution of genetic testing in endocrine disorders

Abhijit Dixit  
Nottingham.

Developments in next-generation sequencing technology have revolutionised the landscape of genetic testing for heterogeneous genetic disorders. There is an emerging need for closer cooperation between endocrinologists and clinical geneticists, including the setting up of multidisciplinary clinics. Examples from a range of endocrine disorders and syndromes diagnosed by targeted single gene testing, multigene panel tests and whole exome/genome sequencing techniques will be presented and role of the clinical geneticist in the paediatric endocrine clinic will be highlighted.

DOI: 10.1530/endoabs.45.S2.1

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### S2.2

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Abstract unavailable.

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## Symposia 3 Complications of Diabetes

### S3.1

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#### Mitigating against future vascular disease. Do statins have a role in children and young people with T1D?

Carlo Acerini  
Cambridge.

Despite recent advances in diabetes care and modest improvements in glycaemic control, Type 1 diabetes (T1D) remains a major risk factor for early onset vascular disease, and is associated with a tenfold increase in cardiovascular related and all-cause mortality compared to the general population. Evidence of vascular endothelial dysfunction and early subclinical atherosclerotic disease can be detected during childhood, and is significantly more prevalent in children and adolescents with T1D in whom vascular changes appear to be soon after diagnosis and accelerate during puberty. The pathogenesis of these vascular abnormalities can in part be attributed to the underlying dyslipidaemia that occurs in T1D. Early management and treatment of abnormal lipid levels is advocated and should not be delayed given that optimised glycaemic control alone is unlikely to normalise lipid profiles. Treatment with oral HMG-CoA reductase inhibitors (i.e. statin agents) has been shown to be highly efficacious and safe at reducing LDL cholesterol (LDL-C) levels and at decreasing the risk of first cardiovascular disease events, including stroke and myocardial infarction, in adult patients with or without diabetes; irrespective of severity of the initial lipid profile. Statins may have effects other than the reduction in cholesterol levels, including inhibition of arterial smooth muscle cell proliferation, prevention of oxidation of LDL-C, plaque stabilisation, effects on macrophages, improvement of endothelial dysfunction, as well as anti-inflammatory and anti-thrombotic effects. Currently, experience of using statins in children has been limited to those with disorders of lipid metabolism such as familial hypercholesterolaemia, where the safety profile of treatment with these drugs has been excellent. There thus appears to be sound rationale for using statin agents in young people with T1D, particularly in those patients with risk factors or signs of early (micro)vascular disease, however the clinical benefits and long-term cost-effectiveness of treatment in this setting are yet to be determined. Ongoing clinical trials and future longitudinal studies should hopefully address these outstanding issues and are eagerly awaited.

DOI: 10.1530/endoabs.45.S3.1

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### S3.2

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Abstract unavailable.

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### S3.3

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## Symposia 4 Living life with Diabetes

### S4.1

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#### Diabetes and an eating disorder - my experience

Poppy Watkins  
Nottingham.

I was diagnosed with type 1 diabetes when I was 10 years old. Then in 2014, when I was around 15 years old, I began developing an eating disorder which was diagnosed as a combination of both anorexia and bulimia tendencies. After struggling with the condition, as it got increasingly worse, by myself for around 4 months I was referred to CAMHS. Having an eating disorder made my HBA1C



very unsteady and rather high (but never above 9%/ 75 mmol/mol), which in turn made me suffer with headaches and migraines and the constant feeling of tiredness. After around a year and a half of counselling from CAMHS and additional private 'Tapping' therapy, I began getting better and the bulimia tendencies began to fade. It was around the 2 year mark I was discharged from CAMHS. My HBA1C took roughly 9 months after being discharged from CAMHS to return to a normal healthy level. Eating disorders in young people with diabetes are more common than people realise and can take many different forms. I hope that by sharing my story, I can raise awareness of this and also show that it is possible to recover and do well.

DOI: 10.1530/endoabs.45.S4.1

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## **S4.2**

### **Diabetes and eating disorders make strange bedfellows: Challenges for young people and clinicians**

Deborah Christie  
London.

#### **Introduction**

Young people with an eating disorder are likely to have a morbid preoccupation with weight and/or shape associated with a dread of fatness, a determined avoidance of food with dramatic loss of weight (Anorexia nervosa) or binge-eating followed by self-purging through self-induced vomiting, use of laxatives or diuretics (Bulimia Nervosa). Diabetes is uniquely placed to offer opportunities for weight and shape control without overt avoidance of food. It is increasingly recognised that adolescents may manipulate their insulin dose and/or diet because of weight and shape concerns in ways that may not be immediately or easily identified as symptoms of an ED.

#### **Methods**

Estimates of the prevalence of ED in young people with diabetes vary however it is well recognised that poor glycaemic control may therefore reflect insulin omission in association with disordered eating which may be driven by weight and shape concerns as well as additional emotional disorders.

#### **Results**

Classical approaches to eating disorder diagnosis and management need to be modified to incorporate the specific demands of diabetes regimens. Clinicians need to take into account potential insulin omission, dietary dissatisfaction or manipulation, body dissatisfaction and family functioning as well as high numbers of admission to hospital and/or failure to attend clinic appointments.

#### **Conclusion**

Aspects of proven eating disorder treatments may be helpful but must be modified to take into account the demands of the diabetic regimen to include insulin requirement, levels of acceptable metabolic control, body mass, diabetes related dietary restrictions and the relationship between the family as well as the diabetes team. The presentation will describe the evidence base for interventions as well as consider practice based evidence. The personal perspective of a young person who lives with diabetes and has been bullied by an eating disorder will provide a unique insight into this challenging clinical dilemma.

DOI: 10.1530/endoabs.45.S4.2

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## **S4.3**

Abstract unavailable.

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# Diabetes Professionals Session

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## DP1.1

### Safeguarding and diabetes – social care perspective

Tracey Nurse  
Nottingham.

#### Introduction

Following a child death in Nottingham city, concerns emerged around unmet medical needs. As a result joint work took place with health colleagues to establish a shared understanding of medical neglect and impact on the child. This highlighted the need to strengthen the process for identifying and managing such cases.

#### The Methods

Social care developed a local protocol for managing cases where medical neglect heightened child protection concerns.

#### Results

- Local protocol now embedded and has been applied particularly in cases involving children with diabetes where medical needs not consistently met, and concerns exist which may cross threshold into child protection.

#### Discussion / Conclusion

- Now embedded in Children's Social Care.
- Multi-agency seminars have taken place to increase awareness of medical neglect in particular in relation to diabetes.

Need for early identification and early intervention.

DOI: 10.1530/endoabs.45.DP1.1

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## DP1.2

### Systemic Psychotherapy: an effective tool for treating children and young people diagnosed with Type 1 Diabetes

Esther Robertson  
Nottingham.

The Best Practice Tariff standards for paediatric diabetes state that each patient must have an annual assessment of their emotional health related to their diabetes. The assessment determines whether input to their care by a clinical psychologist is required and if so, they should have timely access to this or, as appropriate, children and young people's mental health services. Locally a Systemic Psychotherapist (Family Therapist) rather than a clinical psychologist undertakes this role. We decided to look at the utility of family therapy, and its effectiveness in delivering therapeutic intervention for children and young people diagnosed with Type 1 Diabetes. The presentation will aim to provide a paradigm of theoretical concepts and techniques underpinning family therapy. This will be achieved by selecting one aspect of family therapy, notably Narrative Concepts, which will be demonstrated using a 5 minute video clip of a family therapy session. The primary emphasis is to invite the participants to focus on the interactions in the here\_ and\_ now and see how past experiences can have a profound effect on the present. It also explores the link between the present and past. Research is embedded in the continuous development of family therapy. I will, therefore, conclude by offering material on current research studies which are evaluating the efficacy of this service.

DOI: 10.1530/endoabs.45.DP1.2

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## DP2.1

Abstract unavailable.

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## DP2.2

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## DP3.1

Abstract unavailable.

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## DP3.2

### Lipohypertrophy: Optimising insulin delivery and enhancing self-care behaviours

Carole Gelder  
Leeds.

#### Introduction

Lipohypertrophy (LH) is common in children and young people (CYP) with diabetes on both insulin injection and infusion therapy. Suboptimal injection and rotation, the presence of LH as well as increased use of insulin have all been associated with glycaemic variability, hypoglycaemia and raised HbA1c. Evidence based and data driven recommendations led to the Forum for Injection Technique 4th edition UK consensus document (FIT 2016). The latest edition also includes insulin infusion and psychological recommendations which have the potential to influence and enhance self-care behaviours and optimise health outcomes.

#### Methods

Contribution to an international audit provided a unique opportunity to benchmark local knowledge and skills in injection and infusion technique, rotation and LH detection against a dataset involving over 13000 participants. Interactive workshops comprising modelling by trained experts aided by real life volunteers with diabetes enabling hands on experience. This approach facilitated a unique opportunity to hone clinical examination technique in a safe learning environment with protected time.

#### Results

Real life examinations integrated with critical awareness of the evidence base provided opportunities for structured reflection on clinical practice. HCP's distinguished changes in skin texture due to LH whilst differentiating between muscle definition, the presence of faeces in the bowel, injection and infusion LH (more subtle in the latter) as well as locating transition zones to establish and monitor LH mass size.

#### Discussion / Conclusion

Notable benefits include tangible changes in routine care provision and enablement of self-management behaviours in this core aspect of diabetes care. Enhancement of self-care behaviours including more frequent site examination (to detect and prevent LH) and infusion site management (to expose and act on silent occlusions earlier, minimising interruptions to insulin flow) have the potential to further reduce the burden of care and optimise overall health outcomes.

DOI: 10.1530/endoabs.45.DP3.2

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# Endocrine Nurse Session

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**EN1.1**

**Ipsen BSPED Nurse Prize: Review of the nurse specialist's role in caring for children and young people with Cushing's syndrome**

Lee Martin  
London.

**Introduction**

The valuable and innovative work carried out by Paediatric Endocrine Nurses is not always recognised. The Ipsen BSPED Endocrine Nurse prize provides this group with a valuable platform to promote expertise and best practice; not just within their group but also to the wider multi-disciplinary team.

**Discussion**

Paediatric Cushing's syndrome (CS) is a very rare, life threatening disorder and the diagnosis/treatment of this condition is extremely challenging. Our centre is the major UK/European referral centre for children with suspected CS. Since 1982, we have investigated over 100 children and adolescents with suspected CS; 60 of these cases going on to be diagnosed with the syndrome. The aim of the project was to identify the unique role of the Paediatric Endocrine Nurse Specialist in the management of children affected by CS. It also explored how the Nurse Specialist improved and tailored the service to implement best clinical practice for the child and their family.

DOI: 10.1530/endoabs.45.EN1.1

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**EN1.2**

Abstract unavailable.

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**EN1.3**

Abstract unavailable.

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# Oral communications

## Oral Communications 1 – CME

### OC1.1

#### **Pan hypopituitarism – Is it secondary to brain tumour and its treatment?**

Ved Bhushan Arya & Helen Spoudeas  
Great Ormond Street Hospital, London, UK.

A 10-year old boy presented with 12-months history of headache, vomiting, declining school performance and change in behavior. There was no visual disturbance. Neurological examination was normal. Weight and height were between 50<sup>th</sup>–75<sup>th</sup> centile. CT head showed a large, partly calcified mass in the sellar region with acute hydrocephalus. Dexamethasone was immediately commenced and care was transferred to the neurosurgical centre.

MRI brain confirmed partly cystic, partly solid intra- and supra-sellar mass with displacement of anterior visual pathway and obstructive hydrocephalus. Pre-operative endocrine investigations showed normal prolactin, normal free T4 with low TSH, normal IGF1/IGFBP3 and normal serum sodium and osmolality. Serum cortisol was low (34 nmol/l), however this was measured post-commencement of dexamethasone.

Initial surgical management involved endoscopic cyst-aspiration and Ommaya reservoir insertion. Dexamethasone was stopped post-surgery and early morning cortisol after 48 hours was satisfactory (364 nmol/l). Subsequently tumor excision was undertaken (histology: adamantinomatous craniopharyngioma). Post-surgery, triphasic response (diabetes insipidus - syndrome of inappropriate ADH secretion - diabetes insipidus) was observed. Management involved intense monitoring of fluid balance, serum and urine electrolytes/osmolality and stat DDAVP doses until permanent diabetes insipidus was clearly established. Perioperative hydrocortisone cover was provided. Measurement of serum cortisol (pre-hydrocortisone dose) at 7 am, 8 am and 9 am (37, 41 and 41 nmol/l) indicated ACTH deficiency. Low fT4 (5.4 pmol/l) and low TSH (0.7 mU/l) post-operatively suggested TSH deficiency.

At discharge, the proband was on DDAVP, Levothyroxine and Hydrocortisone. Post-discharge, investigation with combined pituitary function testing (Growth Hormone [GH] stimulation, LHRH and TRH testing) showed absent GH, LH/FSH and TSH response, confirming GH deficiency, gonadotropin and TSH deficiency. GH treatment was commenced. In view of near-complete tumor resection, multi-disciplinary supra-regional discussion forum decided against radiotherapy treatment. Recurrence of craniopharyngioma was noticed 1-year after surgery, for which a second resection was undertaken after multi-disciplinary discussion.

#### Conclusions

Pituitary reserve should be assessed, if possible, before surgery to ascertain whether the deficit is secondary to tumor or its treatment. Anticipation of triphasic response (DI-SIADH-DI) and appropriate management is critical. Recurrence rate of craniopharyngioma is high without adjuvant radiotherapy. The difficult decisions regarding optimal treatment strategy are best taken in a supra-regional/national forum.

DOI: 10.1530/endoabs.45.OC1.1

### OC1.2

#### **Lysinuric protein intolerance: A cause of secondary IGF-I deficiency with raised growth hormone levels and osteoporosis**

Emily Cottrell & Talat Mushtaq  
Leeds Teaching Hospitals NHS Trust, Leeds, UK.

A 7.7 year old girl born to consanguineous was assessed for poor growth; height –3.2 SDS, weight –2.7 SDS, BMI –0.8 SDS. Examination revealed chubby cheeks, abdominal obesity, relatively thin limbs and a suggestion of mid-face hypoplasia. There was no scoliosis or other dysmorphic features.

Investigations found a 46XX karyotype and negative coeliac screen. Pituitary function testing revealed high basal Growth Hormone (GH) of 6.5 ug/l, rising to 25.5 ug/l, but with undetectable IGF-1 (<3.2). An IGF-1 generation test performed following 4 days of GH (0.035 mg/kg/day) displayed no increment in IGF-1. DNA analysis for a GHR mutation was negative. In tandem she was also investigated for a microcytic anaemia (Hb 113 g/l), neutropenia (1.4) and a raised LDH 1070 (160–430) and ferritin 898 (10–322). A bone marrow aspirate was normal. Metabolic investigations showed a pattern of amino acids consistent with lysinuric protein intolerance (LPI).

LPI is a rare autosomal recessive metabolic disorder affecting amino acid transport. The condition typically presents after an infant is weaned, with recurrent diarrhoea and vomiting especially following protein rich meals. It may have a multisystem clinical presentation including growth, haematological abnormalities and rarely osteoporosis. The diagnosis is based on biochemical findings, including increased urine concentrations of lysine, arginine and

ornithine but with low concentrations in the plasma. Molecular testing identifies two SLC7A7 pathogenic variants in more than 95% of individuals. Treatment includes citrulline and a low protein diet.

As LPI may be associated with osteoporosis, the bone health was further investigated. The Bone density Z-scores were –5.0 & –3.1 SDS at the Lumbar Spine (Bone Mineral Apparent Density) and total body respectively. A spine X-ray revealed multiple vertebral crush fractures associated with tenderness on palpation. Treatment with intravenous bisphosphonates improved the bone pain. Although low GH levels have been reported in LPI, IGF-1 deficiency with high GH has not been described. Furthermore, osteoporosis is rare presentation of LPI. In the investigation of growth abnormalities or recurrent fractures in childhood, an index of suspicion should be maintained in the presence of prevailing clinical or biochemical findings and LPI should be considered.

DOI: 10.1530/endoabs.45.OC1.2

## Oral Communications 2 – CME

### OC2.1

#### **Dyshormonogenesis secondary to two thyroglobulin gene mutations**

Elsbeth Ferguson & Paul Dimitri  
Department of Endocrinology, Sheffield Children's NHS Foundation Trust, Sheffield, UK.

#### Introduction

Dyshormonogenesis accounts for approximately 10–15% of cases of congenital hypothyroidism. Although relatively uncommon, the presence of a neonatal goitre should raise suspicion of thyroid dyshormonogenesis. Advances in genomic sequencing have identified errors at all stages of the thyroid hormone synthesis pathway. We present a case of a fetal goitre with the infant subsequently being diagnosed with dyshormonogenesis secondary to two separate thyroglobulin gene mutations.

#### Case Report

At twenty weeks gestation, routine fetal ultrasonography identified the presence of an anterior neck mass. Fetal goitre was subsequently confirmed on antenatal MRI scan. Maternal history was unremarkable. Maternal thyroid function was normal and maternal thyroid antibodies were negative.

At birth, a goitre was present but there was no evidence of airway compromise. Thyroid function tests performed after delivery revealed TSH > 100 mIU/l and T4 1.9 pmol/l. An ultrasound of the neck showed enlargement of the thyroid gland, no mass and no evidence of surrounding vessel or tracheal compression. A diagnosis of congenital hypothyroidism secondary to dyshormonogenesis was made. The infant was commenced on thyroxine and within four weeks thyroid function normalised.

In the first two years of life, TSH proved to be unstable, with T4 in normal range, despite good compliance. Consumption of even small amounts of milk in close proximity to thyroxine dosing were found to have a significant effect on thyroxine absorption in this patient.

Subsequent genetic investigation revealed the patient has a compound heterozygote mutation in the thyroglobulin gene (P.R296X/P.R787X), with both parents confirmed as being a heterozygote for mutations within separate parts of the gene.

#### Conclusions

This case demonstrates the process of investigation of fetal/neonatal goitres and allows revision of the thyroid hormone synthesis pathway. The diagnosis of dyshormonogenesis is discussed along with highlighting the problems with thyroxine absorption due to consumption of certain foods.

DOI: 10.1530/endoabs.45.OC2.1

### OC2.2

#### **A novel mutation in thyroid pathobiology in families with X-linked intellectual disability?**

Amish Chinoy & Indi Banerjee  
Department of Paediatric Endocrinology, Royal Manchester Children's Hospital, Manchester, UK.

Although congenital hypothyroidism is sporadic in the majority, recessive and X-linked inheritance can also occur in monogenic disorders. In familial cases, the finding of genetic variation could identify specific phenotypes and unravel thyroid pathobiology.

We describe three siblings born to non-consanguineous parents. The index case, a boy, presented at 1 year of age with severe developmental delay, expressive aphasia and hypotonia. Thyroid function showed elevated TSH and fT3 levels,

with fT4 being in the normal range. Thyroid ultrasound scan was normal and anti-TPO antibodies and anti-TSH-receptor antibodies were negative. He was treated with levothyroxine with reduction in TSH levels. A similar clinical phenotype was present in his younger brother, who was also treated with levothyroxine. Their elder sister had borderline hypothyroidism with elevated fT3 levels and mild learning disability. Genetic investigations excluded mutations in MCT8, MCT10, TRa1 T3 and Dio3 mutations. High resolution hybridisation arrays and next generation sequencing identified a hemizygous mutation in an X-linked gene in all children and their mother.

This X-linked gene mutation is associated with intellectual disability, short stature and behavioural issues, as observed in the family. However, a thyroid phenotype has not been reported. It would be important to recognise abnormal thyroid function in children with X-linked intellectual disability. The mechanism by which this mutation may cause thyroid dysfunction remains to be established, although we hypothesise a role in thyroid hormone transporters, as the phenotype is similar to children with MCT8 mutations.

DOI: 10.1530/endoabs.45.OC2.2

## Oral Communications 3 – CME

### OC3.1

#### A case of rare type of Rickets with unidentified genetic aetiology

Ved Bhushan Arya, Caroline Brain & Jeremy Allgrove  
Great Ormond Street Hospital, London, UK.

A 3-years-old young girl, born to Caucasian non-consanguineous parents, presented with bowed legs, noticed since the age of 18-months. She had no significant past medical or family history. On examination, her height was  $-1.3$  SDS (Mid parental height  $+1.87$  SDS). She had widened wrists, genu varum and rachitic rosary. She had areas of skin hyperpigmentation on left forearm and anterior thigh.

Investigations showed low 25-OH Vitamin D (35 nmol/l), normal serum calcium (2.35 mmol/l), low serum phosphate (0.68 mmol/l), elevated alkaline phosphatase (570 u/l) and normal PTH (6.3 pmol/l). X-rays of wrists confirmed rickets. Treatment with a 3-months course of 3000 IU daily of cholecalciferol resulted in no biochemical and radiological improvement. Follow-up investigations showed normal 25-OH Vitamin D (146 nmol/l), normal serum calcium (2.46 mmol/l), persistently low serum phosphate (0.77 mmol/l) and elevated serum alkaline phosphatase (657 u/l).

In view of low serum phosphate, tubular reabsorption of phosphate (TRP) was measured which was normal (81%; normal 70–100%). When TRP was corrected for low serum phosphate, it confirmed urinary phosphate wasting (TmP/GFR 0.56; normal range 1.10–2.70) and suggested a diagnosis of hypophosphataemic rickets. Elevated serum FGF23 levels (215 HRU/ml; Normal  $<100$ ), confirmed FGF23 mediated phosphaturia. Treatment with alphacalcidol (30 ng/kg) and oral phosphate (3 mmol/kg/d) resulted in gradual improvement in rickets.

No mutation was identified on sequencing of *PHEX* gene, excluding X-linked hypophosphataemic rickets, the commonest cause of hypophosphataemic rickets. Subsequently Sanger sequencing of *FGF23*, *DMP1* and *ENPP1* was performed, which did not identify any mutation either, excluding autosomal dominant and recessive hypophosphataemic rickets. Investigations (urine amino acids, urine glucose and tubular damage markers) for Fanconi syndrome were negative as well. Although the skin lesions were not classical of McCune-Albright syndrome and there was no evidence of fibrous dysplasia or endocrinopathy, sequencing of *GNAS1* from lymphocyte DNA and subsequently fibroblast DNA was undertaken, which was normal. Punch biopsy of the skin lesions was performed, which ruled out the diagnosis of epidermal naevi (known to be associated with hypophosphataemic rickets). Unfortunately FGF23 staining of sections of skin lesions is not available to establish these skin lesions to be the source of FGF23 and cause of hypophosphataemic rickets.

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### OC3.2

#### A rare cause of rickets

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#### Introduction

Nutritional rickets due to vitamin D and dietary calcium deficiency is common in the UK. However, nutritional rickets secondary to hypophosphataemia is rare. We present a rare case of hypophosphataemic rickets secondary to use of hydrolysed infant formula.

#### Case description

A 4 month old infant presented to ED with breathing difficulty. He was diagnosed to have bronchiolitis and admitted for further management.

He was born at 31 weeks by spontaneous vaginal delivery and required brief ventilatory support for the first 48 hours and was discharged home at 6 weeks. He had required repeated change in formula feeds due to constipation and recurrent vomiting. He was commenced on the hydrolysed formula Neocate for presumed cow's milk protein allergy at the age of 3 months.

#### Investigations and management

A chest radiograph performed to assess for lower respiratory tract infection suggested rickets and was confirmed on a knee radiograph. There was no family history of rickets. There were no clinical features of rickets except for mild physiological bowing of legs. Investigations revealed a normal plasma calcium, raised alkaline phosphatase (1000 iu/l) and normal parathyroid hormone (24 ng/l) with reduced plasma phosphate (1.23 mmol/l). Vitamin D deficiency was excluded due to sufficient serum 25(OH) levels (60 nmol/l). Hypophosphataemic rickets was suspected. Tubular reabsorption of phosphate of 99.5% excluded renal tubular losses.

#### Outcome

In the absence of other causes of rickets, nutritional hypophosphataemic rickets secondary to poor absorption of phosphate on a hydrolysed formula was suspected. He was commenced on phosphate supplements and one alpha calcidol which was subsequently stopped as he had a raised 1,25 dihydroxyvitamin D ( $>250$  pmol/l). The occurrence of hypophosphataemic rickets in the setting of the hydrolysed formula Neocate was confirmed following discussion with a colleague in the United States (case series awaiting publication).

#### Conclusion

Clinicians should exercise caution in the use of hydrolysed formula especially in the absence of objective evidence of cow's milk protein allergy. Specialised formula feeds should be initiated following thorough investigations. Infants on hydrolysed formula should have close monitoring of growth and nutritional status.

DOI: 10.1530/endoabs.45.OC3.2

## Oral Communications 4 – CME

### OC4.1

#### The clinical utility of Co-peptin measurement in paediatric endocrine practice

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#### Background

Arginine Vasopressin (AVP) measurement is difficult. When available there has historically been a lengthy interval between sampling and a result. Co-peptin is a 39 amino-acid glycopeptide that is derived from a pre-prohormone consisting of AVP, neurophysin II and co-peptin. It is released in an equimolar ratio with AVP into the circulation. Co-peptin is stable and can be used as a surrogate marker of AVP release in hyper and hypo-osmolar disorders. Many laboratories now measure copeptin because it is a useful marker of cardiovascular disease. The result is frequently available within a matter of hours. Levels are usually in the range 1 to 12 pmol/l and may be  $>20$  pmol/l in nephrogenic diabetes insipidus. We report two cases where the measurement of co-peptin levels provided the clinician with prompt, diagnostic feedback.

#### Case reports

**Case 1:** An 8 years old child with epilepsy, developmental delay and a ventriculo-peritoneal (VP) shunt for hydrocephalus secondary to neonatal meningitis presented with status epilepticus. A cranial CT scan did not demonstrate new pathology and full septic screen revealed streptococcus pneumonia meningitis. A revision of the VP shunt was performed and he was treated with antibiotics for 6 weeks. During the admission he developed hyponatraemia but was not clinically hypovolaemic. Hyponatraemia became more severe with intravenous fluid therapy including normal saline. Thyroid function and early morning cortisol level were normal and renin activity was suppressed. The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) was suspected and

	Day 14	Day 31	Day 34
Serum Sodium (mmol/L)	129	130	132
Serum Co-peptin (pmol/L)	13.7	10.1	9.5



confirmed by an inappropriately measurable co-peptin at the time of hyponatraemia.

**Case 2:** A 22 month old girl presented with a urinary infection and sepsis. She required fluid resuscitation and diabetes insipidus was considered because of initial hypernatraemia. Further investigations demonstrated an elevated serum co-peptin of 24.9 pmol/l when serum sodium was 150 mmol/l which ruled out cranial diabetes insipidus (CDI).

#### Conclusion

We have shown that copeptin can be used as surrogate marker of AVP release and can facilitate the diagnosis or exclusion of disorders such as CDI and SIADH.

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## Oral Communications 5 – Endocrine

### OC5.1

#### Effect of KRN23, a fully human anti-FGF23 monoclonal antibody, on rickets in children with X-linked hypophosphatemia (XLH): 40-week interim results from a randomized, open-label phase 2 study

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In XLH, high circulating FGF23 causes hypophosphatemia, rickets, and short stature. In our Phase 2 study, 52 XLH children (ages 5–12 years,  $\leq$  Tanner 2) were randomized to receive KRN23 subcutaneously biweekly (Q2W) or monthly (Q4W). Serum phosphate (Pi) was measured biweekly. KRN23 dose was titrated (maximum 2 mg/kg) targeting age-appropriate serum Pi concentrations.

The first 36 subjects had a mean 6.6 years of standard-of-care treatment before washout. Serum Pi increased from baseline in all subjects to near normal levels (mean increase 0.30 mmol/L at 38 weeks;  $P < 0.001$ ) and was more stable with Q2W dosing; hyperphosphatemia did not occur. KRN23 significantly improved rickets, assessed by the Thacher Rickets Severity Score (RSS), with greater improvements seen with Q2W dosing (44% reduction;  $P = 0.0126$ ) and particularly in higher-severity rickets patients (baseline RSS  $\geq 1.5$ ) (59% reduction;  $P < 0.0001$ ). Using the Radiographic Global Impression of Change (RGI-C;  $-3 =$  worsening;  $+3 =$  complete healing), Q2W dosing improved rickets by  $+1.6$  ( $P < 0.0001$ ) with the higher-severity rickets subset showing substantial healing ( $+2.0$ ;  $P < 0.0001$ ). Alkaline phosphatase, a marker of rickets severity, decreased. Most treatment-related adverse events (AE) were mild, most commonly a transient injection site reaction (39%). One child experienced a serious AE and was hospitalized for fever/muscle pain that improved and continues in the trial. No clinically significant changes occurred in serum or urine calcium, serum iPTH, or renal ultrasound. In summary, KRN23 improved

phosphorus homeostasis and rickets in children with XLH, with an acceptable benefit-risk profile.

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### OC5.2

#### Functionally significant reductions in white matter in patients with congenital adrenal hyperplasia

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#### Background

Management of patients with CAH remains challenging. There is increasing evidence to suggest that failure to optimize treatment during childhood not only affects final height but also leads to psychological and psychiatric problems, reflecting an underlying effect on neural development. Previous qualitative structural T2-weighted MRI studies have identified white matter hyper-intensities in up to 46% of CAH patients. The nature and functional relevance of these abnormalities remains unknown.

#### Objective and hypotheses

We aimed to identify novel MRI brain biomarkers of CAH using quantitative imaging and to examine their association with cognitive abnormalities.

#### Method

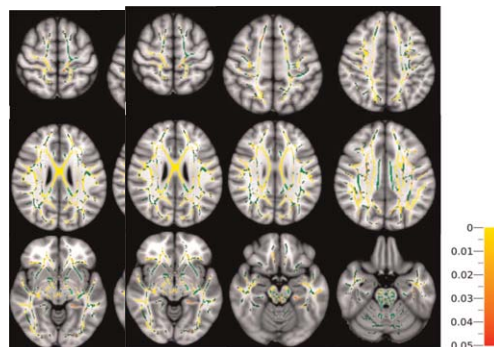
All participants completed subtests of the Cambridge Neuropsychological Test Automated Battery and underwent brain volumetric, magnetic resonance spectroscopy and diffusion tensor imaging. Freesurfer (neural volumes and cortical thickness), TARQUIN (metabolites) and Tract Based Spatial Statistics (fractional anisotropy) were used for neuroimaging data analyses. ANCOVA were performed to compare groups, adjusted for multiple comparisons. Partial correlations were performed to assess the relationship between MRI markers and neuropsychological measures controlled for age and socioeconomic status.

#### Results

Seventeen females with 21-hydroxylase deficiency and eighteen age-matched healthy females were recruited (32.7 and 28.6 years,  $P = 0.25$ ). Patients with CAH had significantly lower episodic memory, learning and spatial working memory ( $P < 0.001$ ) scores. Chiari 1 malformations (defined as downward displacement of  $> 5$  mm of the cerebellar tonsils through the foramen magnum) were identified in 4 of the 17 patients. Patients with CAH had significant reductions in total brain volume ( $P = 0.02$ ), corpus callosum volume ( $P = 0.03$ ), hippocampal N-Acetyl Aspartate ( $P = 0.03$ ) and choline ( $P = 0.002$ ), brain fractional anisotropy (Figure A,  $P < 0.01$ ) and parahippocampal cortical thickness (B, left, C, right,  $P < 0.05$ ). There were significant relationships between; corpus callosum volume and spatial working memory ( $P = 0.001$ ), parahippocampal thickness, episodic and working memory ( $P < 0.05$ ), hippocampal choline and rapid visual information processing ( $P < 0.02$ ).

#### Conclusion

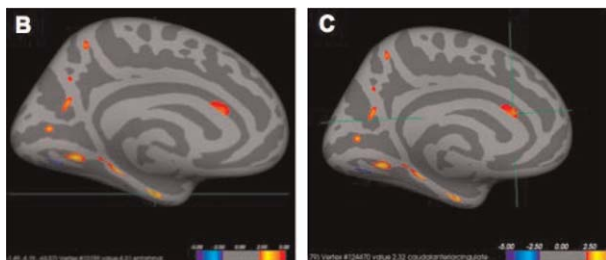
For the first time we have identified central nervous system imaging biomarkers of clinically significant cognitive abnormalities in patients with CAH. Further studies are required to determine the age of onset of these abnormalities and to develop preventative strategies.



A. Mean FA skeleton overlaid on the mean FA map. Regions of the mean FA skeleton in green represent areas where there were no significant differences in FA values in the patients with CAH compared to controls. Areas in red/yellow are regions where the FA was significantly lower in the CAH group. Colour map indicates the degree of significance for red and yellow regions.

		All Patients		Patients with Baseline Total RSS $\geq 1.5$		
		Baseline	Wk 40	Baseline	Wk 40	
Mean Total RSS	All (N=36)	1.4	1.0*	All (N=18)	2.3	1.2 <sup>#</sup>
	Q2W (N=18)	1.5	0.9*	Q2W (N=9)	2.4	1.0 <sup>#</sup>
	Q4W (N=18)	1.3	1.1	Q4W (N=9)	2.2	1.4*
Mean RGI-C	All (N=36)		+1.4 <sup>#</sup>	All (N=18)		+1.9 <sup>#</sup>
	Q2W (N=18)		+1.6 <sup>#</sup>	Q2W (N=9)		+2.0 <sup>#</sup>
	Q4W (N=18)		+1.2 <sup>#</sup>	Q4W (N=9)		+1.7 <sup>#</sup>

\*  $P < 0.05$ , comparing Wk 40 to baseline, <sup>#</sup>  $P < 0.001$ , comparing Wk 40 to baseline.



QDEC analysis demonstrating significant reductions in parahippocampal cortical thickness in female patients with CAH compared to controls.

Areas in red/yellow are regions where cortical thickness is significantly lower in the CAH group in the left (B) and right (C) hemisphere. Green lines indicate the parahippocampal region.

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### OC5.3

#### Mutations in *SGPL1*, encoding sphingosine-1-phosphate lyase, cause a novel form of primary adrenal insufficiency with steroid resistant nephrotic syndrome

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#### Background

Primary adrenal insufficiency (PAI) is most commonly congenital in children. PAI is genetically heterogeneous with some gene defects causing syndromic disease. A third of patients have no genetic diagnosis meaning their prognosis is uncertain. We recently investigated families with a novel combination of PAI and steroid resistant nephrotic syndrome.

#### Objective and hypotheses

To discover the genetic defect underlying this syndrome.

#### Method

Whole exome sequencing (WES) was performed in two families with Sanger sequencing of *SGPL1* to confirm segregation and screen further families.

#### Results

By WES and Sanger sequencing three different mutations in *SGPL1* were identified in four families. All mutations were homozygous in affected individuals and heterozygous in their asymptomatic parents. Kindred 1, three patients had a novel missense mutation [c.665G>A; p.R222Q], the index case presented with PAI (8 m), developed focal segmental glomerulosclerosis (FSGS) at 2.5 y and received a kidney transplant aged 5 y. A younger sibling with similar clinical history (not sequenced) died (4 y) whilst an older sibling (8 y) and a cousin (3 y) have only PAI. Kindred 2, a child presenting with PAI had the p.R222Q mutation and at age 3.7 y has no renal phenotype. Kindred 3, a female baby presenting with PAI (6 m) had a novel in-frame deletion, [c.1633\_1635delTTC; p.F545del] and developed FSGS (5 y) on follow-up, additional features included ichthyosis and neurological symptoms. Kindred 4, two affected siblings manifesting PAI, ichthyosis and nephrotic syndrome (<1 yr) had a canonical splice site change, [c.261+1G>A; p.?], the male sibling additionally presented with micropenis, unilateral cryptorchidism and neurological symptoms.

#### Conclusion

We have identified a novel, potentially progressive, disorder incorporating PAI and nephrotic syndrome amongst other features. Sphingosine-1-phosphate lyase (*SGPL1*) executes the final decisive step of the sphingolipid pathway, initiating irreversible cleavage of the lipid signalling molecule sphingosine-1-phosphate (S1P). This novel syndrome highlights the importance of the sphingolipid

metabolic pathway in adrenal function. A genetic diagnosis for patients with this form of PAI is important for correct treatment, genetic counselling and screening for co-morbidities.

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### OC5.4

#### Characteristics of Vitamin D supplementation programs for the prevention of rickets in infants and young children in Europe: Factors influencing compliance

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#### Introduction

Nutritional rickets is a growing public health concern in at-risk populations despite existing prevention programs and health policies.

#### Aims

To compare infant and childhood vitamin D supplementation policies and strategies across Europe and explore factors influencing adherence.

#### Methods

Representatives of the ESPE bone and growth plate working group and other experts in the field of infant vitamin D supplementation across Europe were asked to complete a questionnaire relating to their national health policy and child care programs, societal factors, and details on strategy implementation. Kendall’s tau-b correlation coefficient was used to assess the effect of individual factors and the total number of factors ( $n=11$ ) on estimated country-specific adherence rates.

#### Results

Responses were received from 28 European countries, of which 27 (96%) had a national vitamin D policy in place (96%). Fifty % (14/28) of countries commence supplements on day 1–5, 46% (13/28) on day 7–21, and only one country (the UK) starts supplements not before 6 months of life. There was a wide variation in the recommended duration of vitamin D supplements (1–4 years, to lifelong in at risk populations). Five countries (18.5%) reported adherence rates from national statistics; others were estimates of experts working in the field. Good ( $\geq 80\%$ ), moderate (50–79%) and poor adherence ( $<50\%$ ) was reported by 59% (16/27), 30% (8/27) and 11% (3/27) of countries, respectively. The UK reported the lowest adherence rate of all European countries (20%). Specific factors significantly associated with good adherence were: 1) supplementation of both breast and bottle fed infants ( $P=0.02$ ); currently recommended by 81% of countries. 2) Availability of family financial support ( $P=0.04$ ); currently practised in 89% of countries. 3) Checking adherence to supplementation at routine child care visits ( $P=0.001$ ); currently practised by 59% of countries. Adherence was also positively associated with the total number of factors ( $P<0.001$ ).

#### Conclusions

Good adherence to vitamin D supplementation is associated with relatively simple factors such as offering universal supplementation and checking adherence at routine childcare visits. Supplementation should be adopted independent of the mode of feeding. Interestingly, financial family support and not free vitamin D supplies enhanced compliance.

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### OC5.5

#### The performance of early childhood Human Chorionic Gonadotrophin (HCG) testing to investigate male undervirilisation

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#### Background

The 3 day human chorionic gonadotrophin (HCG) test is commonly performed to investigate male undervirilisation. However, the utility of routine HCG testing for male undervirilisation in early childhood and correlation with pubertal progress is unclear.

**Aims**

To review performance of the 3 day HCG test for diagnosis and outcomes.

**Methods**

Standard 3 day HCG test data were analysed in 130 boys of age <3 years with undervirilised male genitalia over a 15 year period in a single regional centre. Androgen response measured by mass spectrometry was correlated with diagnostic outcomes in all and with pubertal progress in 14 (11%) boys >11 years of age. Undervirilisation was characterised by findings of micropenis (stretched penile length <2.5 cm), hypospadias, undescended testes and External Masculinisation Score (EMS). Puberty was delayed if there was no sign of onset or progress by age 12 years.

**Results**

Nineteen (15%) boys had primary hypogonadism/adrenal dysfunction and 11 (8%) boys had hypogonadotrophic hypogonadism with the cause for undervirilisation being unknown in 100 (77%) boys. Stimulated testosterone concentration (T-stim) and ratio of stimulated to basal testosterone (T-ratio) declined after 1.5 years, suggesting gonadal unresponsiveness to HCG beyond age 2 years. Lower T-stim ( $P=0.002$ ) and T-ratio ( $P=0.01$ ), but not EMS ( $P=0.38$ ), were associated with a primary adrenal/testicular diagnoses (P-dx). The combination of short penile length and hypospadias was correlated with lower T-ratios ( $R^2=0.5$ ,  $P<0.001$ ). A cut-off T-stim >12.5 nmol/l excluded P-dx [Odds ratio (OR) 3.3 95% CI (1.1–10.5),  $P=0.04$ ], while the composite variable [T-stim <12.5 nmol/l or T-ratio <20] had the greatest probability of predicting P-dx [OR 95%CI 7.3(3.2–16.7),  $P<0.001$ ]. In older boys with information on puberty, higher T-stim [median (range) 12.1(7.3–32.3) v 9.3(0.3–13.1),  $P=0.24$ ] and T-ratio [18.9(1.6–69.7) v 10.2(1.0–43.7),  $P=0.46$ ] trended towards spontaneous puberty than delayed puberty.

**Conclusions**

The 3 day HCG stimulation test yields a primary adrenal/testicular diagnosis in 15% of undervirilised boys. Testosterone response to HCG correlates with the severity of undervirilisation; a generous response may exclude underlying pathology and predict spontaneous pubertal progress.

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**OC5.6**

**Cytochrome p450 side chain cleavage enzyme (CYP11A1) mutations: Phenotypic variability and identification of p.E314K as a recurrent, pathogenic variant**

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**Background**

*CYP11A1* encodes the P450 side chain cleavage enzyme which initiates the steroidogenic cascade by conversion of cholesterol to pregnenolone. Severe (or classical) deficiency of this enzyme is characterised by disordered sexual differentiation in addition to adrenal and gonadal insufficiency. However partial loss-of-function mutations of *CYP11A1* can present as isolated glucocorticoid deficiency (IGD). We describe 16 patients with both novel and known mutations in *CYP11A1* who presented with varied clinical phenotypes.

**Patients and methods**

Whole exome or targeted (Haloplex) next generation sequencing (NGS) was performed in patients with adrenal insufficiency of unknown aetiology. The p.E314K variant (rs6161; c.940G>A) of *CYP11A1* has a minor allele frequency of 0.0024 and is predicted benign. We postulated that it alters splicing and assessed its effect using an *in vitro* splicing assay.

**Results**

The following mutations in *CYP11A1* were detected in 16 patients by NGS: homozygous p.A359V (2 non-pigmented sisters with IGD), homozygous p.R451W (1 classic patient), compound heterozygous mutations p.I279Yfs\*9 and p.\*522Rext\*68 (2 siblings with IGD) and p.R120Q and p.Q395K (a patient diagnosed with lipid adrenal hyperplasia). In the remaining 10 patients, with variable presentations, sequencing revealed the presence of compound heterozygosity for a p.E314K mutation with coexistent p.R424\*, p.R439\*, p.I279Yfs\*9, c.990G>A (splice mutation), c.426-2A>G, p.L335P (2 siblings) or c.790\_802del (3 brothers with pigmentation, low cortisol and salt loss but normal puberty). In all 16 cases the variants were biallelic and never seen together in parents or unaffected siblings. Although predicted benign the p.E314K variant is enriched in our patient cohort with an allele frequency =0.015 ( $P<0.01$ ).

**Conclusion**

Previously considered a benign variant, the p.E314K occurs more frequently than expected in patients and we predict that it is pathogenic when in combination with

a severe disruptive change on the other allele. We hypothesize that it affects the gene at the RNA level, perhaps altering splicing, or that it represents a marker for another deleterious change within the gene. This and other partially inactivating mutations of *CYP11A1* often leads to mild phenotypic presentation including isolated hypocortisolaemia and normal sex development.

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**OC5.7**

**Frequent occurrence of DUOX2 and DUOXA2 mutations in cases with borderline bloodspot screening TSH who develop 'True' congenital hypothyroidism**

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The UK newborn screening programme for congenital hypothyroidism (CH) facilitates prevention of neurodevelopmental delay in CH by enabling prompt diagnosis and treatment. Although the UK Newborn Screening Programme Centre (UKNSPC) defines a borderline bloodspot screening TSH (bsTSH) concentration as 10–20 mU/l, the lower cutoff used at Great Ormond Street Hospital (6 mU/l), enables diagnosis of true and transient CH in cases missed using UKNSPC criteria. We hypothesised that mutations in *DUOX2* and its accessory protein *DUOXA2* may be common in borderline CH cases and have broader management implications.

We screened 40 term babies with eutopic gland-in-situ, including 21 with Asian/Chinese ethnicity (53%). Biochemical recruitment criteria comprised a 1st bsTSH measuring 6–20 mU/l, and confirmatory venous TSH (vTSH) >25 mU/l. *DUOX2* was sequenced initially, followed by *DUOXA2* in mutation negative cases. Mutations were classified as pathogenic based on *in silico* predictions including molecular modeling for *DUOX2* mutations affecting the peroxidase-like domain.

In total of 19 cases (47.5%) harboured likely disease-causing mutations in either *DUOX2* ( $n=13$ , 32.5%) or *DUOXA2* ( $n=6$ , 15%) and confirmatory venous thyroid hormone levels in mutation-positive cases demonstrated subnormal mean free T4  $9.1 \pm 0.8$  (NR 12.5–24.6 pmol/l). Initial or repeat bsTSH was below the UKNSPC cutoff (10 mU/l) in 42% of mutation-positive cases. We detected 7 rare novel *DUOX2* mutations and 6 novel *DUOXA2* mutations; two *DUOX2* mutations (p.Q570L, p.F966Sfs\*29) were recurrent and occurred more frequently ( $MAF \leq 0.01$ ). Significant enrichment of *DUOXA2* variants in our cohort compared with healthy populations (15% vs 1%,  $P=1.70 \times 10^{-5}$ ) supported an aetiological contribution of both monoallelic ( $n=5$ ) and biallelic mutations ( $n=1$ ).

Recommended TSH screening cut offs fail to detect individuals with true dysmorphogenesis who develop at least moderate CH, despite borderline bsTSH concentrations. Targetted sequencing of *DUOXA2* and *DUOX2* in such cases will have a high diagnostic yield, especially in Asian/Chinese populations, and genetic ascertainment will facilitate prompt diagnosis in familial cases.

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**OC5.8**

**Understanding the Utility of Performing Endocrine & Genetic Investigations in Boys with a Suspected Disorder of Sex Development**

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**Introduction**

Evaluation of XY DSD requires a combination of endocrine and genetic tests. It is unclear whether these two sets of investigations should be performed stepwise or in parallel.

**Aims**

The aim of the study was to document the range of endocrine and genetic abnormalities identified in all XY boys who were investigated at one specialist multidisciplinary service.

**Methods**

Case records were reviewed to collect information from all 46 XY boys who presented for evaluation of atypical genitalia in Glasgow between 2010 and 2015. Detailed phenotypic information including external masculinisation score (EMS), biochemical and genetic diagnosis was studied.

**Results**

boys with median EMS of 9 (range 1,11) were included. Associated malformations (AM) were present in 39 (32%) with 14 (11%) having a recognisable syndrome. The median EMS of those with or without AM was the same at 9 (1,11). A family history of DSD was present in 16 (13%) and consanguinity in 3 (2%). An endocrine abnormality of gonadal function was present in 28 (23%) with a median EMS of 8.3 (1,10.5). These abnormalities included a disorder of gonadal development (DGD) in 19 (15%), LH deficiency (LHD) in 5 (4%) and a disorder of androgen synthesis (DAS) in 4 (3%). In the remainder, there were 91 (75%) cases of non-specific disorder of undermasculinisation (NSDUM), 2 (2%) cases of disorder of Müllerian development (DMD) and one case (1%) of cloacal anomaly. Of 43 cases (NSDUM, 30; DGD, 10; LHD, 3) who had array-CGH, copy number variants (CNVs) were reported in 13 (30%) (NSDUM,9; DGD, 4) with a median EMS of 8.5 (1.5,11). Limited gene panel analysis in 61 (NSDUM,41; DGD,15; DAS,2; DMD,2; Cloacal Anomaly,1) identified variants in 6 (10%) (NSDUM,3; DGD,1; DAS,2) with a median EMS of 6 (3,9). CNVs were detected more frequently in cases that had associated malformations ( $P=0.03$ ).

**Conclusions**

In boys with suspected XY DSD, the likelihood of identifying an abnormal diagnostic test seems to be unrelated to the appearance of the external genitalia. In addition, there is no association between a genetic and endocrine abnormality. A parallel genetic and endocrine approach for evaluating DSD needs further consideration.

DOI: 10.1530/endoabs.45.OC5.8

**Oral Communications 6 – Endocrine****OC6.1****The intra- and inter-user reliability of testicular volume estimation – a simulation study**

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**Background**

Measuring testicular volume (TV) by orchidometer is a standard method of pubertal staging in boys. A paucity of evidence exists as to its inter and intra-user reliability and the impact of clinicians' gender, training and experience on the accuracy of measurements. Specifically engineered prosthetic models of different size testes were developed to investigate the reliability of TV estimation.

**Method**

The study was conducted over the three-day BSPED meeting in November 2015. Three child-sized mannequins displayed latex scrotum containing prosthetic testicles of 3 ml, 4 ml, 5 ml, 10 ml and 20 ml. Demographic data, paediatric endocrinology experience, TV examination training, information on examination technique were collected anonymously and TV estimations performed. Delegates were asked to repeat their measurements later during the meeting. Scrotum order was changed daily to minimise recall bias.

**Results**

In total of 208 delegates participated (158F, 50M): 50% consultants, 30% trainees, —9% clinical nurse specialists, 11% other. The majority of participants (60%) had less than 5 years experience in clinical endocrinology, 19% had practiced for over 10 years. Only 25.5% had received formal training in TV estimation. There was variability in examination technique, with the majority preferring the patient recumbent (54%) and using both look and feel for estimation (59%).

Participants measured TV accurately on 30% of occasions. Underestimations were made on 40% of measurements and overestimation on 30%. Males and females were similarly inaccurate, males estimating correctly on 31.4% of occasions and females on 29.7%. Experience improved accuracy with consultants scoring accurately 31.7%, paediatric trainees 28.4%, nurse specialists 27.2% and

newly qualified doctors 11.1% of the time. Inaccuracies were highest at the smallest volumes: 57% overestimating 3 ml testis (largest coefficient of variation, 57.8%), compared with 17% for the 20 ml testis (smallest coefficient of variation, 31.9%).

**Conclusion**

Overall TV estimation accuracy was poor. There was considerable variation between subjects and at lower volumes. This is clinically pertinent considering the different management decisions made at smaller volumes. Seniority improves measurement estimation. Delegate feedback supported more training and developing these models for teaching simulation.

DOI: 10.1530/endoabs.45.OC6.1

**OC6.2****Systematic trial of Nifedipine in children with Hyperinsulinaemic Hypoglycaemia due to mutations in the ABCC8 gene**

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**Introduction**

Several previous case reports have described the use of the calcium-blocker Nifedipine for the treatment of hyperinsulinaemic hypoglycaemia (HH). These cases are a collection of transient/permanent forms of HH, with known/unknown genetics, where Nifedipine has been used either as monotherapy or in combination with other medications. There have been no previous reports of any systematic trial of Nifedipine use in patients with HH due to mutations in the *ABCC8* gene.

**Methods**

Prospective study assessing the glycaemic response to Nifedipine in children with HH due to mutations in *ABCC8* gene and diazoxide-unresponsiveness. Nifedipine was administered at a starting dose of 0.25 mg/kg/day and increased to a maximum dose of 2.5 mg/kg/day. The information collected included family history and HH history (presentation, genetics, histology/18F-DOPA PET scan).

**Results**

In total of 11 patients (6 females) were trialled on Nifedipine at a median age of 0.44 years (range 0.14–3.77). The genetic mutations in *ABCC8* gene were: homozygous in 3 cases, paternally inherited heterozygous in 4 and compound heterozygous in 4. 18F-DOPA PET scan demonstrated a focal lesion in 2 cases and the rest were diffuse HH disease. 1 subject had Nifedipine in monotherapy, whilst the rest had it in combination with octreotide/glucagon/diazoxide or comstarch. After a median of 6.5 (3–23) days of maximal (2.5 mg/kg/day) of Nifedipine therapy none of the patients showed any improvement in glycaemic control and patients continued to have hypoglycaemic episodes.

**Conclusion**

Nifedipine therapy is ineffective in patients with HH due to mutation in the *ABCC8* gene.

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**OC6.3****Reversible 5 $\alpha$ -reductase 2 deficiency in Hypothyroidism**

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**Introduction**

In total of 5 $\alpha$ -reductase 2 is vital in sexual development of male foetus; its deficiency causes impaired virilisation due to defective conversion of testosterone to dihydrotestosterone and is an important cause of Disorders of Sexual Development (DSD). We report 3 cases of severe primary acquired auto-immune hypothyroidism, which show a similar picture of 5 $\alpha$ -reductase deficiency (5ARD) on urine steroid profile (USP) and reversible following adequate thyroxine replacement therapy.

**Case Reports**

Case 1: 13 year old boy with poor growth was finally diagnosed as primary hypothyroidism (TSH > 100 mU/l; FT4 4 pmol/l). USP performed due to small penile size and lack of pubertal development showed 5ARD with hypothyroidism reversing when euthyroid, prompting USP review in subsequent cases.

Case 2: 11 year old girl with short stature was confirmed as auto-immune hypothyroidism (TSH >100 mu/l; FT4 0.9 pmol/l). USP showed 5ARD during untreated stage, which reversed completely on thyroxine replacement therapy.

Case 3: 11 year old boy with poor growth was diagnosed as profound hypothyroidism (TSH >100 mu/l; FT4 undetectable). USP showed 5ARD; awaiting repeat USP following treatment.

#### Results

In total of 3 patients with severe hypothyroidism showed 5ARD and normalisation of 5 $\alpha$  reductase steroid markers with thyroxine replacement. The ratios of 5 $\alpha$ /5 $\beta$ -reduced tetrahydrocortisol were 0.02, 0.08 and 0.10 in Case 1, 2 and 3 respectively (Normal: Mean 1.04; SD 0.89). Ratios for Case 2 after 2 & 4 months of treatment were 0.36 & 1.69. Ratios for the 5 $\alpha$ /5 $\beta$ -reduced androstenedione metabolites were less abnormal, indicating a specific impairment of the 5 $\alpha$ -reductase 2 isoform in hypothyroidism.

#### Conclusion

In total of 5 $\alpha$  reductase-2 deficiency is a rare disorder leading to incomplete male genitalia development in patients with 46XY DSD. Untreated or undiagnosed hypothyroidism is a potential cause of reversible 5 $\alpha$  reductase-2 deficiency. Altered steroid metabolism in hypothyroidism, if undetected may lead to erroneous results and interpretation of USP; thus excluding hypothyroidism in diagnostic work ups for DSD, especially patients with late presentations is extremely important.

#### Novel insight

We have demonstrated altered steroid metabolism in hypothyroidism – a completely reversible picture of 5ARD with adequate thyroxine replacement therapy; if undetected, may lead to errors in interpreting USP results whilst investigating DSD.

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## OC6.4

### Impact of intercurrent illness on calcium homeostasis and hypoparathyroidism management

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#### Introduction

Hypoparathyroidism is typically managed with calcitriol/alfacalcidol. Close monitoring of serum calcium is required as under-treatment causes symptomatic hypocalcaemia while over-treatment will cause nephrocalcinosis. We report three cases who demonstrated resistance to treatment during an intercurrent illness, necessitating increase in medication doses and monitoring.

#### Case series

**Case 1:** Two-month-old boy with newly diagnosed hypoparathyroidism due to *GCMB2* mutation normalised his calcium on standard treatment with alfacalcidol and calcium supplements. He however developed bronchiolitis during admission, resulting in precipitous drop in corrected calcium (1.53 mmol/l) and seizures, requiring intravenous calcium infusion and significant increase in medication to normalise serum calcium (alfacalcidol 400 ng/day to 1500 ng/day, and calcium supplements 12 mmol/day to 48 mmol/day). He eventually needed recombinant PTH to achieve calcium homeostasis.

**Case 2:** A male infant diagnosed with hypoparathyroidism at birth responded to standard treatment. At 2 months he presented with bronchiolitis and recurrent hypocalcaemic seizures, requiring increase in dose of alfacalcidol (400 ng/day to 1500 ng/day) and calcium supplementation. However, following resolution of illness, he required rapid reduction in dosage due to hypercalcaemia.

**Case 3:** A six-month-old boy with Sanjad-Sakati syndrome on standard treatment for hypoparathyroidism presented with symptomatic hypocalcaemia following viral gastritis. He required increase in dose of alfacalcidol upto 3000 ng/day to normalise serum calcium. He was however lost to follow-up and presented again at 2 years of age with symptomatic hypercalcaemia (cCa > 3 mmol/l) and severe nephrocalcinosis. To normalise his serum calcium and prevent further progression of nephrocalcinosis, he was commenced on recombinant PTH.

#### Conclusion and implications for clinical practice

Intercurrent illness in infants with hypoparathyroidism can lead to marked resistance to standard treatment and symptomatic hypocalcaemia. The underlying

pathophysiology remains unknown, but would seem to involve more than just intolerance to oral medication and feeds. During such periods, close monitoring of calcium levels is required, with quick escalation in medication doses, as well as reduction to baseline on recovery to prevent over-treatment. Parental education is recommended, with future research evaluating the possible role of 'sick-day' rules similar to adrenal insufficiency.

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## OC6.5

### A novel methodology using high resolution thermal imaging to detect vertebral fractures in children with osteogenesis imperfecta

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#### Background

Vertebral compression fractures are common in children with osteogenesis imperfecta. Current imaging methods for fracture detection (X-ray and DXA) use ionising radiation. High Resolution Thermal imaging (HRTI) is a non-invasive, non-ionising method that detects infrared radiation energy emissivity to an accuracy of 0.04 °C, providing a quantitative and qualitative map of temperature distribution. Given that the alteration in blood flow in vertebral fractures acutely and chronically results in temperature change we hypothesised that HRTI may detect thermal variation in vertebral fractures in patients with OI.

#### Methodology

Prior to routine DXA and X-ray scans, twelve consented participants aged 5–18 with OI and known vertebral fractures had metal discs (diameter 0.85 cm) fixed at 4 cm to the right of each spinous process.

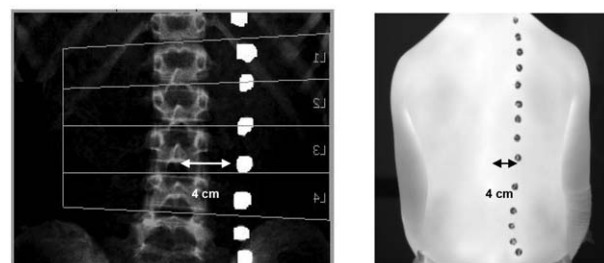
Thermal imaging of each subject's back was performed for two minutes at a capture rate of thirty frames per second using the Flir T630sc HRTI camera. Genant semiquantitative (GQ20) visual grading was used to define vertebral fracture position and severity on DXA or radiographs and then correlated with the metal disc position on thermal images (figure). TI recordings were compared to DXA and X-ray images using MATLAB® (Matrices Laboratory: version 8.3, R2014a). The temperature percentage change (TPC) of fractured and non-fractured vertebrae relative to adjacent skin areas (region of reference:ROR) was analysed using paired t-tests.

#### Results

Mean age of the patients was 11.7 (3.9). Two-thirds of the cohort had OI-type I, with the remaining classed as type III or IV. TPC between fractured thoracic vertebrae ( $n=11$ ) and the ROR was significant (1.27% (1.07);  $P=0.007$ , CI:0.45 to 2.09) whereas TPC between the non-fractured vertebrae and ROR was not (0.97% (1.01);  $P=0.064$ , CI: -0.08 to 2.03). Lumbar fractures ( $n=3$ ) were too few to draw conclusions. TPC of the least severe fractures (GQ20-D1) was also significant (1.14% (1.14);  $P=0.01$ , CI:0.36, 1.92), implying that the least severe fractures could be identified on TI.

#### Conclusions

Preliminary work suggests HRTI may be a novel non-radiation approach to identifying vertebral fractures in OI. Larger studies are needed to substantiate current findings and to determine whether fracture severity and position influence thermal emissivity.



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**OC6.6****Predictive factors of an underlying genetic defect in children with short stature and suspected growth hormone insensitivity (GHI)**

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**Background**

GHI insensitivity (GHI) presents with growth failure, IGF-1 deficiency and normal/elevated GH (basal > 5 µg/l and/or peak > 10 µg/l). GHI encompasses a spectrum of clinical and biochemical abnormalities. Associations between phenotypic characteristics and genetic defects remain obscure.

**Objective**

Identify phenotypic predictors of underlying genetic defects in GHI.

**Methods**

In total of 102 children (62M) median age 6.2 yr with short stature and suspected GHI (mean height -4.5 SDS; mean IGF-1 -2.6 SDS, mean peak GH levels 29.6 mcg/l) underwent genetic analysis (including candidate gene and whole exome sequencing). Phenotypic evaluation was performed at referring centres. Subjects with genetic diagnosis were compared with those with no diagnosis using an unpaired t-test and univariate/multivariate logistic regression analysis to assess age, sex, height SDS, IGF-1 SDS, consanguinity, ethnicity and peak GH levels.

**Results**

Genetic sequencing identified likely causative variants in 49/102 (48%) patients (GHR [31], IGFALS [4], OBSL1 [6], CUL7 [2], CCDC8 [1], PTPN11 [2], SOS1 [1], H19 hypomethylation [1] and MatUPD7 [1]). Mean height SDS was significantly lower in those with a genetic diagnosis (-5.2 vs -3.8,  $P=0.0005$ ; 95% CI 0.6-2). There was no difference in age, sex and IGF-1 SDS between the two groups. Significant univariate phenotypic predictors for underlying genetic defects were lower height SDS ( $P=0.001$ ; 95%CI 0.47-0.83, OR 0.62), consanguinity ( $P=0.0001$ ; 95% CI 5.3-44.1, OR 15.27), non-Caucasian ethnic heritage ( $P=0.0001$ ; 95%CI 3.4-26.2, OR 9.5) and higher peak GH levels ( $P=0.009$ ; 95%CI 1.008-1.058, OR 1.03). In the multivariate model, lower height SDS and consanguinity remained statistically significant.

**Conclusion**

Lower height SDS, consanguinity and non-Caucasian ethnicity were the strongest predictors for finding a genetic defect in GHI. IGF-1 level was not a helpful predictor and may reflect the wide inter- and intra-assay variation between centres. These findings highlight the importance of careful phenotyping to guide genetic investigations.

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**OC6.7****Early treatment with rhGH in patients with Prader-Willi syndrome results in improved height with no respiratory adverse effects**

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**Background**

Prader-Willi syndrome (PWS) is a complex genetic disorder caused by lack of expression of paternally inherited imprinted genes on Chr15q11-q13. rhGH has beneficial effects on growth, body composition and development. Starting age, dose titration and monitoring remain controversial.

**Objective**

To study retrospectively children who presented in our multidisciplinary PWS clinic and assess response to rhGH treatment in terms of auxology, IGF1 concentration and potential complications.

**Method & Patients**

In total of 47 patients (male 27, female 20) were followed up; 5/47 were lost to follow-up and 2/47 refused rhGH treatment. 40 patients were treated with rhGH, all had detailed sleep studies before, and six weeks after starting treatment.

**Results**

Treatment started at a mean age of 2.1 ± 2.6 years (range 0.58-12.8), 45% of patients ( $n=18$ ) started rhGH before the age of one (0.58-0.97 years). 15% ( $n=6$ ) had evidence of sleep apnoea, requiring non invasive ventilation before starting rhGH. Mean starting rhGH dose was 0.025 mg/kg/day (0.5 mg/m<sup>2</sup>/day) increased to 1 mg/m<sup>2</sup>/day following the second sleep study. At one year, mean

dose was 0.7 ± 0.2 mg/m<sup>2</sup>/day. Pre-treatment mean height was -1.65 ± 1.1 SDS (-4.47 to 0.37 SDS), with a weight of -1.43 ± 1.8 SDS (-5.5 to 3.3) and BMI of -0.46 ± 1.6 SDS (-3 to 4). After one year there was an increase of 1.37SDS in Ht (mean -0.28 ± 0.94, range -2.4 to +2.3), with a mean weight of -0.24 ± 1.8 SDS (range -4.0 to 3.7) and BMI of 0.08 ± 2.2 SDS (-3.0 to 4.6). No patient had worsening respiratory status and 2/6 patients discontinued ventilatory support. One patient paused treatment during spinal surgery and restarted afterwards. IGF1 was > +2.0 SDS in 60% of patients and the dose of rhGH remained unchanged with repeat yearly IGF1 measurement.

**Conclusion**

Early treatment with GH results in improved height in the first year with no adverse effect on respiratory function. We recommend dose titration using auxology and IGF1 concentration.

DOI: 10.1530/endoabs.45.OC6.7

**OC6.8****Outcome of hyperthyroidism diagnosed in childhood and adolescence**

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**Background**

Long term remission in paediatric onset hyperthyroidism (HT) is low at 20-30% compared to 40-50% in adult onset HT. There are very few studies which report long-term follow-up of paediatric onset HT especially into adulthood and factors which can predict a need for definitive treatment in the long-term.

**Objectives**

To evaluate the long-term outcome of paediatric onset HT with follow-up into adulthood and identify any early predictors of a need for definitive therapy.

**Methods**

Retrospective analysis of those diagnosed to have HT under the age of 18 years and follow-up data available. At follow-up, comparison was made by categorising them into three groups: those who underwent definitive therapy (DT) i.e Thyroidectomy/Radioactive iodine (RAI), those who remained on Antithyroid drugs- ADT (MT) and those achieved complete remission (CR).

**Results**

In total of 61 patients (49 females, 12 males) were identified to fulfil criteria for the study. Median age at diagnosis was 15.1 years (range: 3.6-18) with 34% between 16-18 years. All 61 patients were treated with ATD at diagnosis. Duration of first course of ATD varied from < 1 year in 7%, 1-2 years in 26%, > 2 years in 46% and ATD never discontinued in 21%. 69% of those with < 1 year ATD relapsed compared to 79% with ATD > 2 years (median duration of treatment 31.5 m [range 24-96 m]).

At follow-up, median duration since diagnosis was 8.75 yrs (range 2.0-20.7 yrs) and median age at follow-up was 23.2 yrs (5.6-36 yrs). 32% (20/61) had undergone definitive treatment (DT group) - 16% ( $n=10$ ) RAI and 16% ( $n=10$ ) surgery, 36% (22/61) still on ATD (MT group) whilst 32% (19/61) had undergone full remission (CR group). Comparison between the three groups did not identify any statistically significant difference for predictor factors at diagnosis including age, T4 and free T4 levels, Thyroid peroxidase antibody levels and duration of first course of CBZ treatment.

**Conclusion**

Long-term complete remission of paediatric onset HT in our study was 32%. There were no predictors identified that could help predict long-term outcome, especially into adulthood.

DOI: 10.1530/endoabs.45.OC6.8

**OC6.9****A single centre experience of Differences/Disorders in Sex Development (DSD) over 20 years**

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**Introduction**

Differences/Disorders in Sex Development (DSD) represent a diverse range of conditions that present at various stages of life. A multidisciplinary team (MDT) approach is required to reach a specific diagnosis and management plan, but few large single centre studies of the range and prevalence of diagnoses have been undertaken.

**Method**

Medical records of all children with DSD discussed at a single MDT between 1-Jan-1996 and 31-Dec-2015 ( $n=580$ ) were retrospectively reviewed to evaluate the referral patterns and diagnoses; clinical features, biochemical data and genetic analyses were considered.

**Results**

A total of 271 (1996–2005) and 309 (2006–2015) children were discussed in two respective decades. The relative proportions of DSD categories were similar across two decades (Sex chromosome DSD [SCDSD]: 8.1%/12.0%; 46,XX DSD: 29.2%/25.9%; 46,XY DSD: 62.7%/62.1% in 1996–2005/2006–2015 respectively). Overall, 300/580 children were discussed in their first year of life, with an increase in the number and proportion of children referred earlier in the second decade (2006–2015) (185 versus 115; 59.8% versus 42.4%). Specific diagnoses among children discussed in their first year of life for SCDSD ( $n=30$ ) included 45,X/46,XY and X variants ( $n=21$ ), 47,XXY variants and children with 46,XX/46,XY chimerism ( $n=3$ ). Most children with 46,XX DSD ( $n=87$ ) had congenital adrenal hyperplasia (CAH) ( $n=58$ ), the rest having ovotesticular DSD ( $n=4$ ), isolated clitoromegaly or cloacal anomalies. Among 46,XY DSD ( $n=183$ ), specific molecular diagnoses were reached in 39 children (including disease-causing variants in SF1, WT1, SOX9, STAR, HSD3B2, HSD17B3, AR, and SRD5A2). Most ( $n=112$ ) of the others were 46,XY boys with severe hypospadias and often associated features including intra-uterine growth restriction, and/or renal, cardiac or syndromic anomalies. Relatively few 46,XY females presented in infancy (30/109), but molecular diagnosis was reached in 20/23 46,XY females born within the last 10 years.

**Conclusion**

Children with a heterogeneous range of conditions were referred to the DSD MDT at our centre. Understanding the relative prevalence of those conditions is very valuable. Molecular analysis is useful in reaching a specific diagnosis and directing management, but the underlying pathophysiology in most 46,XY children with severe hypospadias currently remains unknown, and could include genetic, epigenetic, and/or environmental factors.

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**Oral Communications 7 – Diabetes****OC7.1****Hypercholesterolaemia screening in type 1 diabetes – a difference of opinion**

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**Background**

The National Institute for Health and Care Excellence (NICE) guidelines on childhood type 1 diabetes (T1D) do not recommend cholesterol screening. However, the National Paediatric Diabetes Audit (NPDA) has an annual cholesterol measure (> 12 years) as a key outcome indicator. This is confusing for professionals managing children with T1D.

**Methods**

An online survey was sent to 280 members of the Association of Children's Diabetes Clinicians assessing cholesterol screening practice.

**Results**

About 87 (31%) responded. About 94% measure cholesterol in their patients. About 33% annually on all patients, 40% using annual measurements only in the over 12-year-old population. About 7% routinely using fasting samples and 41% use only a non-fasting sample. In addition to total cholesterol, 67% also measure triglycerides, HDL and LDL cholesterol levels. About 63% used no guidelines to decide treatment/further investigation. NICE guidelines and ISPAD (International Society for Paediatric and Adolescent Diabetes) were the most commonly used. A 'high' cholesterol varied from >4.5 to >8 mmol/l, with 40% giving no response or specific level. Action following a cholesterol level that was above the threshold for treatment included 42% who would refer to a dietician, 14% who would refer to a lipidologist and 2% who would commence a statin. About 16% would refer to a dietician and a lipidologist. About 10% would refer to a dietician and commence a statin. About 3% would refer to a lipidologist and dietician as well as commence a statin. About 13% of professionals would not take any further action. Only 14% of clinicians had started statin therapy in their diabetes clinic in previous 5 years.

**Conclusion**

Whilst the majority measure cholesterol in children with T1D, there is marked variability in sampling, patients screened and action taken if considered abnormal. It is debatable whether cholesterol measures should be undertaken,

certainly more than once and whether it should feature as key outcome in the national audit in future.

DOI: 10.1530/endoabs.45.OC7.1

**OC7.2****The development of an e-learning package to support education staff with the management of type 1 diabetes**

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Currently in the UK children and young people with diabetes receive variable provision of care and support in educational settings. There are concerns that this impacts on the young person's glycaemic control, their quality of life, and their educational performance and outcome. Whilst most paediatric diabetes teams provide training for school staff, it may take several days, even weeks, after diagnosis before a diabetes educator is able to attend the school to provide education and support.

The aims of this project were to develop a comprehensive, consensus-based, e-learning package that would inform education providers about diabetes and provide a framework for the best practice management and support of young people with type 1 diabetes in schools. This package was not intended to replace the visit from the specialist nurse but to complement this and allow the young person to return to education at the earliest possible opportunity. This was achieved by convening a series of multi-agency stakeholder workshops including clinicians, patients/families, teachers, and voluntary sector representatives, to discuss the content and format that this package should take. These discussions were then developed into two e-learning modules (basic and advanced) by a core team of diabetes educators from 3 regional diabetes networks.

The modules provide guidance to all key parties involved in the day to day support of young people with diabetes, including expected roles and responsibilities, and legal obligations. The basic module is aimed at all staff to raise their general awareness of type 1 diabetes. The advanced module is for those staff designated specific responsibilities for supporting the young person with type 1 and goes into greater depth regarding the management and treatment of diabetes in the school setting. These modules have been positively received by education providers, and are endorsed by the National Children and Young Person's Diabetes Network.

DOI: 10.1530/endoabs.45.OC7.2

**OC7.3****SEREN (structured education: Reassuring empowering nurturing); a new structured education programme for diabetes in Wales, UK**

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**Background**

Education in diabetes is a fundamental component of self-management. Health care systems that have structured education from diagnosis have demonstrated improving trends in HbA1c. Within Wales, education for Children and Young People (CYP) was delivered informally and this deficiency was highlighted in the National Paediatric Diabetes Audit. While structured education is being delivered in some parts of the UK, there is no overarching programme covering the entire range of CYPs with diabetes, from diagnosis to transition to adulthood.

**Objectives**

Following basic training in the principles of structured education, a working group consisting of Health Care Professionals (HCPs) and parent representatives

was set up in 2013 with a view to develop a tailored programme. The philosophy of the programme is to “Empower the CYP and family to manage diabetes from diagnosis right through and including transition to adult services”.

#### Methods

Work commenced with existing education materials that were being used within Wales. We developed shared interactive and age appropriate resources that are aligned to the education key stages for the UK (1,2, 3+4). The resources include an interactive story board, age based workbooks and activities. There is a detailed curriculum for the educators which is accompanied by an education/assessment record - this will enable standardisation of diabetes education across Wales. The programme is accompanied by a quality assurance process with formal evaluation.

The first module “Diabetes at Diagnosis” for age 11years +, piloted in September 2015 helped to refine these resources.

#### Results

Feedback from educators and users has been positive.

#### Conclusion

The first phase of the programme was launched in March 2016 after training of HCPs within Wales. The other key stages (with a Welsh translation) will follow and additional modules such as sport, pumps, annual updates, transition to secondary school and adulthood are planned.

We would like to take the opportunity to share our journey with you.

DOI: 10.1530/endoabs.45.OC7.3

## OC7.4

### Accuracy and patient experience of the novel flash glucose monitoring system in children and young people with type 1 diabetes mellitus

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Alder Hey Children’s Hospital, Liverpool, UK.

#### Background

FreeStyle Libre flash glucose monitoring system (FSL) has recently gained popularity as it can potentially reduce the number of finger prick capillary blood glucose tests (CBG). Initial short-term studies in adults have demonstrated accuracy although there is no paediatric data available to date. We aimed to assess the accuracy of FSL in children and young people and evaluated the user experience in routine clinical practice.

#### Methods

About 310 datasets of corresponding CBG and FSL readings were available from 8 T1DM patients (8–18 years) who were enrolled in two-week trial of FSL. A detailed questionnaire was completed at the end of the trial period.

#### Results

The mean (+SD) variation of the FSL readings compared to CBG was 0.92 mmol/l (+1.18)]. The overall mean absolute relative difference (MARD) was 10.9% and 12% of the episodes had a discrepancy of > 2 mmol/l. The mean number of swipes per day was 10 and FSL revealed an average of 8% time spent in the hypoglycaemic range. The mean (+SD) variation during hypoglycaemia (< 4 mmol/l) was 0.42 mmol/l (+0.32)]. About 88% of values were within the reference standard ( $\pm 0.83$  mmol/l) at glucose concentrations less than 5.6 mmol/l. The sensor lasted for an average duration of 7 days. All patients rated convenience and ease of use as high (4–5 out of 5) on a self-measured scale with 75% reporting an improved quality of life with FSL. A substantial percentage of young people found FSL to be more “socially acceptable” than finger prick testing.

#### Conclusions

We report the first paediatric data on patient experience and accuracy of FSL in routine clinical practice. FSL provides more data on glucose levels/trends and patients find the system convenient for routine use. Although the overall accuracy is reasonable, some extreme variations are noted. Only around half of the patients stated that they would rely on FSL for dose calculations/hypoglycaemia management. The limited longevity of the sensor in routine clinical practice has potential cost implications. Further long term studies of a larger sample size are required to understand the accuracy, long term efficacy and safety of FSL in children and young people.

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## OC7.5

### Establishing a paediatric diabetes sports service

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#### Background

There is growing recognition of the importance of sports/exercise in children and young people (CYP) with type 1 diabetes (T1DM) [NICE guidance 1.2.47–1.2.53]. In 2014 our Paediatric Diabetes service set up a Diabetes Sports clinic run by a paediatric diabetologist and dietician and an adult diabetologist. Appointments were offered to families of CYP with T1DM who are ‘elite sportspersons’—performing at competitive levels, or regional/national levels. We have held 4 clinics and seen 18 families. Clinic aims include: reducing the number and severity of hypos in children doing a lot of sport, giving advice on dietary intake during/after sport, and generally improving confidence about being active with sport.

#### Method

A service-user audit was performed to assess patient/user satisfaction. Eighteen questionnaires were sent out, 14 were returned (=78% response rate). We also audited the number of hypos in the 3 months before the Diabetes Sports Clinic appointment and in the 3 months following the clinic.

#### Results

- About **86%** of families were ‘very satisfied’ or ‘satisfied’ with the pre-clinic information they received (including details of information that would be useful for them to collect prior to coming to the appointment).
- About **100%** of families were ‘very satisfied’ or ‘satisfied’ with the length of the clinic appointment (40minutes), the knowledge of the MDT team, and found the discussion in clinic useful.
- About **93%** of families ‘strongly agreed’ or ‘agreed’ that they were able to make improvements to their child’s care using information provided in the Diabetes Sports Clinic (7% neither agreed nor disagreed).
- About **100%** of families were ‘very likely’ or ‘likely’ to recommend the clinic to family or friends with T1DM and **93%** of families believe they would benefit from a follow-up appointment.
- There was a reduction in hypo episodes in **73%** of patients who attended the clinic (no change in 9%).

#### Conclusion

We are very encouraged by these results and we plan to expand the service to cover the region. We also held a Family Sports Education morning in May which was very well received, and we have written detailed family information leaflets on T1DM and exercise.

DOI: 10.1530/endoabs.45.OC7.5

## Oral Communications 8 – Diabetes

### OC8.1

#### Coeliac disease screening in children with type 1 diabetes mellitus: Is it time for a new approach?

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<sup>1</sup>Oxford Children’s Hospital, Oxford, UK; <sup>2</sup>Oxford Foundation School, Oxford, UK.

#### Objectives

Recently updated NICE guidelines (2015) on coeliac screening for children with Type 1 diabetes mellitus (T1DM) recommend just one initial screen for coeliac disease (CD) at the time of T1DM diagnosis and thereafter **only** if symptomatic. This is in contrast to the recommendation for on-going annual screening for autoimmune thyroid disease (ATD). Our unit has historically performed annual screening for both ATD and CD. Our study aimed to establish whether current NICE recommendations for CD screening were sufficient, or if indeed they could result in missed diagnoses.

#### Methods

We performed a cross-sectional review of patients attending our Paediatric Diabetes Service to identify those with CD and ATD. Further analysis established how the diagnosis of CD had been made, the timing of the diagnosis compared to onset of and duration of T1DM, and presence or absence of symptoms. We performed an extensive review of national and international screening guidelines, comparing these against the new NICE guidelines.



**Results**

Of the 342 children within our Paediatric Diabetes Service, we identified 28 patients with CD (8.2%) and 20 with ATD (5.8%). Only 28% of CD diagnoses were made from initial new diabetic screening bloods whereas 56% were diagnosed from annual review bloods. One patient (4%) presented with symptoms outside of annual review (no data in 12%). 44% of the cohort were diagnosed with CD within the first year of T1DM diagnosis but 12% were diagnosed after 5 years with T1DM.

Several alternative guidelines recognised the increased incidence of CD in the first 5 years after diagnosis of T1DM, and therefore advocate more screening within the initial 5 years.

**Conclusions**

Previous literature suggests that CD is significantly less prevalent than ATD in T1DM. UK studies suggest a prevalence of 4.4–5.8% of CD in children with T1DM. Our results show a higher prevalence of CD than this previous literature has suggested. The majority of cases were asymptomatic and identified by annual review bloods after initial negative screening tests. We recommend that national guidelines should be re-evaluated with on-going yearly screening for CD, at least for the first 5–10 years following diagnosis of T1DM.

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**OC8.2****The role of DNA hydroxymethylation in non-alcoholic fatty liver disease**

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**Introduction**

Non-alcoholic fatty liver disease (NAFLD) has become the most common form of chronic liver disease in children in association with the increasing prevalence of obesity. The underlying mechanisms are incompletely understood, however the accumulation of cholesterol and fatty acid lipotoxins plays an important role. 5-hydroxymethylcytosine (5hmC) is an epigenetic modification generated from 5-methylcytosine (5mC) by the Ten-eleven translocase isoenzymes (Tets). Tet function is modified by glucose metabolites suggesting that Tet enzymes may be a novel modulator of energy homeostasis. We hypothesised that Tet-mediated DNA hydroxymethylation impacts on NAFLD pathogenesis.

**Methods**

C57Bl6/j mice were fed 58% saturated fat (HFD) or control diet for 17 weeks before intraperitoneal glucose tolerance testing and analysis of liver histology. Genome-wide profiling of 5hmC was undertaken using DNA immunoprecipitation and semiconductor proton sequencing. Hepatic transcriptomic analysis was performed using Illumina WG6 beadchip microarrays. A parallel HFD-fed mouse cohort with was switched to control diet for 12 weeks to reverse the phenotype. Human embryonic stem cell-derived hepatocytes were challenged with energy substrates lactate, pyruvate and octanoate for 48 hours, with 5hmC and transcriptome analysis.

**Results**

HFD induced obesity, glucose intolerance, insulin resistance and hepatic steatosis; strikingly these changes were reversed after switching to control diet. Whilst the overall global 5hmC profile was not altered by HFD, there was significant genic enrichment of 5hmC in upregulated mediators of cholesterol synthesis and transport (Lss, Sc4mol, Fdps, Hsd17b7, Cyp17a1, Mvd, Cyp1a2, Dhcr7 and Apoa4), with no enrichment in genes with other pathological functions. 5hmC enrichment was abolished following reversal of the NAFLD phenotype. These findings were largely replicated in human hepatocytes exposed to high-energy substrates with specific 5hmC enrichment in genes synthesising and transporting lipotoxic molecules (PLIN2, CIDEC, APOA4, ACADVL, HMGCS2, APOA5, CYP2J2, IGFBP1, PPAP2C, ACSL1, APOC3, ANGPTL4, NRG1) and no enrichment in upregulated genes of alternative function.

**Conclusion**

In these models of NAFLD, overnutrition induces genic hydroxymethylation with concurrent transcriptional activation specifically in genes driving the synthesis and transport of lipotoxic molecules. Such changes are reversible strengthening the functional association. We suggest that Tet-mediated hydroxymethylation may be an important mechanism in NAFLD pathogenesis and progression.

DOI: 10.1530/endoabs.45.OC8.2

**OC8.3****Comparison of Insulin sensitivity measures between overweight and obese children and adolescents of South Asian and White Caucasian ethnicity**

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University Hospitals of Leicester, Leicester, UK.

**Background**

WHO has recommended that adults of South Asian (SA) ethnicity need to have lower body mass index (BMI) cut-off to define overweight and obesity compared to White Caucasians (WC). The background for this is the increasing evidence that obesity-related morbidities are much higher at a lower BMI among SA compared to WC adults.

**Objective**

The aim of our study was to evaluate differences in measures of insulin sensitivity amongst children and adolescents classed as overweight or obese of either SA or WC ethnicity

**Method**

Retrospective analysis of medical records of all children and adolescents defined as overweight or obese using BMI and British 1990 growth reference BMI charts were used as the criteria to define each group. Ethnicity data was based on self reporting by the family. Comparison between the two groups included fasting glucose, insulin, homeostasis model assessment (HOMA-IR), 120 minutes glucose levels after oral glucose tolerance test (OGTT) and HbA1c. Statistical analysis was done using PRISM software.

**Results**

A total of 143 patients who fulfilled criteria were identified. 67 (47%) were SA and 76 (53%) WC. Age and sex distribution between the two groups were identical. SA group had a lower mean BMI (SA  $32.1 \pm 5.9$  vs WC  $36.4 \pm 7.7$ ;  $P=0.0003$ ) and lower mean BMI SDS (SA  $3.0 \pm 0.7$  vs WC  $3.5 \pm 0.7$ ;  $P<0.0001$ ) compared to WC. HbA1c levels (SA  $40 \pm 8$ mmol/mol vs WC  $37 \pm 5$ ,  $P=0.02$ ), Fasting insulin (SA  $32.8 \pm 21.4$  miu/l vs WC  $25.3 \pm 17.0$ ;  $P=0.03$ ) and HOMA-IR index (SA  $7.2 \pm 5.1$  vs WC  $5.3 \pm 3.8$ ,  $P=0.02$ ) was significantly higher in the SA compared to WC. Fasting glucose and 2 hour glucose after OGTT were not statistically significant between the groups. 2 children in WC and 4 in SA were diagnosed with Type 2 Diabetes.

**Conclusion**

Our study reveals that obese and overweight children and adolescents of SA had significant abnormality of insulin sensitivity markers at a lower BMI compared to WC. This highlights the need to consider lowering the BMI threshold cut-off to define overweight and obesity among SA children and adolescents similar to those recommended in adults.

DOI: 10.1530/endoabs.45.OC8.3

**OC8.4****Effect of weight loss on Resting Energy Expenditure in pre- and post-pubertal obese children**

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**Background**

In obese adults, caloric restriction leads to a reduction in energy expenditure, and it is this compensatory adaptive down-regulation that is cited as one of the causes of weight regain in adults. There are currently insufficient data to establish if this phenomenon also occurs in obese children who lose weight and whether puberty affects this adaptive response.

**Objective**

We hypothesised that obese children who lose weight have less 'reflex' changes in Resting Energy Expenditure (REE) (that may drive weight regain), compared with obese adolescents with a similar degree of weight change.

**Method**

Prospective cohort study. 41 subjects; 21 obese pre-pubertal children (age 3–7 years; 11 male) and 20 obese adolescents (age 14–18 years; 10 male). Obesity defined as BMI  $>2.4$  SDS. Subjects recruited as either 'reducers' (relative/absolute weight loss of  $\geq 10\%$  in preceding 9–15 months) or 'maintainers' (controls). REE measured using Medgem® indirect calorimetry in all 41 participants at baseline and REE measured at follow-up in 23 subjects, 6–21 months later (average 10.6 months); 13 obese pre-pubertal children (6 male) and 10 obese adolescents (5 male).

**Results**

At baseline, REE (Kcal/day) in pre-pubertal weight reducers and maintainers had similar mean values (SD) of 1197(274) and 1246(160), but post-pubertal reducers had 252 kcal lower REE compared to post-pubertal maintainers, 1852 (279) and 2104 (393) respectively. When REE was expressed as Kcal/Kg/day (division of mean REE by mean weight in each group), baseline values for the pre-pubertal reducer and maintainer group and the post-pubertal reducer and maintainer group were 25.4, 23.7, 18.9 and 17.8 Kcal/Kg/day respectively. At follow-up, values were 28, 25.5, 18.4 and 16.6 Kcal/Kg per day respectively. Therefore compared with baseline, changes in REE/Kg per day between baseline and follow-up measures were +2.6 in pre-pubertal reducers, +1.8 in pre-pubertal maintainers, -0.5 in post-pubertal reducers and -1.2 in post-pubertal maintainers.

**Conclusions**

Pre-pubertal children have a greater REE compared to post-pubertal adolescents, which would help them to maintain weight loss. Larger studies are needed to explore the relationship between weight loss and REE in pre and post pubertal children.

DOI: 10.1530/endoabs.45.OC8.4

**OC8.5****Biomedical outcomes of weight loss associated with intragastric balloon therapy supported by a life style programme in severe adolescent obesity**

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<sup>6</sup>Department of paediatric endocrinology, Lady Cilento Children's Hospital, South Brisbane, Australia.

**Background**

Severe obesity in childhood is associated with significant morbidity including systolic hypertension, fatty liver, obstructive sleep apnoea, dyslipidemia and type 2 diabetes. Evidence that even small changes in BMI SDS bring about significant clinical benefit is strong.

**Objectives**

To assess the impact of weight loss associated with intragastric balloon therapy supported by a life style programme on biomedical outcomes (glucose metabolism, blood pressure, lipid profiles) in severely obese adolescents and to observe any changes in incretin, ghrelin and adipokine hormones.

**Methodology**

A 2-year cohort study of 12 adolescents (BMI >3.5 SD, Tanner stage >4) following 6 months intragastric balloon placement. Subjects underwent anthropometry, oral glucose tolerance test, measurement of basal and stimulated incretins and adipokines at 0, 6 and 24 months.

**Results**

Mean weight loss at 6 months was 7.1 kg (ICI -27,12.8],  $P$  value = 0.005), (5% body weight) but weight loss was sustained in only 20% patients at 2-years. Insulin area under the curve following OGTT improved at 6 months ( $P < 0.05$ ). As individuals tended to regain weight following balloon removal HOMA scores and fasting insulin levels increased but Insulin AUC remained below pre intervention levels. There was also a fall in HbA1c at 6 months that was maintained despite weight regain ( $P < 0.005$ ). There was a significant increase in fasting GLP-1 over the 24 months ( $P = 0.04$ ). The area under the curve (AUC) for GLP-1 also improved at 24 months despite weight regain. The significant drop in GIP at 6 months ( $P < 0.001$ ) was not sustained at 24 months. We noted moderately strong inverse correlations between percentage weight loss and change in GLP-1 AUC ( $r = -0.45$ ) and ghrelin ( $r = -0.51$ ) at 6 months. Clinically relevant improvements were also seen in blood pressure, liver function at 6 months.

**Conclusion**

Short-term weight loss and clinically relevant improvement in obesity related complications were seen after 6 months of intragastric balloon therapy. Benefits were sustained in some patients but not the majority at 2 years.

DOI: 10.1530/endoabs.45.OC8.5

**OC8.6****Is abuse associated with adolescent overweight and obesity?:****A population cohort study**

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Julian Hamilton-Shield<sup>2,3</sup>

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<sup>3</sup>Bristol Royal Hospital for Children, Bristol, UK.

**Background and Objectives**

Abuse in childhood is associated with obesity in adult life. However, little is known about the relationship between abuse and obesity during childhood or adolescence. The aim of this study was to investigate, using a birth cohort study, whether there was an association between pre-adolescent child abuse and overweight and obesity in later childhood. We hypothesised that abuse and obesity may be associated.

**Methods**

Using data from the Avon Longitudinal Study of Parents and Children (ALSPAC), which is a cohort involving 13978 children, we analysed BMI (body mass index) ( $\text{kg}/\text{m}^2$ ) at ages 13 and 16 years and repeated measures of parentally reported abuse up to 11 years of age. The sample in this analysis comprises 4205 adolescents with complete data for child abuse variables collected during childhood and BMI at both 13 and 16 years. Abuse was categorised as emotional, physical or sexual. In a sub-sample, a longitudinal analysis utilising serially-collected BMI measurements (at 13, 16 and 18 years) was conducted to identify whether abuse resulted in different trajectories of BMI during adolescence.

**Results**

Using linear regression analysis, adjusting for sex and family adversity, we found no significant association between child abuse of any kind and obesity or BMI z-scores at 13 or 16 years. The rate of reported abuse was 0.47% for sexual which was lower than previous figures, 5.6% for physical and 15.3% for emotional which were similar to previously reported rates. The longitudinal analysis revealed no significant association between childhood abuse and the pattern of BMI change during adolescence.

**Conclusions**

We did not find a relationship between pre-adolescent child abuse and adolescent obesity in this cohort. Furthermore, as these data were prospectively collected, we challenge the assumption that adolescent obesity is linked to previous child abuse as has been reported for obesity in adult life. Therefore, based on the findings of this study, paediatricians need not assume that pre-pubertal child abuse is a potential causal factor or consequence of childhood obesity. A further longitudinal study utilising both parental and child reports with data record linkage and including neglect, the fourth type of child abuse, would be desirable.

DOI: 10.1530/endoabs.45.OC8.6

**OC8.7****Clarifying the natural history of human insulin receptoropathy**

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**Background**

Insulin resistance is the reduced responsiveness of the body to the glucose-lowering activity of insulin. It is usually associated with obesity, but in a minority of patients, this is not the case. Single gene mutations can often be found in such patients, some of which affect the insulin receptor (INSR). There is a spectrum of genetic insulin receptoropathies. These can be considered as two groups. One group comprises rare, severe, autosomal recessive disorders: Donohue syndrome (DS) and Rabson-Mendenhall syndrome (RMS). The other group consists of Type A Insulin Resistance (TA), which is typically autosomal dominant.

**Aims**

To investigate the effect of different degrees of INSR function on birth weight, and on the biochemical profile, including HDL-Cholesterol, Triglyceride, and Adiponectin. Previous research has shown that patients with DS and RMS have reduced birth weight, and that patients with human insulin receptoropathy typically have preserved or elevated adiponectin levels, and do not have metabolic dyslipidemia (hypertriglyceridemia and low HDL-Cholesterol levels).

**Methods**

Patient notes were reviewed to add to an incomplete database of 185 patients with INSR mutations collected between 1992 and 2015. The mean values of birth weight, HDL-Cholesterol, Triglyceride, and Adiponectin were compared for patients with DS, RMS, and TA, using Student's t-tests.

**Results**

The mean birth weight for DS patients was significantly lower than for RM or TA patients ( $P < 0.0005$ ). The mean HDL-Cholesterol for DS patients was significantly lower than for TA patients ( $P < 0.005$ ). The mean Triglyceride in

TA was significantly lower than in DS ( $P < 0.05$ ), and significantly higher than in RM ( $P < 0.005$ ). The mean Adiponectin did not vary significantly between DS, RM, and TA patients.

#### Conclusion

Patients with different degrees of INSR function have significantly different birth weights and measurable biochemical results. These findings of differences between degrees of INSR function add to previous research which found characteristic biochemical results for insulin receptoropathies as a group. These differences in biochemical results could be further studied, to help direct genetic sequencing in patients for specific INSR mutations.

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## Oral Communications 9 – Nurses

### OC9.1

#### A review of junior doctors' knowledge of the management of newborn disorders of sexual development

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#### Introduction

Disorders of sexual development (DSDs) are estimated to occur in 1 in 4500 births. This potentially represents one baby born every other day in the UK. We aim to explore how Mersey foundation and paediatric trainees deal with newborn babies with possible DSD and identify if there is a need for further training in this subject.

#### Methods

An online survey composed of 10 questions was distributed amongst foundation and paediatric trainees in Mersey deanery. The questions targeted history taking, examination, investigations and management.

#### Results

About 51 trainees completed the questionnaire. About 9(18%) were foundation and 42(82%) were paediatric trainees. Half of respondents (53%) were unaware of the local DSD pathway.

Only 18% reported that they would include all of the relevant points in history taking. About 14% reported that they would not know what questions to ask if they were faced with a baby with possible DSD. About 53% of trainees were unsure what to look for in their clinical examination. About 84% of trainees would refer the suspected DSD babies to urologist, 4% would refer to the general practitioner, 6% would arrange for follow up in general paediatric clinic and only 6% would refer to the DSD coordinator. About 75% of the trainees appropriately would not assign a gender until proper parental counselling and involvement from endocrine and urology teams. About 84% would also correctly monitor serum electrolytes until CAH excluded with 84% requesting an abdominal ultrasound. About 69% would check the 17-hydroxy-progesterone level after first 48 hours of baby's life. However reassuringly, 90% would get their on-call consultant to be involved with parental counselling. About 94% expressed a need for more training in this subject.

#### Conclusion

This survey illustrates a gap in foundation and paediatric trainees' knowledge about what to ask and what to look for in babies with suspected DSD and a worrying lack of knowledge of local policy on the management. It was reassuring that 90% of the trainees would seek advice from a senior. We plan to repeat this survey among other professionals who perform baby checks including senior doctors and to include information on DSD in our junior doctor teaching and training programme.

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### OC9.2

#### Autonomy, self-injection and adherence in patients on GH treatment

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#### Introduction

Strategies for optimising adherence in patients with growth hormone disorders often focus on enabling them to achieve autonomy in the management of their

treatment, including self-injection of growth hormone (GH). However, there is a scarcity of published data on the effectiveness of this approach. We conducted a survey to elicit responses from UK endocrinologists and endocrine nurses, to investigate 'real-world' clinical practices around the initiation of self-injection and patient education, and to identify barriers that hinder the success of these strategies and their impact on adherence.

#### Methods

An online survey was distributed to 198 endocrine healthcare professionals. The survey consisted of 19 questions designed to discover the various practices across centres, and to gauge respondents' views on the relationship between patient autonomy, GH self-injection and adherence.

#### Results

There were 61 responders, 42 of them nurses and 19 of them consultant endocrinologists. The majority (40) worked with paediatric patients, 17 with adult patients, and 4 with both. Optimum ages for initiating self-injection were judged to be between 7 and 10 years, although this depended on individual patients. The most common reason for initiating self-injection was a request from the child (79%), followed by parental request. Other reasons included moving to secondary education and following established centre practice. The majority of respondents (88%) thought self-injection was important and over half (54%) believed it would improve adherence. However, there was a general absence of guidelines in place to facilitate transition to self-injection. The main benefits of self-injection identified included boosting independence and confidence, taking ownership and control of treatment, and increasing patient freedom and flexibility. Barriers to achieving this included patient maturity, fear of injections or needles, poor dexterity, visual impairment, learning difficulties, parental attitudes and availability of support at home. Measures that could increase uptake in self-injection included increased nurse involvement, patient education and training, home visits, change of device and boosting parental commitment.

#### Conclusions

Self-injection was considered beneficial for patient well-being and likely to improve adherence, but clinicians and patients face numerous challenges. This survey highlighted some valuable issues around patient self-injection and adherence that should be explored further.

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### OC9.3

#### Managing overweight and obese children and young people in a district general hospital in England

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#### Background

In England 15% of children are obese and 29% children are overweight (including obese). This data has huge implications for children and young people's (CYP) quality of life and increased risk of complications as young adults, also has great costs implications for the NHS. If we can identify and support the overweight and obese CYP and their families, we should prevent them from progressing to adult obesity and reduce associated complications.

#### Objective

1. To measure our practice against NICE Guideline: Obesity: identification, assessment and management (CG 189)
2. To identify areas for improvement in our management of obese and overweight children and young people in our Trust.

#### Method

NICE Guideline used as audit standard - (CG189). We performed a retrospective review of patient notes of patients seen in paediatric clinics from May 2014 to July 2015 (15 months). An audit questionnaire was created, and was completed based on information from clinical notes.

#### Results

About 47 children identified as being obese/overweight by consultant colleagues. Out of those, 37 notes were analysed, 6 deemed unsuitable for analysis, 4 notes could not be obtained in time.

Statistics obtained from analysis of data: 62% given general lifestyle advice. About 19% given a weight management programme. About 21% given behavioural change advice/referred to psychologist. About 5.4% parents asked to consider

their own weight. About 16.2% given information on health risks. About 2.7% given information on realistic targets. About 24.3% given information on voluntary/organisational groups. About 75.7% followed up by a paediatrician. About 51.4% followed up by dietician. About 13.5% followed up by psychologist.

Conclusion

We are good at giving general lifestyle advice, but have to involve the whole family in the life style modification plan.

We have to document better information given to CYP and their parents regarding health risks posed by their condition for the future.

We have to be better at working together in an multi-disciplinary team (MDT) approach to ensure cohesive follow up plans.

We proposed to create a leaflet to give to CYP and their parents documenting health risks/ realistic targets/ organizations available to help them.

We consider developing a one-stop obesity clinic with MDT approach (paediatrician, dietician and psychologist).

DOI: 10.1530/endoabs.45.OC9.3

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# Poster Presentations

**Adrenal****P1****Assessment of parental knowledge of the management of acute illness in children on long-term steroids**

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**Introduction**

Children on long-term steroids are at risk of Addisonian crisis during acute illnesses unless their dose is increased. To prevent this parents receive teaching on correct management if their child becomes unwell. We looked at the effectiveness of this education by assessing parental knowledge.

**Methodology**

Parents of all children taking long-term steroids under paediatric endocrinology at our hospital between November 2015 and May 2016 were sent a questionnaire regarding the management of acute illnesses in their child. It was based on local and regional guidelines for steroid management. To maximise response rates questionnaires were also distributed opportunistically during attendances on the ward or outpatients.

**Results**

Out of the 15 of the 22 respondents 100% (15/15) knew their child's steroid dose, when to seek help and who to contact if their child became unwell. 7% (1/15) did not have an in date hydrocortisone injection at home and 33% (5/15) did not feel confident administering the injection themselves. 87% (13/15) knew to increase the steroid dose during illnesses but only 67% (10/15) knew to give IM hydrocortisone during illnesses if oral steroids were not tolerated, and 73% (11/15) knew to give it for a serious injury. Finally only 40% (6/15) knew to specify a paramedic ambulance when phoning for emergency help.

**Discussion**

Our survey demonstrates that further improvement in parental education is needed in this group of carers. As there is no national guidance on steroid management during illness we intend to perform a survey (via BSPED membership) of parental knowledge with the aim of creating a national patient information leaflet as well as a clinic checklist. Meanwhile in our clinic a separate leaflet will be introduced that clearly outlines how to alter steroid doses during acute illness as well as a clinic stamp to remind clinicians to check injection expiry date and offer further injection training to parents. We have also written to our regional ambulance service to get clarity on whether a paramedic ambulance is required or whether a standard ambulance crew carries and can administer IM hydrocortisone in our patients (information will be available at the BSPED meeting).

DOI: 10.1530/endoabs.45.P1

**P2****Assessment of staff knowledge of the management of acute illness in children on long term steroids in a large DGH offered Tertiary Paediatric Endocrine services**

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**Introduction**

Children on long-term steroid treatment are at risk of developing an Addisonian crisis during an acute illness unless their steroid dose is increased appropriately. It is essential for all staff involved in the care and management of such patients (Paediatric Nurses, Paediatric Doctors, ED Doctors) to be familiar with the relevant management guidelines.

**Methodology**

Between November 2015 and May 2016 Paediatric and ED nursing and medical staff (F1 to Consultant) were surveyed to assess the level of knowledge of local guidelines at a large DGH offering a Tertiary Paediatric Endocrine service.

**Results**

Forty-One responses were analysed (11 nurses and 30 doctors of which 4 were ED doctors). 85% (35/41) of staff knew to measure blood glucose and 90% (37/41) blood pressure on arrival but only 47% (14/30) of doctors knew to request U&E and laboratory glucose. 54% (22/41) of staff knew to treat hypovolaemia with an

IV fluid bolus and 88% (36/41) to treat hypoglycaemia with fast acting glucose (orally or IV). 83% (25/30) of doctors knew to contact the on-call consultant and 93% (28/30) where to find the dose of hydrocortisone. 95% (39/41) of staff knew to give IV/IM hydrocortisone to seriously unwell children and 83% (25/30) of doctors knew to increase the oral dose if oral medicines were tolerated in moderately unwell children.

**Discussion**

Our survey covered a representative section of the majority of the staff likely to be in contact with this patient group. The knowledge of the acute treatment of seriously unwell children was high as was where to located local guidelines. The survey highlighted that there was a knowledge gap in the initial investigations needed, the treatment of hypotension and management of those children who were moderately unwell but not in acute crisis. We aim to set up teaching sessions targeted at not only junior doctors in Paediatrics (at induction) but also senior doctors and most importantly staff in ED, where these patients may often be initially seen and assessed, whilst also publishing the management guidelines on the hospital wide intranet. We hope to complete the audit cycle at the end of 2017.

DOI: 10.1530/endoabs.45.P2

**P3****Rationalising the number of cortisol assays in our low dose synacthen test**

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**Objectives**

Secondary Adrenal Insufficiency is diagnosed using an ACTH stimulation test. There is no clear evidence that either a Low dose Synacthen Test (LDST) or a Short Synacthen Test is more superior in diagnosis. In our service, we routinely use LDST to investigate adrenal function. There is a lack of standardisation regarding timing, dose and frequency whilst undertaking a LDST leading to diagnostic inconsistencies. We routinely measure baseline cortisol levels, then at 10, 20, 30 and 60 minutes post Synacthen administration. Our aim was to evaluate whether we could rationalise the number of tests undertaken and in particular whether stopping the test at 30 minutes would be possible without misdiagnosing adrenal insufficiency.

**Method**

We undertook a retrospective analysis of all LDST results performed by our paediatric endocrine nurses in the last 10 years. Prior to January 2015 our cut off for diagnosing adrenal insufficiency was a maximum cortisol < 500 nmol/l; after 12th January 2015 the laboratory cortisol assay changed to being more sensitive and specific so our threshold reduced to < 450 nmol/l.

**Results**

198 tests were analysed. 25% (50 out of 198) had a maximum cortisol level at 20 minutes, while 40% demonstrated this maximum level at 30 minutes (79 out of the 198). 30% of the cortisol levels peaked 60 minutes post the Synacthen dose. The rest were maximum at various other times. Since Jan 2015, 3 cortisol levels were maximum at 60 minutes. Of these, 2 were insufficient at 30 minutes but sufficient cortisol was attained by 60 minutes. In the same period, no test showed a maximum cortisol level at 10 minutes.

**Conclusion**

Analysing cortisol at 10 mins post synacthen did not aid the diagnosis of adrenal insufficiency and could safely be omitted from the protocol. Omitting the 60 min sample however would result in a number of children being diagnosed inappropriately with adrenal insufficiency. Although this would affect only a small proportion of individuals (2 out of 31), as the diagnosis has such important implications for management we would recommend that analysis of cortisol levels 60 min post synacthen is maintained.

Figure showing maximum cortisol levels at various times post synacthen dose

Time of Cortisol Assay	Number of maximum results
10 mins	5
20 mins	50
30 mins	79
45 mins	1
60 mins	60
60 mins or N/A	3

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## P4

**Misleading biochemical picture in infants prior to the confirmatory diagnosis of Congenital Adrenal Hyperplasia (CAH)**

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**Introduction**

Adrenal insufficiency is a rare cause of life-threatening hyponatraemic collapse in the neonatal period. The initial investigations taken at the time of presentation, and prior to the institution of hydrocortisone, are a key step in the diagnostic pathway.

**Aim**

We present a case series where the initial biochemical test results could have led to a delay in diagnosis or early discontinuation of hydrocortisone.

**Case 1:** Female (46,XX) term infant presented with genital ambiguity with non-palpable gonads. Initial electrolytes at day 4 of age were normal with normal peak cortisol response (Table 1). Urinary steroid profile (USP) confirmed a diagnosis of 21-Hydroxylase deficiency, which allowed initiation of salt and steroid replacement, averting an adrenal crisis.

**Case 2:** Term male (46,XY) infant born to mother with 21-hydroxylase deficiency had synacthen test for suspected CAH. The peak cortisol response was satisfactory; infant was discharged with cautious reassurance. However USP later confirmed CAH (3- $\beta$ -hydroxylase deficiency) and infant was commenced on treatment.

**Case 3:** 14-day-old male (46,XY) term infant presented with 14% weight loss, salt-wasting crisis and dehydration. He was commenced on steroid replacement prior to a synacthen test. An elevated serum aldosterone level prior to steroid treatment confused the picture, raising the possibility of pseudohypoaldosteronism. A USP confirmed the diagnosis of CAH (21-OH defect).

**Conclusions**

Two cases showed a normal synacthen response, giving false reassurance of the adrenocortical reserve. This was likely due to cross-reactivity with adrenal fetal steroids. The other showed elevated aldosterone levels, which is occasionally reported due to interference in assay. In suspected cases of CAH, clinicians should be guarded in relying on a single normal or abnormal test. Management should be based on confirmatory USP results.

Table 1 Biochemical results at presentation

Case	Age at presentation (days)	Age at testing (days)	Na (mmol/l)	K (mmol/l)	Aldosterone (pmol/l)	Renin (mU/l)	17-OH-P (nmol/l)	Synacthen test Cortisol (nmol/l) in minutes		
								0	30	60
1	birth	4	137	6.1	-	>500	155	494	531	588
2	birth	3	144	4.9	-	N/A	334	447	466	466
3	14	18	103	6.6	>1000	>500	3220	N/A	N/A	N/A

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## P5

**Reviewing the protocol for the standard short synacthen test**

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**Introduction**

Assessing cortisol status is a key endocrine investigation, to identify those who need glucocorticoid replacement or emergency sickness cover either due to primary or secondary cortisol deficiency or after long-term/high dose steroid treatment causing Hypothalamic-Pituitary-Adrenal axis (HPAA) suppression. A short synacthen test (SST) measuring cortisol levels after administration of Synthetic ACTH at time zero, 30 and 60 minutes is commonly used. A normal response is assay dependent, for our institution historically > 500 nmols/l; >420 nmols/l from Dec 2015 (Roche Gen II).

**Aim**

To examine the SST response in patients investigated for primary, secondary/tertiary hypoadrenalism or adrenal suppression secondary to exogenous steroids.

**Methods**

All SSTs and clinical indication were identified from our departmental database between 1/10/2005 and 1/6/2016.

**Results**

512 consecutive SSTs (437 patients, M=183) were identified, undertaken at various times of day. 382 patients had one test, 41 patients two tests, 8 patients three tests and 6 patients four tests. Median(range) age was 11.3(0.01-21.5) years. Indication and results for SST were: suspected HPAA suppression from exogenous steroids (patients n=139, 82/185 tests, 44% abnormal), suspected secondary/tertiary hypoadrenalism (patients n=181, 36/205 tests, 18% abnormal), suspected primary hypoadrenalism (patients n=73, 13/76 tests, 17% abnormal) and other indication (including chronic fatigue, hypoglycaemia) (patients n=44, 4/46 tests 9% abnormal). Overall, in abnormal and normal tests the cortisol peak was at 60 minutes (n=491), 30 minutes (n=19), at time zero (n=2). 377 tests showed a normal cortisol response with cortisol peak at 30 minutes in n=17 but all also had cortisol normal response at 60 minutes. Peak cortisol by clinical indication; suspected HPA axis suppression from exogenous steroids: 30 min n=6, 60 min n=179, suspected secondary or tertiary hypoadrenalism: 30 min n=8, 60 min n=197, suspected primary hypoadrenalism: zero min n=2, 30 min n=4, 60 min n=70, other indication: 30 min n=1, 60 min n=45.

**Conclusion**

In 96% of SSTs, the diagnostic cortisol peak was at 60 minutes. All of the normal tests with the highest peak at 30 minutes also demonstrated an adequate response by 60 minutes. This study questions the need for a 30 minute cortisol measurement during a SST.

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## Bone

## P6

**Awareness of Vitamin D supplementation guidelines among the junior doctors at University Hospital of Wales, Cardiff**

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**Background**

The prevalence of childhood vitamin D deficient rickets in the UK is rising due to lack of sun exposure. The Department of Health, Royal College of Paediatrics and Child Health (RCPCH) and the National Institute for Health and Care Excellence (NICE) have devised guidelines on vitamin D supplementation during pregnancy, breastfeeding and childhood. A recent Government initiative, Healthy Start vitamins allow access to free vitamin D for women and children from low-income families. Despite these measures, evidence suggests that awareness rate among the doctors remain poor.

**Aim**

To assess the awareness of national (NICE and RCPCH) and local health board guidelines on vitamin D supplementation amongst junior doctors.

**Methods**

A prospective questionnaire was given to two batches of junior doctors randomly during their rotation in the paediatric department at Cardiff and Vale University Health Board.

**Results**

The study period was during September 2014 to March 2015. The total numbers of junior doctors participated in the study were 27. Of which, 48% were ST1-ST3, 26% were ST4 and above, 15% were Foundation year 1 and 2 and rest of the 11% was contributed by staff grade. The results showed only 15% of the junior doctors were enquiring about vitamin D supplements during their admission consultation even though 96% were enquiring about feeding practice. About 63% of junior doctors were checking health board guideline which was based on the RCPCH guidelines. 55% were aware of the Healthy Start Vitamin programme.

**Conclusions**

Most of the junior doctors are not enquiring about Vitamin D supplements during their consultation even though half of them are aware of the local and national guidelines.

**Recommendations**

To raise awareness of the importance of the vitamin D supplementation at the beginning of their placement could be introduced as a part of their hospital induction. Questions about Vitamin D supplementation as well as feeding pattern could be added to the paediatric admission proforma.

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**P7****Craniosynostosis in a case of nutritional rickets**

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**Background**

Nutritional rickets (NR), due to poor dietary calcium intake or vitamin D deficiency is still the most common form of growing bone disease despite the efforts of health care providers to reduce its incidence. Clinical history, physical examination and laboratory evaluation are mainstay of diagnosis.

**Aim**

We report a case of NR where the radiological report was misleading causing significant parental anxiety and delay in diagnosis.

**Case**

Male infant of Afro-Caribbean origin, presented at age 5 months with excessive crying, bulging soft spot in the head and increase in head circumference. He was exclusively breast fed. Born at term gestation, his antenatal scans showed congenital talipes, which were corrected at 2 months of age. Examination and observation was normal with no increase in head circumference over 3 weeks follow up. MRI head was done to rule out any intracranial pathology and reported as sclerotic skull bones with suspicion of osteopetrosis. CT head showed diffuse bone thickening and evidence of craniosynostosis. However, a skeletal survey revealed markedly osteopaenic bones with rachitic changes. Concurrent biochemical picture confirmed the diagnosis of Vitamin D deficient rickets (table 1). Mother was also vitamin D deficient and treatment was commenced. Repeat skull X-ray after a month of treatment showed no clear evidence of craniosynostosis and improving osteopaenia. Close monitoring of the child's head growth will continue.

**Conclusion**

This case illustrates the diagnostic dilemma caused by radiological misinterpretation of MRI head in a florid case of rickets. Early sutural fusion has been reported in hypophosphataemic rickets but we have only been able to find one other case linked to Vitamin D deficiency in the literature. It is important to rule out rickets in children presenting with craniosynostosis.

Age at testing (In months)	Vit D (24–167 nmo/l)	Alkaline phosphatase (100–400 U/l)	Corrected calcium (2.25–2.75 mmol/l)	PTH (14–72 ng/l)	Serum Phosphate (1.45–2.16 mmol/l)	Hb (10–14 g/dl)
5 at diagnosis	<12	4.016	1.96	765	0.64	8.2
7 (after 6 week treatment with vit D)	85	1079	2.5	29	1.86	11

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**P8****Denosumab therapy for hypercalcaemia of malignancy in a young child**

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**Introduction**

Hypercalcaemia secondary to malignancy is rare in childhood. Bisphosphonates have previously been shown to be effective in managing such cases in adults, however caution must be exercised in patients with renal failure or respiratory compromise. Denosumab, a RANKL monoclonal antibody is a very potent inhibitor of osteoclasts and can induce hypocalcaemia. It is not excreted by the kidney. Limited trials in adults have shown denosumab to have greater efficacy compared to bisphosphonates in treating hypercalcaemia of malignancy.

**Case**

A three-year-old girl presented with a brief history of fever, anorexia and vomiting. She was severely hypercalcaemic (cCa 4.88 mmol/l), with an undetectable PTH. She also had evidence of acute kidney injury. Despite hyperhydration and furosemide, the cCa rose to 5.63 mmol/l, and remained elevated following the initiation of calcitonin treatment. Her blood film was suspicious of blasts. A bone marrow aspirate (BMA) was considered crucial at this point to make a diagnosis. Given the situational urgency, and previous reports of hypercalcaemia of malignancy refractory to bisphosphonate therapy, a trial dose of denosumab was administered. The cCa fell to 4.33 mmol/l, enabling a

BMA to be carried out. This confirmed a diagnosis of acute lymphoblastic leukaemia and definitive treatment was started. Normocalcaemia was achieved within 48 hours and sustained.

**Conclusions**

This highlights a rare case of profound hypercalcaemia as a presentation of malignancy in a young child, which responded well to denosumab therapy, enabling an urgent diagnosis to be made and appropriate management to be instigated in a timely manner. Treatment with denosumab may be considered for refractory hypercalcaemia in children, particularly if renal failure is a complication.

**Novel Insights**

This case highlights the youngest child to our knowledge to be treated with denosumab for hypercalcaemia of malignancy. The use of denosumab in the context of severe hypercalcaemia with renal failure, enabled an urgent definitive diagnosis to be made and appropriate treatment of the underlying cause to be initiated in a timely manner. This suggests denosumab may be a viable first line treatment option in cases such as this and its use in children should be considered for further evaluation in clinical trials.

DOI: 10.1530/endoabs.45.P8

**P9****The use of Bone Health Index standard deviation score (BHI-SDS) in the analysis of cohorts with constitutional delay of growth (CGP), Growth Hormone deficiency (GHD), Turners syndrome (TS) and congenital adrenal hyperplasia (CAH)**

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**Background**

BoneXpert software calculates bone health index (BHI) from 100 measurements of cortical thickness and mineralisation of three metacarpals. BHI-SDS is derived from 3,121 X-rays from 231 healthy Caucasian children, corrected for bone age (BA), estimated from the same x-ray.

BHI-SDS is new with relatively unknown clinical utility. Strong correlations between BHI and dual-energy x-ray (DXA) absorptiometry and peripheral quantitative computed CT measurements are reported.

**Objective**

Examine whether BHI-SDS values in children with CDG, GHD, TS and CAH are consistent with previous reports of bone health, measured using conventional methods.

**Methods**

Patients were identified on our database. Age, gender, and BHI-SDS were collected.

**Results**

See table 1 (attached)

**Conclusion/discussion**

BHI-SDS is below the mean in each group. This is consistent with trends reported from DXA studies. BHI reports a measure derived from peripheral skeleton, in contrast to DXA, which uses total skeleton or spine. This may partly account for the differences in magnitude of impairments measured in bone health derived from BA compared from DXA.

The data for CDG patients are interesting. BHI is corrected for BA. This should correct for the effect of delayed skeletal maturation. It may be interesting to repeat this measurement on completion of growth to examine any residual effect on bone health.

Table 1 Table showing age, gender, BHI SDS and comparison with report using conventional methods

	Age (yrs)	Gender (Female:male)	Mean BHI SDS	Report using conventional methods
CDG	7.1–17.1	6: 52	–0.79	No significant difference in CDG and controls
GHD (at diagnosis)	3.7–18.8	31:91	–1.03	Lumbar spine BMD z score –2.92
GHD (+1 yr GH therapy)	4.8–20.1	31:91	–0.20	Lumbar spine BMD z score –1.35
Turners Syndrome	6.3–18.8	–	–0.61	Lumbar spine BMD score –0.87
CAH	1.3–17.4	37:36	–0.41	Total body z score –0.76 Lumbar spine z score –0.29



With the exception (CDG) these data are similar to those reported previously using conventional methods and lend support to use of BHI as a tool to identify and monitor those at risk of impaired bone health.

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## P10

### Chubby cheeks: could it be cherubism?

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#### Background

A 5 year old boy who had been born at 29 weeks gestation presented to the paediatrics clinic with abnormally chubby cheeks. Our patient's great-grandmother had had a similar appearance and his uncle had recently been diagnosed with giant cell granuloma of the jaw. After extensive imaging and genetic work-up, our patient was diagnosed with cherubism: a condition so named because of the resemblance to cherubic putti in Italian art.

Cherubism is a skeletal dysplasia which usually manifests as benign symmetrical swelling of the mandibular and maxillary regions: it normally regresses in adolescence or early adulthood. We review his case and discuss his diagnosis of cherubism as well as exploring some of the common issues affecting children with this rare disease.

#### Objectives and hypothesis

To gain a more full understanding of the diagnosis of cherubism and the current evidence surrounding treatment.

We specifically addressed the following questions:

Is this diagnosis related to the child's prematurity?

Is there a link between this diagnosis of cherubism and the uncle's diagnosis of giant cell granuloma?

Is cherubism related to the child's developing challenging behaviour?

#### Method

The child was followed up from his presentation until his 10th year and his notes were reviewed. A literature review was carried out to find answers to the questions surrounding his case.

#### Results

There is no link between preterm birth and cherubism.

Whilst clinically cherubism may resemble giant cell granuloma, it is unlikely that this boy's cherubism is linked to his uncle's giant cell granuloma, presuming both diagnoses are correct.

Cherubism, like many pathologies resulting in deformity, has been linked to challenging behaviour. It is impossible to tell if this child's behaviour problem is related to his cherubism, his prematurity, neither, or both.

#### Conclusion

This case report gives an overview of cherubism including presentation, progression, complications and current evidence for treatment which suggests that surgical resection should be reserved for very severe cases. There is no evidence supporting medical therapy with calcitonin. The mainstay of treatment involves the prevention of complications such as loss of dentition and psychosocial upset.

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## CME

### P11

#### Early administration of asfotase alfa in a newborn with perinatal hypophosphatasia

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Hypophosphatasia (HPP) is an inherited systemic metabolic bone disease occurring due to mutations in the *ALPL* gene which encodes for tissue-nonspecific alkaline phosphatase (TNSALP), resulting in defective bone mineralisation due to accumulation of inorganic pyrophosphate (PPi). The perinatal form of this condition lays at the most severe end of the spectrum. Enzyme replacement therapy with asfotase alfa, a recombinant fusion protein that includes the catalytic domain of TNSALP and a peptide that targets the enzyme to bone, is now licensed for management of the childhood form of HPP. We report a baby recently born with an antenatal diagnosis of HPP. Parents were healthy and non-consanguineous. A previous pregnancy had been terminated because of deformities in the foetal skeleton, with genetic testing confirming HPP in the foetus and parents being carriers. Antenatally, foetal scans were normal at 16- and

20-weeks. However, scans at 30 weeks gestation showed features of HPP – poor mineralisation of skull bones and shortening of limb bones. Genetic confirmation of HPP was obtained from chorionic villus biopsy sample. She was born by normal vaginal delivery. Intubation was required upon delivery. Asfotase alfa, obtained on compassionate use, was initiated within 12 hours of birth. A skeletal survey showed gross under-mineralisation throughout the skeleton, with the ribs, distal limb bones and skull most severely affected. In view of rib under-mineralisation and likely need for long-term ventilation, a tracheostomy was performed on day 3, along with central venous access. Currently she remains on stable ventilation settings and fully enterally fed with expressed breast milk. Serial antenatal scans and neonatal radiographs demonstrate that there has been progressive worsening of skeletal mineralisation, presumably secondary to accumulation of PPi. We therefore recommend that, in the presence of a family history of HPP, antenatal scans are continued to be performed into later pregnancy for diagnosis and monitoring of severity of HPP. We believe this is the earliest asfotase alfa has been administered to a neonate with perinatal HPP. To what extent this improves outcomes and prevents complications remains to be seen, with close monitoring for craniosynostosis, seizures, tracheomalacia, respiratory deterioration and calcium abnormalities ongoing.

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## Diabetes

### P12

#### Identifying the barriers to effective diabetes 'transitional care'. A qualitative study of patient satisfaction and experiences of transition

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Disparities in the quality of care for patients with type 1 diabetes (T1D) undergoing transition from children's to adult services are well recognised. Poor planning and ill-defined care pathways promote patient disengagement with many becoming 'lost' to specialist follow-up for years. This study sought to obtain the views of young people's experiences of transition to identify perceived barriers to an effective and rewarding transition experience. A qualitative questionnaire was distributed to all youth with T1D aged 14–19 yrs, undergoing 'transition' (June–Sept 2015) within a regional diabetes network in the UK. Areas explored included views on clinic process; information provided and access to structured education. 189 youth participated in the survey. 74% reported discussing transition with their diabetes team prior to the first appointment. 81% had a good understanding of transition and its aims/objectives; yet only 66% had been given written information about this. During clinics, patients received input from either a paediatric (63%) or adult diabetologist (24%). Only 53% felt that teams explained things well to them, and that there was sufficient time to explore (69%) and address (65%) their concerns. 88% reported receiving structured education during the transition process. 94% indicated a preference to see the same team members during visits and preferred clinics to be scheduled mid afternoon (3–5 pm), on a working day (50%) and at their local hospital (80%). Narrative feedback highlighted recurring themes including communication style; information giving / sharing and constancy of support. Our study provides evidence that youth with T1D deem consistency of care, providing timely and relevant information and being listened to and treated like an adult as indicators of rewarding and engaging transitional diabetes care. The voice and opinions of young people with T1D should be used to develop care pathways that reflect their specific needs and requirements.

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### P13

#### Practical Elements for Successful Recruitment of Patients and Families with Newly Diagnosed Type 1 Diabetes (T1DM) into a Research Study

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#### Background

The paediatric diabetes team at our Children's Hospital were part of a national clinical trial considering whether long term outcomes are better for patients on

MDI (multiple daily injection therapy) or insulin pump therapy from diagnosis. Patients and their families had to be approached, consented and treatment for the trial commenced within two weeks of diagnosis. Many centres struggled to recruit, but this was not the case with our centre.

#### Aim

Our aim was to maximise recruitment into the clinical trial, considering all ethical and practical issues.

#### Methodology

We looked at what contributed to our successful recruitment strategy. Families were approached at the very first meeting and the research discussed alongside the initial diabetes education and discussion of the diagnosis. Repetitive discussion of the study at each subsequent meeting, in a positive manner, gave the families the knowledge to make informed choices. Families were also shown pumps as well as injection devices, so that they had some understanding of what they were undertaking. All eligible families were approached; including families whose first language was not English, children with autism and those with safeguarding needs. The whole team discussed the study and every team member was equally committed to its success. Patients were all recruited before they had left the hospital after the initial diagnosis, even if they had to return to start pump therapy.

#### Conclusions

Several factors led to the success of over 60 patients being recruited (more than double the initial target). All members of the team (PDSNs, Consultants, dietitians and support workers) - fully embraced the study within the already established research culture of the Children's Hospital. The diabetes team ensured that the patients' and families' best interests were primary, balancing a strong belief in the study with maintenance of the families' newly built trust in our service and provision of the very best care.

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## P14

### Identifying the barriers to diagnosing type 1 diabetes in young people in the primary care setting

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#### Objectives

In the UK the majority of young people presenting for the first time with signs and symptoms of type 1 diabetes (T1D) are initially seen by general practitioners (GPs). Mis- or delayed diagnosis is not uncommon, and it increases the risk of diabetic ketoacidosis-related morbidity. This study seeks to identify the specific challenges faced by GPs in this setting in order to develop effective care pathways and recommendations for improving the timely diagnosis of T1D.

#### Methods

An online survey questionnaire was distributed to all GPs in Cambridgeshire and Peterborough CCG. Questions asked included: demographic information; clinical knowledge on diagnosis of child T1D; referral pathways; equipment access; and training experiences.

#### Results

551 GPs were directly approached. 63 responded (11.4%) and were representative of GPs in England in terms of prior experience. 38 (63%) responders had diagnosed T1D in a child before. Once T1D was suspected, 87 and 100% would perform urinalysis and a finger-prick blood test respectively on the day of presentation. However, 38, 19, and 27% also chose to test for venous blood glucose, fasting blood glucose and HbA1C respectively to confirm their diagnosis. All responders would arrange urgent (same day) referral to hospital or call the local children's diabetes team for advice. All respondents had access to a standard glucometer, but 23% used it less than once a year. 43% described their previous T1D training as barely adequate or inadequate, and the majority (82%) indicated that further training was required.

#### Conclusions

Our study provides evidence that more training/education on child T1D in primary care is needed. Whilst there was appropriate use of urinalysis and finger prick blood testing, education targeted at raising the awareness for T1D and avoiding unnecessary tests that may result in delay in diagnosis, are required.

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## P15

### Severe acute renal failure requiring dialysis in children with diabetic ketoacidosis

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#### Introduction

Acute renal failure (ARF) is a rare but life-threatening complication of severe diabetic ketoacidosis (DKA) in children.

#### Aim

To characterise the presentation, treatment and clinical course of children with DKA complicated by severe ARF requiring renal support.

#### Method

Retrospective notes review of patients aged < 16 years admitted in 2011–2016 to 3 UK regional paediatric intensive care units (St George's Hospital, London, Leeds Children's Hospital and Bristol Royal Hospital for Children) with DKA complicated by ARF requiring renal dialysis.

#### Results

[Median (range)]. Five (male=2, female=3) cases with type 1 diabetes aged 13.5(9.6–15.9) years were identified, including 4 newly diagnosed and 1 known patient with poor compliance. All presented in winter between December and April. Length of PICU stay was 8(2–20) days. Four were ventilated for 3.5(3–11) days, and 3 required inotropic support. At presentation, HbA1C was 148(90–173) mmol/mol and glucose 35(28–47) mmol/l. Blood gas analysis showed an initial pH of < 6.8 in all patients, base excess between unrecordable and –28, bicarbonate between unrecordable and 4.6 mmol/l; and took 2(2–3) days to normalise. Level of dehydration was estimated at 8(7–10)%. All required additional fluid boluses on clinical judgement and, received intravenous fluids and insulin 0.05–0.1 U/kg according to national DKA protocol. Intravenous antibiotics were given to all (positive blood cultures (*n*=0), positive respiratory secretions with staphylococcus aureus (*n*=2) and streptococcus pneumoniae (*n*=1)). None had a previous history of renal impairment. Abnormal renal function was evident from admission with presenting urea 16.9(9.2–29) mmol/l, creatinine 144(82–289) umol/l; and peak urea 21.3(17.4–51.3) mmol/l, creatinine 375(279–903) umol/l. All underwent haemodialysis for 8(1–13) days and renal function normalised after 2 months (9 days–14 months). Renal imaging during initial presentation reported increased echogenicity in 2 and bilateral mild hydronephrosis in 1 patient(s). Hypertension was reported in 2 patients who were both treated by amlodipine that was later discontinued when blood pressure normalised.

#### Conclusions

Severe ARF in DKA was associated with extremely low blood pH < 6.8 and evidence of hypovolaemic shock at presentation. Haemodialysis was effective and all made a full recovery of renal function. However, future risk of chronic renal impairment remains unclear and long term renal surveillance is required.

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## P16

### An Audit of the Paediatric Diabetes Out Of Hours Advice Service using the Best Practice Tariff Criteria

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#### Background/Introduction

The Best Practice Tariff was introduced in 2012 in England and Wales to provide adequate funding and ensure quality care for all children with Diabetes. The tariff criteria states that units must provide "24 hour access to advice and support" including "24 hour expert advice to other healthcare professionals". The aims of this audit were to: evaluate the Nottingham Children's Hospital out of hours paediatric diabetes service, determine its effectiveness and its compliance with the Best Practice Tariff standards.

#### Methods

All out of hours calls between December 2015 and June 2016 were logged and further details were entered into a spreadsheet. Details included: reason for the call, whether local guidelines were followed, if the diabetes consultant was contacted, whether the patient was admitted and subsequent follow up. Data was then analysed to see what proportion of responses to out of hours calls met the criteria and whether the system used is effective.

**Results**

35 calls were logged, with an additional 22 being initiated by diabetes consultants to families of newly diagnosed patients or those recently started on pump therapy. Of the 35 calls, 26 were family members requesting advice from the paediatric medical registrar on call. All the advice given followed local guidelines and a diabetes consultant was contacted for advice in 60% of cases. 9 calls were from health professionals and went directly to the paediatric diabetes consultant on call. The main issues requiring advice were hypoglycaemia (6), hyperglycaemia (9), inter-current illness (10), insulin pump problems (7), perioperative advice (1), diabetic ketoacidosis (3) and missed doses of insulin (1). 5 patients (14%) required admission: 2 for hyperglycaemia, 2 for hypoglycaemia, 1 unrelated to diabetes. 6/35 patients were under a different diabetes team, with no follow up information. Of the remaining 29, 22 (75%) received a phone call from the diabetes specialist nurse on the next working day.

**Conclusion**

The out of hours service provided by Nottingham Children's Hospital is an effective system which allows families (and health professionals) to receive appropriate advice at home (hospital) and helps to prevent unnecessary admissions. It fulfils the criteria outlined by the Best Practice Tariff.

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**P17****Acute surgical abdomen masquerading as diabetic ketoacidosis**

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**Introduction**

Diabetic ketoacidosis (DKA) can be easily confirmed with the triad of hyperglycaemia, metabolic acidosis and ketonaemia/ketonuria when suspected. DKA presenting as acute abdomen sometimes is well known, but not vice versa. We describe a rare presentation of acute abdomen with stress hyperglycaemia masquerading as DKA.

**Case Report**

2 year old boy presented with abdominal pain for 8 hours, vomiting & lethargy and tachypnoea & tachycardia. A working diagnosis of new onset diabetes with DKA was considered as he had hyperglycaemia (blood glucose 22.2 mmol/l) and severe metabolic acidosis (pH 7.09, base excess -12.8 mmol/l & bicarbonate 12.5 mmol/l); he received cautious fluid bolus (10 ml/kg), gradual dehydration correction over 48 hours and continuous low dose intravenous insulin infusion (0.05 units/kg per hr). He also had lowish blood pressure (94/42 mmHg) and poor urine output; first urine sample obtained 12 hours after admission revealed mild ketonuria (trace) only. Over the next 24 hours, insulin infusion was weaned & stopped due to hypoglycaemia despite glucose infusion, metabolic acidosis persisted and abdominal signs appeared indicating possible peritonitis. An urgent laparotomy revealed internal hernia with strangulated small bowel, due to mesenteric non-attachment; the mesentery was fixed and untwisted small bowel was viable and did not need resection.

**Discussion**

Establishing diagnosis of DKA is often straightforward if hyperglycaemia, metabolic acidosis and ketonaemia/ketonuria are evident; inappropriate mild or no ketonuria for the degree of acidosis, low urine output and hypotension should alert a clinician to explore other causes of acidosis. Excessive fluid administration is detrimental to patient outcomes with DKA, whereas septicaemia or shock patients need enthusiastic fluid replacement therapy. Erroneous diagnosis of DKA prevents adequate fluid administration in septicaemia or shock patients, worsening the clinical situation.

**Learning points**

Hyperglycaemia is a high urine output state due to obligatory osmotic diuresis; thus low urine output is unusual in DKA unless renal function is compromised. Low urine output and hypotension are two good clinical indicators for septicaemia or shock even in a DKA patient and warrants careful reassessment - as avoiding excessive fluids is important in DKA whereas aggressive fluid resuscitation is needed for septicaemia or shock.

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**P18****Hypoglycaemia – are children carrying the right sugars?**Luke Gibbons<sup>1,2</sup> & Vaseem Hakeem<sup>3</sup><sup>1</sup>College London Medical School, London, UK; <sup>2</sup>Royal Berkshire NHS Foundation Trust, Reading, UK; <sup>3</sup>Royal Free London NHS Foundation Trust, London, UK.**Objective**

Assess whether attendees to a paediatric diabetes clinic are carrying their blood-glucose monitors and short-acting glucose to identify and treat hypoglycaemia.

**Background**

The National Institute for Health and Care Excellence recommends children with type 1 diabetes should always have access to blood-glucose monitoring and a fast-acting glucose to treat episodes of hypoglycaemia. This study assessed the paediatric population at Barnet and Chase Farm Hospitals and whether further education about managing hypoglycaemia is needed.

**Methods**

Over a 3-month period, all attendees to the paediatric diabetes clinic at Barnet and Chase Farm Hospitals were invited to complete a questionnaire. They were questioned on whether they had their blood-glucose monitor and "hypo treatment" with them and what their hypo treatment was. Their treatments were classified as 1) fast-acting glucose, 2) slow-acting carbohydrate in addition to fast-acting glucose, or 3) unsuitable for the treatment of hypoglycaemia.

**Results**

70 children and adolescents responded to the questionnaire. Of these, 64 (91%) reported they were carrying their blood-glucose monitor and 57 (81%) reported they were carrying a hypo treatment. Of those carrying a hypo treatment, 56 of the 57 reported carrying a treatment classified as a fast-acting glucose. In addition, 11 also reported carrying a slow-acting carbohydrate. The one respondent classified as unsuitable was solely carrying a slow-acting carbohydrate. When comparing age ranges, the percentage who reported carrying a fast-acting glucose are: 2–4 years (100%), 5–7 years (86%), 8–10 years (81%), 11–13 years (83%), 14–16 years (79%) and 17–18 years (75%).

**Conclusion**

The vast majority of children carry a hypo treatment with a fast-acting glucose in their kit. These results are encouraging. However, there is a small group where greater education and encouragement may be needed, particularly as children age and develop greater independence.

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**P19****It's all about the HbA1cs but don't forget the LFTs...**

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**Introduction**

Mauriac first described a syndrome in 1930 of growth failure, delayed puberty and hepatomegaly in children with type 1 diabetes. This was in the era prior to long acting insulin analogues being available. With the now widespread availability of various insulin analogues and near patient testing to optimise glucose control, this syndrome was presumed to be of historical interest only. There are increasing reports in the literature of the resurgence of this once forgotten clinical entity. We hereby report a case of glycogenic hepatopathy.

**Case Report**

A 14 year old male type one diabetic with chronic poor glycaemic control (HbA1c 81 mmol/mol) despite intensive multidisciplinary input presented with a one week history of generalised abdominal pain, anorexia and vomiting. Clinical examination revealed a normal BMI with hepatomegaly. Routine liver function tests demonstrated markedly elevated AST (peak 5294 U/l, range 5–40 U/l), GGT (peak 578 U/l, range 10–71 U/l) and ALT (peak 1064, range 4–41 U/l). Baseline investigations including coagulation, liver autoimmune screen, virology, alpha 1 antitrypsin, copper, iron and metabolic screen were all normal. Abdominal ultrasound revealed a diffusely enlarged and echogenic liver in keeping with fatty infiltration. Oesophagogastroduodenoscopy revealed changes consistent with coeliac disease. He was then referred to a tertiary Liver Unit for further investigation and proceeded to a liver biopsy. This revealed moderate steatosis with glycogenated nuclei in a well glycogenated biopsy in keeping with a diagnosis of glycogenic hepatopathy. Liver function tests improved with increased glycaemic control.

**Conclusion**

Glycogenic hepatopathy is a rare entity with an elusive pathophysiology. Despite this, a high index of suspicion is warranted in poorly controlled type 1 diabetics

who present with abdominal pain, hepatomegaly and elevated transaminases (notably AST). At present, an invasive liver biopsy is necessary for diagnosis. The condition can improve with improved glycaemic control and increased clinical attention from the multidisciplinary team. Research assessing the long term outcomes is warranted.

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## P20

### Acute mononeuropathy as a first presentation of Type 1 Diabetes Mellitus

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#### Introduction

Diabetic neuropathy is often a late manifestation of diabetes. Moreover its incidence in the paediatric age group is very rare. We present here a case of motor neuropathy as a first presenting feature of Type 1 diabetes mellitus.

#### Case Report

A fourteen-year-old girl presented with right foot drop, which had progressively worsened over the last ten days. There was no other CNS or systemic involvement. Parents denied any history of pain, paraesthesia or loss of sensations. On specific questioning the patient had osmotic symptoms and weight loss over the preceding 2 months. She was noted to have a high stepping gait and was unable to dorsiflex her right foot. Preliminary tests showed blood glucose levels of 24 mmol/l with HbA1c of 118 mmol/mmol. Further investigations revealed positive Islet Cell antibodies, raised Anti GAD and IA2 antibodies-which confirmed type 1 diabetes mellitus. Other investigations including electrolytes, thyroid function tests, full blood count, vitamin D, vitamin B12 and folate levels were all normal. Nerve conduction studies demonstrated a mixture of axonal damage and focal demyelination of right peroneal nerve at the knee. The patient was started on Multiple Daily Injection Insulin Regimen as per protocol and the foot drop recovered within a period of 2 months.

#### Conclusion

Though diabetic neuropathy is more common in Type 1 diabetes it usually does not manifest until long after onset of diabetes. Whilst it has been reported more frequently in adults we only found one other case report of mononeuropathy as a first presenting feature of diabetes in a child. We present this case to underline the importance of diabetes assessment in otherwise healthy patients presenting with neuropathy. This case also reiterates the fact that improving glucose control rapidly reverses slowing of nerve conduction in diabetes.

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## P21

### Efficacy and uptake of an education clinic integrated into an MDT clinic for children with type 1 diabetes

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#### Introduction

The Best Practice Tariff states that units must provide a structured education programme which should be 'tailored to the child's needs, both at the time of initial diagnosis and ongoing updates'. Traditionally, there has been poor uptake of our education sessions with attendance rates of 20% (range 0–30). Therefore, an integrated education clinic was introduced which combined education within a multidisciplinary (MDT) clinic session for ongoing patient and carer teaching. Parents and children were educated separately (by doctors and nurse-dietitian teams respectively) and children were further divided into age groups to allow tailored advice giving. Family members other than primary care givers involved in the care of the child, friends and siblings were also invited. The aims of this audit were to assess the feasibility and effectiveness of the integrated education clinic by examining the uptake of the clinic together with the feedback from each session.

#### Methods

Attendance rates were calculated by looking at those who attended out of the total number of invitees. At each clinic, both patients and their family members received a feedback form which assessed: knowledge on the chosen topic (sick

day rules), confidence in using the knowledge, awareness of local Out of Hours policy and overall experience of the education clinic, both before and after the session.

#### Results

In total of 63 feedback forms were assessed over 4 such clinics, (response rate >95%) Attendance rates were 80.7%. Overall, 97% of parents said that would recommend the session to others, with 85% saying that they preferred to have the education sessions separate from their children. The education clinics increased understanding of sick day rules – 92% of parents indicated that they fully understood the topic after the session compared to 43% beforehand. Parents indicated that they were more informed regarding out of hours contact numbers as a result of the session – for example, knowledge of the pager number increased from 34% – 47% with a similar increase regarding its operating hours (27%–40%).

#### Conclusion

The integrated education clinic improved attendance, allowed for tailored advice giving and increased both knowledge and confidence in the ongoing management of diabetes.

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## P22

### Structured education and competency in adolescents and families with type 1 diabetes mellitus (T1DM)

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#### Background

The Paediatric Diabetes Team at Southampton Children's Hospital provide a home annual review service for children with T1DM led by Paediatric Diabetes Specialist Nurses. They provide patients and families with support, advice and re-education. Service-users have reported positive feedback regarding effectiveness and relevance of education provided. However, many patients, particularly adolescents, still suffer reduced quality of life (QOL) and life-threatening but preventable hospital admissions. Competency assessment may clarify the reasons for this.

#### Aims

This pilot, exploratory study aims to determine whether home annual reviews are effective in educating patients and families, and whether better patient/parent competency is associated with higher QOL.

#### Methods

In total of 11 home annual reviews of adolescent patients were attended. Patients and parents completed a competency assessment before and after the structured education, as well as Paediatric QOL Inventory Generic Core Scale and Diabetes Module questionnaires. Additionally, qualitative interviews were conducted with patients and parents to identify important themes surrounding diabetes management.

#### Results

A Wilcoxon signed-ranks test indicated an improvement in patients' competency scores post-education (before Median=81.1% [IQR=67.6–86.5] vs. after Median=89.2% [IQR=75.7–91.9],  $n=11$ ,  $P=0.003$ ). Parents' post-education scores also significantly improved (before Median=86.5% [IQR=77.7–90.5] vs. after Median=91.9% [IQR=88.5–97.3]  $n=10$ ,  $P=0.005$ ). Spearman's rho showed a significant strong, positive correlation between parent-reported core QOL and parents' pre-education competency scores ( $n=10$ ,  $r_s=0.88$ ,  $P=0.001$ ). The interviews demonstrated issues important to the adolescents include self-perception, independence and impact on education, and for parents, independence and fear of hypoglycaemia.

#### Conclusions

The quantitative results show that competency scores were generally high in most participants, even before education, indicating information had been retained from previously. Nevertheless, scores still significantly improved, demonstrating to the Paediatric Diabetes Team that home annual reviews are effective in improving knowledge and competency. The association between parent competency and parent-reported QOL for their child may be explained and significantly affected by personal anxieties and stresses. Qualitative data indicates most participants are confident in T1DM management. Increased support may be beneficial in minimising the impact of T1DM on self-perception, independence and education. Further study is required to explore factors leading to poor self-management in emergency settings as well as other reasons for preventable admission.

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**P23****Unusual presentation of a rare metabolic disorder in an adolescent with T1D with recurrent DKA and steatohepatitis**

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**Introduction**

Early onset diabetes mellitus and poor glycaemic control can predispose to various long-term complications. NICE recommends regular assessment starting at 12 years of age to diagnose micro/macro vascular complications and neuropathy for appropriate management. Rare undiagnosed metabolic disorders could pose diagnostic and management challenges. We report an unusual presentation of a rare metabolic disorder in an adolescent with type-1 diabetes mellitus (T1D).

**Case report**

A 14-year-old boy with early onset diabetes at 18 months of age presented with abdominal pain, hepatomegaly and weight loss (Weight SDS -4.3, Height SDS -2.9). Hepatological assessment showed deranged transaminases (ALT & AST elevated up to 150-250 IU/l) and hypercholesterolaemia (total cholesterol >9.5 mmol/l & LDL >6 mmol/l) but normal screening bloods for common liver disorders. The liver biopsy showed fatty infiltration suggestive of steatohepatitis.

Over the next 3 years he was admitted with multiple DKA episodes precipitated by infections including recurrent axillary abscesses requiring surgical interventions. During these episodes he was noted to have very high transaminases (ALT >1000, AST >4000 IU/l) and persistently high lactate levels (4-8 mmol/l). Interestingly the transaminase levels improved quickly whenever DKA/infection resolved. Urine organic acid analysis revealed 3-methylglutaconic aciduria. A mitochondrial respiratory chain study in muscle was normal and exome sequencing did not reveal any mutation in the genes related to mitochondrial disorders.

Subsequently he developed severe burning sensation and electric shock like shooting pain in his lower limbs suggestive of peripheral neuropathy. His deep tendon reflexes and sensory assessment using monofilament were normal. Serum B<sub>12</sub> and folate levels and thyroid function tests were normal. Doppler of his lower limbs was normal and his symptoms were managed with Pregabalin and Amitriptyline with limited success. Echocardiogram revealed mild ventricular hypertrophy. The constellation of clinical features including peripheral neuropathy, steatohepatitis, hepatomegaly, cardiac hypertrophy and methyl glutaconic aciduria points towards a new genetic/metabolic syndrome related to diabetes mellitus.

**Conclusion**

The case illustrates the importance of investigating for underlying rare metabolic disorders in patients with T1D presenting with recurrent episodes of DKA and lactic acidosis.

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**P24****A case of Mauriac Syndrome**

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Mauriac syndrome is a rare complication of poorly controlled type 1 diabetes (T1D) characterized by growth failure, hepatomegaly, elevated transaminases and cushingoid features. We report a case of an eleven year old boy with Mauriac syndrome.

**Case Study**

An eleven year old Caucasian boy, known to have T1D from 7 years of age with poor glycaemic control and high HbA1c noted to have abdominal distension with hepatomegaly at his clinic visit. It was also noted that his height centile moved from 9th to 2nd centile. Ultrasound confirmed hepatomegaly. He had raised alanine transaminase and gamma glutamyl transferase, total cholesterol and triglycerides. Autoantibodies, glandular fever screen, ceruloplasmin, alpha 1 antitrypsin, hepatitis, coeliac screen and drug history were negative. His Insulin like growth factor 1 (IGF1) was low. A possible diagnosis of Mauriac syndrome was considered. A liver biopsy confirmed Glycogen hepatopathy (GH) and, in the clinical context, that of Mauriac syndrome.

**Background**

He was born at 35+4 weeks gestation to teenage Caucasian parents. Due to severe neglect and developmental delay, care was taken over by dad and step mum after social services involvement at 1 year of age.

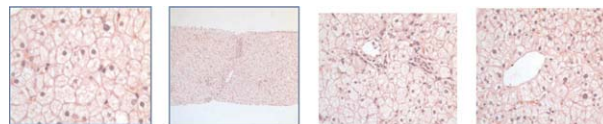
Secondary to difficult childhood he had severe attachment disorder needing mental health input for few years. Early childhood challenges had huge impact on his diabetes management. He was non compliant with his treatment. There were many behavioral issues at school. He expressed several times how he hated his diabetes. He was started on pump therapy. With step-mother's, diabetes team support his liver function tests normalized following improved glycaemic control.

**Discussion**

Our case demonstrated hepatomegaly, liver dysfunction, growth faltering and hypercholesterolemia secondary to poorly controlled diabetes. The proposed mechanism of growth delay is decreased glucose in tissues, IGF1 in circulation, and resistance to growth hormone. GH is reversible with improved glycaemic control.

**Conclusions**

Increased awareness of GH in clinicians will prevent delay in diagnosis and management. Our case highlights the importance of growth monitoring, focused examination in diabetes follow up. Health-care encounters should focus regularly on challenges in daily lives which can significantly affect management of diabetes.



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**P25****Management of Paediatric Diabetic Ketoacidosis: An Audit**

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**Introduction**

NICE Guidelines NG18 (published 2015) advocate a more conservative approach to management of diabetic ketoacidosis (DKA) in children and young people up to the age of 18, in an attempt to reduce the risk of cerebral oedema.

We aimed to assess if management of DKA in children at Manor Hospital was compliant with hospital guidelines, that were based on BSPED guidelines (issued 2009). We analysed the difference in total fluid administered if the new DKA guidelines were in place, specifically in the case of young people.

**Method**

We retrospectively audited case notes of all patients up to the age of 19 years admitted to Walsall Manor Hospital with DKA between 1st July 2014-31st July 2015 ( $n=13$ ). A standardised proforma was used to collect data, which was then analysed.

**Results**

Current hospital policy advocates that young people after their 16th birthday are managed by the adult medical team. The adult DKA Guideline is based on recommendations of Joint British Diabetes Societies Inpatient Care Group recommendations (2013).

The age range was 10 to 18 years. Ten patients were treated using the paediatric and three were treated using the adult guidelines.

There was one significant fluid calculation error found in a patient treated with the paediatric guidelines, although the patient did not come to any harm. No fluid calculation error was found in those patients treated with adult guidelines, though one patient developed fluid overload not requiring active treatment. Mathematical modelling of fluid given in the first 12 hours of treatment shows that a young person would receive 40-70% less fluids if treated as per NICE NG18 instead of adult DKA Guidelines.

In terms of other complications, there were 12 episodes of hypoglycaemia, but no episodes of hypokalaemia in the 13 patients.

**Conclusion**

The risk of cerebral oedema is greatest in the first 12 hours of treatment. Patients between the ages of 16-19 treated with adult guidelines would receive significantly more intravenous fluid compared to paediatric guidelines, potentially increasing their chance of cerebral oedema.

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**P26****Ensuring complete data for the national paediatric diabetes Audit – An Approach Using Python**

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**Introduction**

Diabetes teams need to keep electronic data records for supporting participation in the National Paediatric Diabetes Audit (NPDA), and other governance activities. NPDA benchmarks diabetes services against each other, and services are keen to make sure their data is accurate so that it gives a good reflection of their service. Twinkle is a specialised database that is widely used for this purpose.

Twinkle allows units to produce specific reports on their patients as a CSV spreadsheet, the format NPDA requires for uploading to their website. However, we found limitations in this process. We found it difficult to identify missing data from the Twinkle database itself using the built in Report Builder. In addition, sometimes data entered onto Twinkle was not appearing on the CSV file.

We therefore explored an alternative approach to this problem.

**Methods**

We developed a computer programme in Python, a basic programming language, to specifically analyse the data in the Twinkle CSV file prior to uploading to the NPDA website. The algorithm could identify young people with missing care processes, whether this was due to the process not being performed, not being entered onto Twinkle, or not being exported correctly to the CSV file. Data could be analysed only for those completing a full year of care.

By generating this list in April, we were able to identify children with missing care processes and add this information if it was available, improving our data completeness. We then generated the list in December, which enabled us to target children with missing data in the last quarter of the April-April audit year, to try and improve the number of care processes completed.

This led to an improvement in key care processes as follows: albuminuria 53.7% to 88.1%; retinopathy 61.1% to 90.5%; foot examination 66.7% to 92.9%.

A similar programme was able to analyse the median HbA1c for a specific time frame. This is not possible directly within Twinkle.

**Discussion**

Alternative approaches may be able to achieve the same result using report builder, or through advanced features of Excel, but this was a solution which we found useful.

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**P27****Audit of screening investigations and delay in referral for children with newly diagnosed type 1 diabetes**

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Gloucestershire Royal Hospitals NHS Foundation Trust, Gloucestershire, UK.

**Aim**

To audit the current practice of investigations for children presenting with type 1 diabetes in our centre and identify delays in referral to secondary care.

**Standards**

Guidelines published by ACDC: Care of the well child newly diagnosed with type 1 diabetes, NICE: "Diabetes (Type 1 and Type 2) in children and young people" August 2015 and local trust guidance "Paediatric diabetes - management of newly diagnosed well child".

**Methods**

In total of 2 year retrospective audit from 2013–2015. Data collected from trust pathology results, discharge summaries and diabetes database.

**Results**

In total of 53 cases were audited. 28% of patients presented in diabetic ketoacidosis. Within the cohort 6 patients (11%) had evidence of delay in diagnosis or referral to secondary care identified by primary care requesting laboratory investigations for diabetes or previous presentations to primary care with symptoms of diabetes.

In total of 92% of patients had a laboratory glucose measured at diagnosis with 8% of patients being diagnosed with diabetes on bedside blood glucose testing only. Just 70% had HbA1c sent at diagnosis with no EDTA sample received by the laboratory being the commonest reason for non-compliance with the standard. 85% of patients had anti-IgA tissue transglutaminase measured at diagnosis of diabetes and 2 patients in our cohort were diagnosed with coeliac disease following a positive screening test. 81% of patients had a complete thyroid screen at diagnosis of diabetes (TPO, T4 and TSH) with 4 patients identified as antibody positive but biochemically euthyroid.

Antibody testing for type 1 diabetes was conducted in 85% of our patients at diagnosis. Of these only 53% had both islet cell (or anti-IA2) and anti-GAD

antibodies measured. In line with our local guidance and the new NICE guidance C-peptide was not measured in 90% of our cohort.

**Conclusions**

No patient had complete investigations for Type 1 diabetes at diagnosis. To combat this we have developed a new diagnosis of diabetes investigation pack aimed at preventing incorrect blood bottles and insufficient samples being sent. Audit results and referral guidelines for children with suspected Type 1 diabetes have been disseminated to primary care via the CCG with the aim of preventing future delays.

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**P28****Lessons learnt from a case of childhood obesity with Hyperosmolar Hyperglycaemic state (HHS) and severe acidosis**

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**Case**

A 14 year-old boy was found semiconscious by his mother following difficulty in sleeping overnight as he felt intermittently hot and cold. He had intentionally tried to lose weight (about 25 kg over 6 weeks). Presenting weight was 81 kg. Following prolonged resuscitation at home, GCS was 12 on arrival to hospital, 8 when intensive care team arrived. pH was <6.9 throughout. First venous glucose was 80 mmol/l (unrecordable on gas and glucometer), first plasma Sodium 119 mmol/l (corrected 141.3 mmol/l), calculated osmolality 338.2 mOsm/kg. Despite cautious resuscitation fluids and hydration volumes, slow reduction of hyperglycaemia (61.9 mmol/l after 6 hours), and close watch of sodium levels (corrected sodium at 6 hours 141.9 mmol/l), the child continued to deteriorate and died in the intensive care unit. Tabulated results will be presented and comparison of treatment of DKA and HHS.

**Conclusion**

There should be a maximum weight to be used in the DKA fluid calculator (although in this case a reduced weight was inputted due to the large volumes worked out on current weight). Post mortem results confirmed Type 1 Diabetes Mellitus. Family could find no evidence of any medication used to control his weight.

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**P29****Audit on metabolic effect of insulin pump therapy vs. pen for children with Type 1 Diabetes**

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**Background**

Insulin pump therapy has been linked to improved HbA1c levels, reduced frequency of severe hypoglycaemic episodes and reduced rates of Diabetic Ketoacidosis compared to treatment with multiple daily injections. Insulin pump therapy was started in 2008 in our unit.

**Aims**

To compare the metabolic effect of insulin pump therapy vs multiple daily injections via pen devices in children with type 1 diabetes in our unit.

**Method**

- Retrospective audit.
- Twinkle Database search for all patients with type 1 diabetes attending our unit between June and December 2015.
- Recorded age, sex, type of therapy and last HbA1c result in 2015.

**Results**

- 218 patients identified (99 female), Age range: 2–17 years, (mean 12.5).
- 25% of total patients using pumps (50% < 12 years, 26% > 12 years of age).

	Pump <12 Years	Pen <12 Years	Pump ≥12 Years	Pen ≥12 Years
<b>Number of Patients (n)</b>	29	58	27	104
<b>Mean Age (Years)</b>	8.1	9.6	14.4	14.9
<b>Mean HbA1c (mmol/mol)</b>	55.6	65.6	59.9	69.8
<b>Patients with HbA1c ≤58 mmol/mol (%)</b>	79.3	27.6	48.1	26.9

- 100% of patients aged <4 years were using pump therapy.
- Patients aged  $\geq 12$  years had a higher mean HbA1c in both pump and pen groups.
- Pump patients had a lower mean HbA1c in all groups.
- The percentage of patients with an HbA1c of  $\leq 58$  mmol/mol decreased significantly in the older pump patient group.
- Girls aged  $\geq 12$  years using pumps were less likely to have an HbA1c of  $\leq 58$  mmol/mol (31% compared to 64% boys).

#### Conclusions

- Pump therapy leads to significant reduction in HbA1c in all age groups.
- Patients aged <12 years tend to have lower HbA1c results, likely due to increased parental supervision.
- The percentage of patients with an HbA1c of  $\leq 58$  mmol/mol is lower in older pump patients, particularly girls.

#### Recommendations

- Pump therapy should be offered to as many suitable patients as possible, considering patient choice.
- Greater attention should be focussed on teenage patients, particularly girls, to try and prevent an increase in HbA1c levels.

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### P30

#### A case of neonatal Diabetes: Diagnostic and management challenges

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We present a patient who was incidentally diagnosed with neonatal diabetes at 4 months of age. Due to his small size his treatment has posed a number of challenges for our team.

#### Case Report

A 4 month old boy presented to the Emergency Department with a petechial rash on his legs. Investigations revealed elevated blood glucose of 26.7 mmol/l but a normal pH of 7.39. He had glycosuria but no ketonuria. There was no history of weight loss or osmotic symptoms. Fasting blood glucose remained elevated at 15.6 mmol/l the following morning. He was commenced on intravenous insulin via a sliding scale. Two days later this was changed to long acting subcutaneous insulin Detemir only. After 4 weeks he was commenced on pump therapy, in conjunction with a sensor and the low glucose suspend function activated.

Further investigations revealed an elevated HbA1c of 113 mmol/mol, normal insulin, low C-peptide and negative pancreatic Antibodies. Genetic testing showed a heterozygous mutation in the INS gene, confirming the diagnosis of permanent neonatal diabetes.

His care has posed a number of challenges for the multidisciplinary Diabetic team due to his small size at diagnosis (weight 7 Kg). We have encountered problems with blood glucose testing (immersion of feet in warm water), unreliability of sensor data, causing the pump to be suspended unnecessarily, and issues with correction doses, which had to be calculated manually. His pump was also stopped for 2 weeks due to gastroenteritis.

Proband is now 3 years of age, with good diabetic control (HbA1c 43–55 mmol/mol), although he continues to have problems with frequent blood glucose testing and his parents manually calculate insulin boluses.

#### Conclusion

All children diagnosed with diabetes at less than 6 months of age should have genetic testing for neonatal diabetes. The treatment of babies with diabetes is very challenging, although as technology advances, it is becoming easier. It is important that a multidisciplinary approach is used and that the family is involved in all aspects of care.

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### P31

#### Introducing Dedicated Annual Review Clinics for Children with Type I Diabetes Mellitus in Gloucestershire: Results from a two-year service improvement and evaluation

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Mihirani Balapatabendi

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#### Introduction

In 2014 the diabetes multidisciplinary team at Gloucestershire Royal Hospital Foundation Trust introduced dedicated annual review clinics for children with

type I diabetes over the age of 8 years. Children receive their Consultant appointment, foot check, annual review bloods and structured education sessions in a single afternoon clinic visit. We present the results of two annual service evaluation projects, which have helped us improve the clinics and allowed us to target the educational needs of our patients.

#### Methods

A Structured feedback questionnaire was designed with strength of agreement questions assessing the quality and timing of education sessions and questions about the physical checks and usefulness of a dedicated annual review clinic. The feedback questionnaire was modified for the 2015 evaluation to capture more information about the educational needs of our patients. Questionnaires were given to all patients attending clinic to complete in the waiting room with a box placed by the outpatient reception to collate responses.

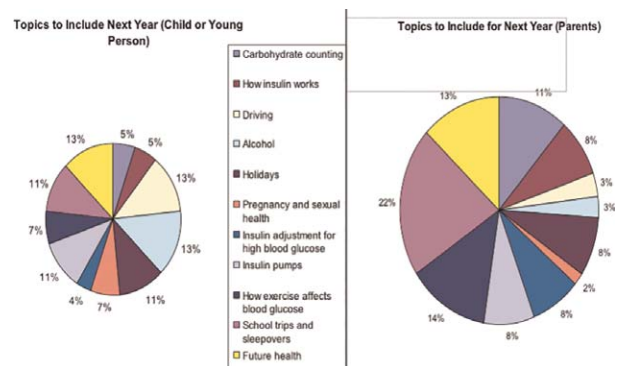
#### Results

In total of 54 questionnaires were received from 147 patients attending annual review clinics in 2014. 54 responses were received from 176 patients attending in 2015. 91% of patients responded positively to the question "Is an annual review clinic useful". Similarly education sessions were highly rated in terms of relevance, usefulness and ability to answer questions. 85% of respondents agreed or strongly agreed that they would use what they had learnt to improve their health.

The 2015 evaluation demonstrated that parents and children had different educational priorities. Our young people were more interested to learn about diabetes and adolescent health issues such as driving, alcohol, pregnancy and sexual health whilst parents valued more practical topics such as insulin adjustment for hyperglycaemia and exercise (Figure 1).

#### Conclusions

Dedicated Annual review clinics are highly rated by our patients and feedback comments largely positive. The results have enabled us to tailor structured education sessions to the needs of our patients and parents. We have seen a reduction in non-attendance rates from 17 patients in 2014 (11.5%) to 11 patients in 2015 (6%) supporting the fact that our service users value the clinics despite the longer duration of appointment.



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### P32

#### Emergency advice for families of children with diabetes – the story of a helpline

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#### Objective

To describe the changes in out-of-hours emergency advice to families of children with diabetes over the last 15 years, the reasons for change and impact on hospital attendance.

The local emergency clinical helpline for children with diabetes (DiabNet) was discontinued in August 2015. We have looked at its service and how it informed the support we deliver today, especially out of hours advice provided currently by paediatric registrars.

#### Background

DiabNet was established in 2000 as a collaboration between three Scottish Health Boards: NHS Tayside, NHS Forth Valley and NHS Fife. This helpline was staffed by Paediatric Diabetes Specialist Nurses using shared protocols and guidelines and was initially open 24 hours a day, 7 days a week. Over the years, it evolved to offer a more tailored service, as changes in diabetes management led to families being better equipped to manage most situations.

Eventually, Diabnet helpline was discontinued as its usage decreased over the years. Families now contact the paediatric registrar on-call for emergency advice.

To support this change, registrars were trained using interactive teaching sessions, flow charts on intranet and a call proforma to ensure a standard approach. Completed forms are used for audit and training purposes.

#### Results

There are 223 children with type 1 diabetes in NHS Tayside. There were approximately 120 calls to the helpline per year. 32 calls were made in NHS Tayside 2014-15 (< 1/week). 35 out of hours calls were logged in the 8 months since withdrawal of the DiabNet helpline, 3 of which resulted in admission.

#### Conclusion

Recommendations from NICE in 2015 suggest that 24 hour emergency advice be available to families of children with type 1 diabetes from "their diabetes team". Few units would be able to support this and paediatric trainees have limited exposure to childhood diabetes. With our current approach, early results suggest that safe and effective advice can be provided by medical trainees with no increased rate of hospital attendance.

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### P33

#### Does increase in funding and service provision improve outcomes of patients with diabetes? An evaluation of HbA1c in paediatric patients with diabetes at Peterborough City Hospital

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Peterborough, UK.

#### Objectives

In April 2013 a new payment tariff was introduced to enable better funding and comprehensive provision of paediatric diabetes care. We aimed to assess if this new tariff and increased resources have improved glycaemic control in children with diabetes.

#### Methods

This was a retrospective analysis of HbA1c, insulin requirements and BMI in all patients under the care of the paediatric diabetes team at a district general hospital for at least 1 year prior to and following the introduction of the tariff.

#### Results

A total of 148 patients were included, 73 (49.3%) were male. Median age at diagnosis was 7 years (IQR 4–10) and median duration of diabetes was 3 years (IQR 1–5). All but 2 patients had type 1 diabetes mellitus. 58 (39.2%) were on a basal bolus regimen, 41 (27.7%) on a continuous subcutaneous insulin infusion (pump) and 48 (32.4%) used multiple methods of insulin delivery during the study period.

The median BMI before tariff introduction was 19.3 kg/m<sup>2</sup> (IQR 17.3–22.1), rising to 21.0 kg/m<sup>2</sup> (IQR 18.2–23.3) after introduction. Median HbA1c was 73.3 mmol/mol (IQR 67–83) prior to and 75 mmol/mol (IQR 66–90) following the tariff introduction (p=0.002). Median increase in HbA1c was 2.5 mmol/mol (IQR –3, 10).

There was no difference in HbA1c by sex, age group or duration of diabetes, and no relationship with initial glycaemic control. No difference was found in HbA1c according to method of insulin delivery. However, patients who started pump therapy after tariff introduction had an improved HbA1c compared to patients already using a pump.

#### Conclusions

We found a marginal worsening of glycaemic control following introduction of the paediatric diabetes tariff. This a rise in HbA1c could be due to increased duration of diabetes, but also could reflect the response of patients to a change in service structure. The improved HbA1c in subgroup of patients started on pump therapy since tariff introduction suggests better patient selection with new pathway and increased resources. Further work should focus on assessing the HbA1c trend in newly diagnosed patients pre-tariff, compared with patients diagnosed since, to determine whether this rise in HbA1c is really related to the service being offered.

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### P34

#### Continuous Subcutaneous Insulin Infusion results in better glycaemic control and reduced insulin requirements in CFRD: Report of 2 cases in children

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#### Introduction

Continuous Subcutaneous Insulin Infusion (CSII) has several advantages over Multiple Daily Injections (MDI) including better hourly delivery and avoidance

of injections. However usage of CSII is significantly less in Cystic Fibrosis Related Diabetes (CFRD) compared to type 1 diabetes and published literature on use of CSII in children and adolescents with CFRD is minimal.

We report two cases where CSII was used in CFRD resulting in a lower Total Daily Dosage (TDD) of insulin and improved quality of life (QOL).

#### Case report 1

M, a seven year old boy was diagnosed to have CFRD at the age of 5. He was initially started on levemir and then MDI with long and rapidly acting insulin with a high TDD of 2.04 units/kg, 11 months after initiating insulin therapy. His HbA1c was 45 mmol/mol (6.3%) in this period.

In total of 11 months after initiating MDI, M was started on CSII at the age of 6. Besides the standard reduction in insulin dose by 30% at the beginning to CSII, the TDD came down by a further of 38% after 9 months. The HbA1c dropped to 40 mmol/mol (5.8%). Repeat CGMS showed stable glucose levels compared to erratic ones on MDI. The family reported improvement in QOL since being on the pump.

#### Case report 2

B, a 14 year old girl was diagnosed to have CFRD at 11 years of age. She was initially started on levemir, then MDI and finally CSII 24 months later due to lipohypertrophy on skin and with an aim to improve QOL. TDD which was 1.63 units/kg came down to 0.84 units/kg one month after starting CSII. HbA1c dropped from 73 mmol/mol (8.8%) on MDI to 67 mmol/mol (8.3%) in the same period. QOL and hypertrophy both improved on CSII.

#### Conclusion

Our cases demonstrate that CSII reduces the insulin requirement in CFRD, with an improvement in general QOL and glycaemic control. CSII should be considered as an option in the management of CFRD. It is likely that a standard approach results in quite significant over treatment with insulin and a tailored CSII regime would optimise doses and control.

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### P35

#### Assessing the impact of a youth worker on diabetes care in adolescents with type 1 diabetes

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Leeds Children's Hospital, Leeds, UK.

#### Background

The inclusion of a youth worker within a transition service can be pivotal to its success.

#### Objective

To assess the impact of a youth worker on diabetes care in adolescents with type 1 diabetes (T1DM) over a 6 month period by measuring HbA1c levels (primary outcome), Personal Development Tool score (PDT), hospital admissions and clinic attendance (secondary outcomes).

#### Method

Prospective cohort study. 20 adolescents (age 14–18 years; 10 males) with T1DM > 1 year. Subjects divided into 2 equal groups depending on HbA1c value; Group 1 HbA1c ≥ 75 mmol/mol and Group 2 HbA1c 58–74 mmol/mol. Intervention: Youth worker input for 6 months with completion of PDT, which assesses 8 areas of diabetes care (marked out of 5, with a total score of 40) by the adolescent at the start and finish.

#### Results

[Mean(SD)]. Age at recruitment for group 1 was 17.2(1.3) years and group 2 was 15.8(1.6) years, and duration of diabetes (9.6 and 9 years respectively). HbA1c at recruitment was 109(20.2) mmol/mol in group 1, and 97.4(21.2) mmol/mol after 6 months. In group 2 HbA1c at recruitment was 63.2(3.7) mmol/mol and 69.5(9.3) mmol/mol after 6 months.

In groups 1 and 2, average PDT score improved after 6 months from 21 to 28 and from 29 to 34 respectively. Average number of hospital admissions (2.6) and clinic non-attendance (3.5) was higher in group 1 compared to group 2 (0.5 and 2.8 respectively). Time in hours spent with the youth worker during the 6 months in group 1 (26.2) and group 2 (28) was comparable. However, more time was spent individually (7.4 hours) than in group time (18.8 hours) with patients in group 1 compared to group 2 (2.7 hours individually, 25 hours of group time). Female patients spent less time with the male youth worker.

#### Conclusions

The youth worker had a positive effect on the diabetes control as demonstrated by reduced average HbA1c values in group 1 and higher PDT scores in both groups after 6 months. The addition of a female youth worker may provide better continuity and diabetes care as self-esteem, coping styles, peer-pressure and identity all have gender elements.

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**P36****A critical review of type 1 diabetes new patient education programme at a single tertiary centre**

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**Introduction**

Good patient education is the key to successful self-management of diabetes. In October 2013, we introduced a revised and extended 'Newly Diagnosed Patient Education Programme' involving 20 structured education sessions delivered by the multidisciplinary team.

**Aim**

To assess the effect of the new patient education programme on HbA1c at the end of two years and compare this to a control group undergoing the old education programme.

**Methods**

All patients diagnosed with type 1 diabetes between October 2013 and October 2014 undergoing the new education programme were included. The control group included the pre-intervention group diagnosed between January-December 2010. Data on HbA1c, patient demographics and psychosocial factors were collected.

**Results**

Twenty four patients (8 males) were included in the study group and 17 (6 males) in the pre-intervention group. The median HbA1c at baseline was significantly different in the two groups (Study=111 mmol/mol vs control=88 mmol/mol,  $P=0.02$ ). HbA1c improved significantly at 3 months in both groups (study=53 mmol/mol and control=46 mmol/mol). HbA1c at 2 years were similar in the two groups (study=70 mmol/mol vs control=74 mmol/mol,  $P=0.59$ ). Psychosocial factors varied greatly between groups, with the study group having higher numbers of social risk factors (CAF 2 vs. 0, split families 9 vs. 3, domestic violence 3 vs. 0, ongoing psychology support 8 vs. 2, clinical depression 2 vs. 0).

**Discussion**

Despite the barriers of increased prevalence of psychosocial factors in the study group the median HbA1c in the two groups were similar at 2 years. There is a downward trend in the median HbA1c of the unit (69 mmol/mol in 2009/10 to 64 mmol/mol in 2015) and upward trend in percentage achieving HbA1c <58 mmol/mol (20% in 2009/10 to 32.7% in 2015), although not reflected in the chosen cohort.

**Outcome**

We are critically reviewing the education sessions to restructure the order to maximise benefits in early weeks. We are considering additional education session at the end of honeymoon period at 9-12 months before the predicted rise in HbA1c.

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**P37****The highs and the lows: Glycaemic control and socio-economic factors in paediatric patients with type 1 Diabetes in Blantyre, Malawi**

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**Background**

Type 1 diabetes mellitus (T1DM) is the commonest paediatric endocrine disorder in Malawi. Chronic diseases such as diabetes are frequently neglected in resource limited settings. The life expectancy from diagnosis of T1DM has been reported to be as low as 1 year in parts of Sub-Saharan Africa. The true incidence of T1DM in Malawi is unknown, however diabetic-ketoacidosis (DKA) is thought to be an overlooked child killer due to misdiagnosis. Lack of investigations, insulin supply, and education are all barriers. There are currently no studies in Malawi which look at glycaemic control or outcomes in this population.

**Aim**

This retrospective study aims to assess glycaemic control, complications and correlate with availability and type of insulin, patient factors and socio-economic status in Malawi's only paediatric diabetes clinic.

**Methods**

Records of all fifty-four children and adolescents with T1DM attending the Diabetes clinic were reviewed. Clinical details including duration of illness, type and dose of insulin, availability of glucometer, symptoms of hypoglycaemia/hyperglycaemia and complications were recorded. Socio-economic details such as educational status, access to a fridge, and mobile phone were also documented.

**Results**

There were 31 males and 23 females ranging from 4-20 years. The median age of diagnosis was 10 years. Twenty five percent did not have access to a glucometer. The median HbA1c for the study population was 11.4%. Overall only 16% of patients had reasonable control (defined as an HbA1c between 6-8%). There were 7 admissions with DKA over this period. One patient came in twice. Two were new diagnoses of T1DM. There was one 1 death from DKA thought to be due to out of date insulin. Forty five percent of patients had access to a fridge to store insulin, and there was no significant difference in HbA1c ( $P=0.68$ ) between children with a fridge and those without.

**Conclusion**

The management of T1DM can be challenging in resource-limited settings as it requires life long follow up and a multi-disciplinary team approach. The median HbA1c is comparable to other studies in low resource settings. This audit highlights additional resources are needed to continue to improve glycaemic control in this population.

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**P38****Introduction of an intensive outpatient education programme is acceptable to parents of children, and young people with newly diagnosed type 1 Diabetes**

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<sup>1</sup>Birmingham Children's Hospital NHS Foundation Trust, Birmingham, UK; <sup>2</sup>University of Birmingham, Birmingham, UK.

**Objectives**

Many successful European centres provide intensive education as 2 week inpatient admissions for newly diagnosed type 1 diabetes. Prolonged inpatient stay is resource intensive and disrupts the family unit. Our centre aimed to determine the feasibility of delivering an intensive education programme in an ambulatory care setting.

**Methods**

The curriculum, introduced in October 2013, comprised 20 hours face to face education by paediatric diabetes nurses, doctors, dietitians, psychologist and social/family support worker (SW/FSW) over 6 weeks. Sessions were scheduled around lunch. Home or diabetes unit visits were provided, as required, for injection support. Families with children diagnosed between October 2014 and November 2015 were provided with an anonymous questionnaire to evaluate programme satisfaction and highlight challenges.

**Results**

There were 54 newly diagnosed in the study period, all of whom participated in the programme. Overall programme attendance rates were high (91%). Questionnaires were completed by 14 (26%) families. 11(79%) were completed by a parent (1 with interpreter). 92-100% of families agreed or strongly agreed sessions delivered by PDSN, Drs or Dietitians were helpful. Sessions rated ambivalent by 17-38% were SW/FSW or psychology delivered sessions, complications and hyperglycaemia. Families report they could attend and reschedule appointments as required. One family reported appointment times caused difficulty in collecting siblings from school. One family raised parking issues. One found the course provided more information than they could manage, others found the pace appropriate.

**Conclusion**

An intensive education programme can be successfully delivered on an ambulatory basis, despite barriers of inner city location, limited parking and a population comprising high prevalence of low socioeconomic status and ethnic minorities. Strategies to address issues highlighted by families are in place to improve accessibility to all.

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**P39****Management of diabetes in a refugee child- the challenges**

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**Background**

Type 1 diabetes is a chronic condition with significant implications on the child, the family and the health services. Management of this condition in a refugee child is fraught with further challenges.

## Methods

In this observational case report, we discuss the challenges in the management of a 10-year-old Somali boy, with type 1 diabetes for the past few years, who presented with Diabetic ketoacidosis.

Table 1 illustrates the challenges faced by the diabetic team during 2-weeks of hospitalisation.

**Further management issues**

Regular input from the team initially twice a week, then weekly with interpreter. Telephonic advice not possible, advised to attend hospital if worried.

Dietary assessment at home with interpreter- looked at menu/weighed the portion sizes/calculated carb content/took pictures/made laminated charts along with insulin doses.

Better daily routine with the child starting school now.

Communication still difficult.

Control better than before, blood sugars still erratic- Chaotic lifestyle, lack of routines, multiple hospital appointments, communication difficulties.

School constantly in touch with the team regarding management at school as unable to communicate with mum.

## Conclusion

Management of diabetes in a refugee opens new challenges to the diabetic team. Along with social and cultural barriers, there are barriers to effective communication leading to difficulties in educating the child and the family. The challenges could be overcome with team work and innovative strategies, but with an increased demand on resources.

Issue	Implications	Remedial measures
Language barrier	Difficult to communicate, check understanding	Used interpreter every single day during admission.
Innumerate	Interpreting blood glucose readings, understanding decimal points understanding highs/lows, dialling insulin doses	Education sessions on the ward - number charts, visual aids. Blocked the decimal points on the meter to avoid confusion.
Care of other siblings during education	Difficulty in getting mum's attention	Ward staff/play therapist input used.
Meal refusal on the ward	Insulin requirement assessment	Home cooked food brought by mum (difficult as she had no transport and child care)

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**P40**

Abstract unavailable.

**P41****High HbA1c pathway for children and young people with poor glycaemic control: process and outcomes**

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## Background

Children and Young People (C&YP) with poorly controlled diabetes are at increased risk of diabetic ketoacidosis (DKA) and long-term sequelae. There is no clear evidence about how best to manage them. NPDA data highlights that UK numbers are in decline, but still constitutes 21.3% of C&YP with diabetes. The

high HbA1c pathway at Nottingham Children's Hospital (NCH) aims to systematically identify and support C&YP with HbA1c >80 mmol/mol. It provides regular contact, school involvement, psychology input, and intensive re-education, including an inpatient stay and referral for social support if necessary.

## Methods

Medical notes of 89 C&YP on the high HbA1c programme at NCH, from March 2012 to September 2015 (42 months) were retrospectively reviewed. Data was analysed using Microsoft Excel.

## Results

In total of 89 C&YP (45 female), median age 15-years, were initiated on the pathway. The median pathway duration was 3 months 14 days, with almost half remaining on for less than 3 months. 4 young people being unable to achieve adequate control within the data collection period. About 30 C&YP were on the pathway at any one time, representing <10% of our clinic population.

In total of 42 (47%) had multiple starts on the pathway, with a median age of 16-years. Median HbA1C on initiation was 89 mmol/mol, with subsequent measurement at 6 months being 77 mmol/mol (where available). Of this group, 5 had social care involvement and 3 were identified as having a CAF in place.

In total of 47 (53%) were started on the pathway only once, with a median HbA1C of 85mmol/mol. Within this cohort, subsequent median HbA1C measurement at 6 months was 69mmol/mol (where available). On average, their pathway duration was 1 month less than those who had multiple starts.

In total of 47 (53%) successfully received 2 weekly contacts with the team, 56 (63%) had an MDT within 6–8 weeks. Carbohydrate counting refreshers were offered in 38 cases and 21 (25%) had psychological input. 21 were admitted for stabilisation.

## Conclusion

The high HbA1c pathway was developed to increase support to those struggling with poor control, to highlight concerns and escalate as necessary. NCH has half the number of C&YP with poor control compared to the national average.

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**P42****The seven wonders of diabetes: An audit of the NICE key age specific care processes**

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## Introduction

NICE CG15 (2004) recommends that diabetic patients aged over twelve years receive seven key care processes. The National Paediatric Diabetes Audit (NPDA) aims to improve outcomes and quality of care in paediatric diabetes. The following describes what proportion of children with type 1 diabetes in our Paediatric Diabetes Unit (PDU) are receiving these seven key care processes in comparison to the NPDA (2013–14).

## Audit Methodology

Patients aged 1–17 years with a diagnosis of diabetes for  $\geq 1$  year on 01/01/15 to 31/12/15 inclusively, were identified using the TWINKLE database. Patients with non-type one diabetes were excluded. Patients were divided into two age groups (<12 yrs and  $\geq 12$  yrs). Data was extracted on HbA1c, Body Mass Index, Blood Pressure (BP), Albumin Creatinine Ratio (ACR), cholesterol and foot examination. Retinopathy screening data was obtained directly from the regional diabetic retinopathy screening service. Completeness rates were calculated for each individual care process in those  $\geq 12$  years of age. A completeness rate for HbA1c and for all seven key care processes was calculated in both groups. Data was compared to the NPDA (2013–2014).

## Outcomes

A total of 226 patients were identified with 30 excluded due to non-type one diabetes. HbA1c was performed in 100% of patients (98.3% NPDA). 52% ( $n=101$ ) were  $\geq 12$  years of age. In this age group, HbA1c and BMI were completed 100% (93.8% and 94% respectively, NPDA). Cholesterol was performed in 97% (54.2% NPDA). 93% of patients had a BP documented (80.2% NPDA). ACR was performed in 85% of cases (48.8% in the NPDA). Foot examination was documented in 82% of patients (45.7% in the NPDA). Formal retinopathy assessment occurred in 54% (51.9% in the NPDA). All seven key care processes were completed in 30% of those aged  $\geq 12$  years (16.1% NPDA). 5% of those <12 years of age had all seven key care processes completed (3% NPDA). Overall, HbA1c and BMI standards are being achieved. Other key standards, especially retinopathy screening, remain suboptimal.

## Change in Clinical Practice

A proforma for annual assessment will be implemented for key care processes to be performed as standard.

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**P42A****An audit on the outcomes of care in paediatric diabetes**

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Royal Belfast Hospital for Sick Children, Belfast, UK.

**Introduction**

NICE CG15 (2004) states that children with diabetes should receive care to achieve optimum control to reduce risk from diabetes complications. The National Paediatric Diabetes Audit (NPDA) aims to improve outcomes in paediatric diabetes. The following describes the outcomes of care in our Paediatric Diabetes Unit (PDU) in comparison to the NPDA (2013-14).

**Audit Methodology**

Patients aged 1–17 years with a diagnosis of diabetes for  $\geq 1$  year on 01/01/15 to 31/12/15 inclusively, were identified using the TWINKLE database. Patients with non-type one diabetes were excluded. Patients were divided into two age groups ( $< 12$  years and  $\geq 12$  years). Data was extracted on HbA1c, Body Mass Index (BMI), coeliac disease and thyroid function in both groups. Data on Blood Pressure (BP), Albumin Creatinine Ratio (ACR), cholesterol and smoking status was obtained in those aged  $\geq 12$  years only. Retinopathy screening ( $\geq 12$  years of age) was directly obtained from the regional diabetic retinopathy service. Data was compared to the NPDA (2013–2014).

**Outcomes**

A total of 226 patients were identified (30 excluded due to non-type one diabetes). HbA1c was performed in 100% of patients (98.3% NPDA) irrespective of age. Mean HbA1c was 67.9 mmol/mol (NPDA 72 mmol/mol). About 63% had an HbA1c between 58–80 mmol/mol (NPDA 58.6%). Mean HbA1c increased with increased duration of diabetes. About 67% used  $\geq 4$  insulin injections per day (NPDA 54.8%). BMI was performed in 100% (NPDA 94%) with most children having a healthy BMI irrespective of age. Thyroid function testing occurred in 97% (NPDA 36.4%). Thyroid dysfunction present in 3% (NPDA 2.3%). Coeliac disease screening occurred in 95% (NPDA 47.6%) with a prevalence of 8% (NPDA 6.9%). About 52% ( $n=101$ ) were  $\geq 12$  years of age. Of these, 93% had BP performed (NPDA 80.2%) with 8% being hypertensive (NPDA 27.5%). About 54% (NPDA 51.9%) had a formal retinopathy screen. ACR occurred in 85% of cases (NPDA 48.8%) with microalbuminuria evident in 16% (NPDA 7.1%). Serum cholesterol was performed in 97% (NPDA 54.2%). About 76% had a total cholesterol  $\leq 5$  mmol/l (NPDA 83.9%). About 1% admitted current smoking (NPDA 2.8%).

**Change Practice**

A proforma for annual assessment has been devised and will be implemented for recording of outcomes to be as standard.

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**Gonadal, DSD and reproduction****P43****Extending the clinical utility of urinary gonadotrophin estimation in turner syndrome**

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**Background**

Girls with Turner Syndrome (TS) are at increased risk of primary ovarian failure. Previous studies have demonstrated that urinary gonadotrophins (UG) can be used as a non-invasive biochemical marker of pubertal status but their value in monitoring and managing girls with primary ovarian failure is unclear.

**Aims**

To determine the range of UG in girls with Turner Syndrome (TS) and its correlation to serum LH and FSH.

**Patients and Methods**

About 16 girls (median age 12.29 year; 5.27 – 20.45 year) with Turner syndrome undergoing assessment of ovarian function had a non-timed spot urine sample for estimation of UG concurrently with estimation of plasma LH and FSH on one occasion ( $n=9$ ) or consecutively ( $n=7$ ). Urinary and plasma gonadotrophins (LH and FSH) were measured by chemiluminescent microparticle immunoassay on

the Abbott architect *i*1600. UG corrected for creatinine excretion were compared to previously published age and sex-matched reference values.

**Results**

Median UG in TS girls were significantly greater than pubertal girls (ULH:Cr TS vs pubertal; 0.31 vs 0.09  $P<0.05$ ; UFSH:Cr TS vs pubertal 3.17 vs 0.20  $P<0.01$ ). ULH:Cr and UFSH:Cr did not correlate with age. There was a significant association between UG ULH:Cr and UFSH:Cr and plasma gonadotrophins ( $P<0.001$  and  $P<0.05$ ). Significant associations were found both for plasma and urinary LH and FSH: ULH:UCr and plasma LH  $r^2$  0.836; UFSH:UCr and plasma FSH  $r^2$  0.7345.

**Conclusion**

UG reflect plasma gonadotrophins concentrations in TS. UG estimation may represent a useful non-invasive method of assessing ovarian function in TS and monitoring the effectiveness of oestrogen replacement.

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**P44****Co-existence of congenital adrenal hyperplasia and bartter's syndrome due to maternal uniparental isodisomy of HSD3B2 and CLCNKB mutations**

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**Introduction**

We present a patient with co-existence of 3 $\beta$ -Hydroxysteroid dehydrogenase type 2 deficiency (HSD3B2) the rarest form of Congenital Adrenal Hyperplasia (CAH) and Bartter Syndrome (hypokalaemic alkalosis secondary to hyperaldosteronism), a unique dual combination of opposing pathologies that has never been reported in the literature.

**Case Report**

A female infant (46XX) born at 34/40 weeks gestation, weighing 2.67 Kg ( $-1.54$  SDS) to non-consanguineous parents presented on day four of life with significant weight loss. Subsequent investigations revealed hyponatraemia hypochloreaemia, metabolic alkalosis, elevated 17-hydroxyprogesterone ( $> 110$  nmol/l), ACTH (553 ng/l; normal:10–50) and renin (2,206 mU/l; normal: 5.4–30). Urine steroid profile suggested HSD3B2 deficiency, which was confirmed by the identification of a homozygous *HSD3B2* mutation [c.745C>T, p. Arg249\*]. Genitalia was normal with no virilisation. She was started on hydrocortisone, fludrocortisone and sodium chloride. Plasma renin concentration remained  $> 500$  mU/l, and she had persistence of the hypochloreaemic alkalosis, and developed a worsening hypokalaemia even after withholding fludrocortisone, hence an underlying renal tubulopathy was suspected. Exome sequencing revealed homozygous deletion in *CLCNKB*, establishing the diagnosis of Bartter syndrome type 3. The mother was found to be heterozygous for both the mutations in *HSD3B2* and *CLCNKB* mutations and the father was negative for both. The co-existence of two rare recessive conditions due to homozygous mutations raised the possibility of uniparental isodisomy (UPD). SNP (Single Nucleotide Polymorphism) microarray analysis confirmed 2 segments of homozygosity on chromosome 1 of maternal ancestry, encompassing both *HSD3B2* and *CLCNKB*. She is managed with high doses of oral sodium and potassium supplements, hydrocortisone, fludrocortisone and indomethacin. The clinical course is complicated by recurrent admissions secondary to severe electrolyte imbalance.

**Conclusions**

UPD, the presence of two identical copies of a given genomic region inherited from one parent, predisposes to recessive diseases, as each heterozygous variant of the parent will be present in the homozygous state, in the child. Thus, identification of a homozygous rare mutation in an offspring of non-consanguineous parents should raise suspicion of UPD. Despite identifying the genetic cause, hypokalaemic alkalosis, the biochemical fingerprint of hyperaldosteronism in a child with CAH remains unexplained and challenges our current understanding of mineralocorticoid-mediated effects in the collecting duct.

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## P45

**5-alpha reductase deficiency: insights into the diagnosis and management of a rare condition**

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**Introduction**

5-alpha reductase deficiency (5aRD) is a rare cause of 46XY DSD, that affects sex development before birth and during puberty. The incidence is unknown; affected individuals have been described from all around the world, particularly in small communities or where consanguinity is common.

**Methods**

A 20-year retrospective review of presenting features, biochemical data and genetic analysis of all patients presenting to a single multidisciplinary team was undertaken.

**Results**

In total, 15 patients with a wide phenotypic spectrum were identified. Thirteen were diagnosed in infancy; two presented with androgenisation in adolescence. Of those presenting earlier, six were raised male, six female and one changed from female to male in early childhood. Two individuals presenting in adolescence had been raised female and one changed to male at this time. Traditional investigations including hCG testing were generally informative but required prolonged stimulation in childhood in order to get a diagnostic T:DHT ratio (baseline ratios were informative in the 3 teenagers, 3days HCG in 7/9 children). Urine steroid profile (USP) showed false negative results in the neonatal period ( $n=2$ ) but was diagnostic after the age of 4–6 months with elevated ratios of 5alpha:5beta metabolites (12/15) and in one case it was sufficient to direct, alone, the genetic diagnosis. Two children had a family history of 5aRD and eight had documented consanguinity. Genetic analysis was informative in all children where available, with population hotspots of p.Arg246Gln in Pakistani ( $n=4$ ) and c.332\_333delTC in Malta ( $n=3$ ). Three children raised female had early gonadectomy but more recently, gonads were left in pending detailed psychological counselling and gender identity assessment, occasionally necessitating the use of GnRH analogues. DHT cream +/- high dose testosterone was used to enhance penile size, with variable effect, in several males.

**Conclusion**

is a rare condition with variable presentation and course, but extremely important to diagnose as personalised management and support is needed. After the first 6 months of life, USP and early genetics can be diagnostic without the need for prolonged stimulation tests. As a subset of children can change their gender identity, careful interdisciplinary support is needed throughout childhood and adolescence.

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**Miscellaneous/other**

## P46

**Blood pressure monitoring and management in young girls with turner syndrome**

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**Background**

Hypertension is common in adults with Turner Syndrome (TS) but less is known about hypertension in children with TS.

**Aim**

To determine the frequency of hypertension in a contemporary paediatric TS cohort and to assess its association with clinical characteristics.

**Patients and methods**

Preliminary analysis of 22 girls with TS attending a designated TS clinic at RHC, Glasgow, with at least 2 blood pressure measurements in the preceding 12 months. Hypertension was defined by systolic or diastolic BP measurement  $\geq 95$ th percentile for gender and height on 2 consecutive visits in one year. Stage 1 hypertension (95<sup>th</sup>–99<sup>th</sup> centile) and stage 2 hypertension ( $> 99$ <sup>th</sup> centile).

**Results**

Median age at last clinic visit was 13 years (4,19), HtSDS  $-2.0$  ( $-3.3, -0.8$ ), BMISDS  $0.3$  ( $-3.2, 3.2$ ). 10/22 had karyotype of 45X,0. None has a history of coarctation of aorta. 8/22(36%) were hypertensive: 4/8 were defined as stage I hypertension and 4/8 as stage II hypertension. 4/22(18%) were on anti-hypertensive therapy, however 2/4(50%) remained hypertensive. Of the other six who were hypertensive but not on treatment, 3/6 have been referred for 24 hour ambulatory blood pressure monitoring.

	Hypertensive (n, 8)	Not hypertensive (n, 14)	P value
Age (years)	14.9 (11.0, 19.6)	12.3 (4.0, 17.6)	0.15
Ht SDS	-1.8 (-3.1, -0.8)	-2.1 (-3.3, -1.0)	0.27
BMI SDS	1.8 (-1.1, 3.2)	0.1 (-3.2, 2.4)	0.02
Bicuspid aortic valves	1/8 (13%)	2/14 (14%)	
Growth hormone	4/8 (50%)	9/14 (64%)	0.51
Oestrogen	4/8 (50%)	6/14 (43%)	0.75
45X	3/8 (38%)	7/14 (50%)	0.57

Multivariate logistic regression analysis for factors associated with hypertension using age (95% CI 0.59 to 1.93), BMISDS (0.96 to 6.47), tanner stage (95% CI 0.25 to 9.01) and karyotype (95% CI 0.09 to 8.15) as independent factors showed that there were no single independent factor associated with hypertension in girls with TS.

**Conclusion**

Our current study demonstrated that 36% of young TS girls were hypertensive based on clinic measurements. No single factor was predictive of hypertension in our study. Optimal monitoring and management of blood pressure in paediatric TS is unclear and deserves future study.

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## P47

**Longitudinal changes in bone density and body composition in post-pubertal adolescents treated with GnRH analogues in a Gender Identity Development Service**

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**Introductions**

Gender Identity Disorder (GID) occurs when a person's gender identity differs from their biological sex, causing distress (gender dysphoria). GID presenting in childhood can dissipate at puberty. If it persists, they may progress to physical interventions. This involves the use of a GnRH analogue (GnRHa) for one year followed by cross sex hormones.

**Methods**

As part of the clinical assessments, adolescents have body composition measurements and annual bone density scans. Two related studies were undertaken 1) Comparison of body composition between bone densitometry (iDXA) vs TANITA measurements (51 children) and 2) Longitudinal changes in bone density and body composition (iDXA) in 26 adolescents who had been on GnRH analogues for a year.

**Results**

The baseline (Pre-GnRHa) study included 51 patients (18 male, 33 female) with a mean age of 16.2 years (range 14.8–17.9). The iDXA recorded 19.5% more body fat (mean 4.6 kg (2.9SD)) and 16.8% less lean mass (mean 7.3 kg (3.4SD)) than the Tanita scales.

The longitudinal study included 26 patients (10 male, 16 female), with the repeat scans done at a mean of 1.1 years after commencing GnRH analogues. The difference in bone density scores between the Post and pre GnRHa scans was: LSBMD  $-0.64$  (0.38 SD), BMAD  $-0.68$  (0.83 SD), TBBMD  $-0.23$  (0.46 SD), TBLH  $+0.03$  (SD 0.52). Analysis was carried out according to biological sex. The BMI Z-score increased by a mean of 0.2. The fat mass increased by a mean of 5.1 kg (7.3 SD), the lean mass and the BMC decreased by 4.5 kg (6.6 SD) and 48.1 g (75.4 SD) respectively.

**Conclusions**

The Tanita body composition scales underestimate the body fat and overestimate lean mass compared to the iDXA. In post-pubertal adolescents, GnRHa for one year increase the BMI and fat mass and reduces lean mass and bone density

values. The clinical significance of these short term changes remain to be determined and whether these can be mitigated by the initiation of cross sex hormones.

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## P48

### Ketotic hypoglycaemia in children with transient congenital hyperinsulinism of infancy

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#### Introduction

Congenital hyperinsulinism (CHI) is a rare genetic disorder of unregulated insulin secretion from the pancreatic  $\beta$ -cells leading to severe hypoglycaemia & permanent neurological deficit if not managed appropriately. Ketotic hypoglycaemia (KH), a diagnosis of exclusion, is by far the most common form of hypoglycaemia in children between 1–5 years of age characterized by recurrent episodes of hypoglycaemia and ketosis.

#### Aim

To identify the prevalence of ketotic hypoglycaemia in children who had previously been diagnosed with transient CHI.

#### Methods

Retrospective data of 142 patients with persistent/recurrent hypoglycaemia was analysed. Diagnosis of KH was confirmed by documented low levels of insulin and C-peptide with appropriately elevated free fatty acids, 3-betahydroxybutyrate, cortisol and growth hormone during hypoglycaemia.

#### Results

Out of the 53 children with transient CHI, 5 children (9.4%) demonstrated KH after resolution of CHI. All were boys with mean ( $\pm$ SD) birth weight of 2.82 kg ( $\pm$ 0.45). The average age of initial presentation with hypoglycaemia was 46.8 hours. The mean blood glucose concentration was 1.98 mmol/l ( $\pm$ 0.72). All patients required high glucose infusion rate initially 13.70 mg/kg per min ( $\pm$ 1.57). 4(80%) children required diazoxide to control the persistent hypoglycaemia [mean dose 7.38 mg/kg per day ( $\pm$ 1.94)]. Diazoxide therapy was discontinued at a mean age of 11.25 months ( $\pm$ 5.25). The mean age of presentation of KH was 18 months ( $\pm$ 2.16). KH developed after an average time period of 6.7 months following the resolution of CHI.

#### Conclusion

Children with transient CHI are at risk of subsequently developing KH at a variable age period. This emphasises the need for close follow up of these children for early identification of KH and to initiate appropriate management. Further studies are required to understand the change in glucose abnormalities from CHI to KH in this group of patients.

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## P49

### Vitamin D status of healthy, low-income, kurdish children in Sulaimani city and Kalar district of Iraqi Kurdistan

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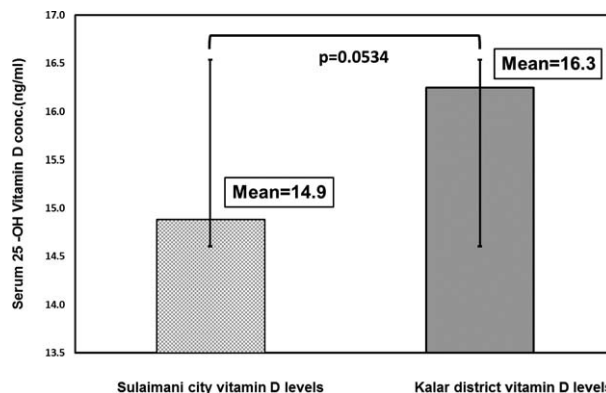
Vitamin D deficiency can cause serious health complications in both adult and children. Recent studies have shown a high prevalence of vitamin D deficiency in children worldwide. Despite the abundance of sunlight in the Middle East, many research groups have confirmed alarming rates of vitamin D deficiency in Middle Eastern population; however vitamin D status among Middle Eastern countries is rarely investigated.

For the first time, this study compared vitamin D levels in children (age 6–12) residing in Sulaimani city with children living in rural Kalar district of Iraqi Kurdistan.

In total of 770 healthy children residing in Sulaimani city and a Kalar district were recruited for this study. Each participant completed a questionnaire about their lifestyle, including socioeconomic background, sunlight exposure and nutritional habits. An electrochemiluminescence binding assay (ECLIA) was used to measure the non-fasting serum concentration of total 25-hydroxyvitamin D (25(OH)D). The difference between vitamin D status of Sulaimani city and Kalar district were compared using student T test for independent samples. A *p* value of less than 0.05 was considered significant.

The mean serum 25-(OH)D concentration in Sulaimani city children (14.8 ng/ml  $\pm$  8.84, *n*=385) was close to vitamin D concentration of Kalar district children (16.12 ng/ml  $\pm$  8.9, *n*=385), *P*=0.053. Of all the children in this study, 77.8% were severely vitamin D deficient (25(OH)D  $\leq$  20 ng/ml), and 11.8% were vitamin D insufficient (25(OH)D=21–29 ng/ml), whereas only 10.4% of the children were vitamin D sufficient (25(OH)D Sufficient  $\geq$  30 ng/ml).

In conclusion, a high percentage of children residing in Sulaimani city and Kalar district had vitamin D deficiency; and there were no significant difference between vitamin D levels of urban inhabitants compared to rural areas. This result suggests that Kurdish children are at high risk of vitamin D deficiency complications. Screening for vitamin D deficiency should be performed in schools, and supplements should be prescribed for children with vitamin D deficiency. Public awareness campaigns are needed to improve vitamin D levels in children.



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## P50

### Hyperinsulinaemia: Demographics of cases in a district general hospital over a 5 year period

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We present the data from cases of hyperinsulinemia that were seen and diagnosed in a district general hospital over a five year period. The cohort included babies with congenital hyperinsulinism (CHI). In the paediatric age group, several were associated with obesity (insulin resistance) group and there was a case on insulinoma.

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## P51

### Altered islet architecture in congenital hyperinsulinism in infancy

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#### Background

Congenital hyperinsulinism of infancy (CHI) is the most common cause of severe hypoglycaemia in children. CHI arises from mutations in ion channel genes (*ABCC8/KCNJ11*), which lead to inappropriate insulin secretion. CHI is also associated with increased cell proliferation and altered islet cell development. The aim of this study was to investigate the composition of the islet capsule in CHI and to relate this to the organisation of islet cells.

#### Methods

Pancreata were obtained from CHI patients following surgery and from autopsy specimens of age-matched control infants. Islet capsule and intra-islet blood

vessels structures were demonstrated after staining diffuse CHI (CHI-D) and control pancreata with PicroSirius Red (PSR). Collagen distribution was quantified using a digital macroanalysis after placing the PSR stained slides under polarising microscopy. Immunostaining was performed to examine the expression pattern of collagen (IV)  $\alpha 1$  chain (COL4A1) in islets and intra-islet basement membranes. Confocal microscopy was used to examine the relationship between COL4A1 and glucagon-secreting  $\alpha$ -cells.

#### Results

PSR staining showed that control islets are surrounded by defined layer of basement membrane (BM). In CHI-D ( $n=7$ , 2–13 months), 75% of islets were incompletely encapsulated compared to only 22% in control islets ( $n=4$ , age 7 weeks–10 months). When collagen content was quantified, CHI-D was significantly lower ( $P<0.001$ ) than control islets and this was found to be associated with a marked decrease in the expression of COL4A1 in CHI-D ( $n=4$ , 2–5 months). Three dimensional imaging using confocal microscopy of CHI-D ( $n=2$ , 5 months) islets revealed that  $\alpha$ -cells were largely dissociated from the islet capsule and capillaries when compared to age-matched controls.

#### Summary/Conclusion

CHI tissue has disrupted islet architecture including a lower collagen content compared to the age-matched control tissues, and the disassociation of glucagon producing  $\alpha$ -cells from the basement membrane. The decreased expression of COL4A1 supports the involvement of islet matrix in the pathogenesis of CHI.

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## P52

### Enhanced islet cell neogenesis and endocrine cell differentiation are pathognomonic with congenital hyperinsulinism in infancy

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#### Background

Congenital Hyperinsulinism in Infancy (CHI) is characterised by inappropriate insulin release from islet  $\beta$ -cells. We currently attribute hypoglycaemia to  $\beta$ -cell dysfunction because of defects in the ion channel genes *ABCC8* or *KCNJ11*. However, the CHI pancreas is also associated with the inappropriate expression of foetal-like transcription factors and enhanced cell proliferation. We hypothesised that islet cell differentiation and neogenesis would also be enhanced in disease.

#### Method

Pancreatic tissue was obtained from 26 patients with CHI following surgery. Eight-five per cent of patients carried *ABCC8* gene defects and 15% carried mutations in *KCNJ11*. Twelve patients had diffuse-CHI (age: 2–13 months) and 14 patients had focal disease (age: 1–10 months). Tissue samples were fixed and processed for use in immunohistochemical analysis. Quantification of both single insulin-expressing cells within ductal epithelia (a marker of differentiation) and islet cell clusters associated with ducts (neogenesis) was carried out and normalised to the area of the tissue section. Control data was obtained from age-match pancreata ( $n=8$ , 1–12 months).

#### Results

Both islet cell differentiation ( $19.4 \pm 4$  cells/cm<sup>2</sup>  $n=12$  vs.  $4.9 \pm 2.9$  cells/cm<sup>2</sup>  $n=8$ ) and islet neogenesis ( $15.2 \pm 3.8$  events/cm<sup>2</sup>  $n=12$  vs.  $0.9 \pm 0.3$  events/cm<sup>2</sup>  $n=8$ ) were enhanced in diffuse CHI tissue in comparison to age-matched controls. To investigate whether these findings were related to gene defects in *ABCC8/KCNJ11* or as a direct consequence of hyperinsulinism, we also analysed focal CHI tissue. In both lesions (somatic loss of maternal imprinting,  $n=11$ ) and non-focal domains (unaffected by *ABCC8/KCNJ11* defects,  $n=14$ ), no differences were found in the incidence of either cell differentiation ( $5.6 \pm 1.6$  vs.  $5.8 \pm 1.3$  cells/cm<sup>2</sup>) or neogenesis ( $1.05 \pm 0.86$  vs.  $1.4 \pm 0.6$  events/cm<sup>2</sup>). Furthermore, these values were not significantly different to control data.

#### Conclusion

Diffuse CHI is associated with a 17-fold increase in islet cell neogenesis and a 4-fold increase in the incidence of islet cell differentiation from duct progenitors. As neither is enhanced in focal-CHI, this suggests that *ABCC8/KCNJ11* defects in progenitor cells are likely to be responsible for inappropriate increases in new islet cell formation in CHI.

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## P53

### Vineland adaptive behaviour scales to identify neurodevelopmental problems in children with Congenital Hyperinsulinism (CHI)

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#### Background

Congenital Hyperinsulinism (CHI) is a disease of severe hypoglycaemia due to insulin hypersecretion, that can be recognised either early or late in childhood. CHI is associated with adverse neurodevelopmental outcomes. The Vineland Adaptive Behaviour Scales Second Edition (VABS-II) is a parent-report measure of intellectual and developmental functioning, which could be used to screen children with CHI for impairments.

#### Aims

To investigate reliability of Vineland to screen developmental problems in CHI.

#### Methods

Vineland questionnaires were completed by parents in 64 CHI children of age  $>1.5$  years for communication, daily living skills, social and motor skills domains. Total and domain scores were converted to standard deviation scores. The Vineland also includes assessment of problematic behaviours, including externalising, internalising and total maladaptive behaviour scores. Vineland was validated in cohort of 9 children with idiopathic ketotic hypoglycaemia (IKH) without neurological problems; repeat variability was assessed in 7 children with CHI.

#### Results

Most children in this cohort presented in the neonatal period (Early-CHI) but 16 (25%) children presented beyond one month of age (Late-CHI). As expected, Vineland scores were in the normal range in IKH (median (range)  $-0.33$  ( $-1.73, 1.13$ )). However in CHI, total Vineland scores were low [ $-0.46$  ( $-3.60, 4.00$ )] across all domains. All Vineland scores were similar on repetition (paired  $t$ -test  $P=0.18-0.95$ ). Vineland scores were inversely correlated with age at presentation ( $P=0.024$ ) and male gender ( $P=0.036$ ) independently. Late-CHI male scores were lower than females [ $-1.40$  ( $-3.60, 0.87$ ) v  $0.20$  ( $-1.07, 1.27$ ),  $P=0.014$ ], with additional 6.5% gender effect on age at presentation ( $P=0.04$ ). Vineland scores showed inverse correlation with the severity markers such as mutations in CHI genes ( $P=0.039$ ) and response to diazoxide treatment ( $P=0.019$ ). Total Vineland scores correlated with independently assessed developmental delay in at least one domain [Odds ratio (OR) (95% confidence intervals, CI)  $0.52(0.38, 0.73)$ ,  $P<0.001$ ]. Total behaviour scores also correlated with developmental delay, mainly for internalising behaviours [OR (95%CI)  $1.30(1.09, 1.55)$ ,  $P=0.005$ ].

#### Conclusions

The Vineland Adaptive Behaviour Scale is a reliable screening tool for maladaptive development and behaviour correlating with developmental delay in children with CHI. Male gender, later age at presentation and severity of disease are independent risk factors for lower Vineland scores correlating with a guarded prognosis.

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## P54

### The profiles of insulin secretory granules are markedly different in $\beta$ -cells of patients with either focal or diffuse Congenital Hyperinsulinism in Infancy (CHI)

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#### Background

The mechanisms responsible for inappropriate insulin release from  $\beta$ -cells in Congenital Hyperinsulinism in Infancy (CHI) have largely focused upon defects in  $K_{ATP}$  channels. Little is known about insulin biogenesis, the profiles of insulin in insulin-containing secretory granules or whether the impact of  $K_{ATP}$  channel defects (due to mutations in *ABCC8* or *KCNJ11*) is the same in diffuse- and focal disease.

**Objective and hypotheses**

We aimed to define the ultrastructural properties of the insulin-containing granules in  $\beta$ -cells from different forms of CHI and to compare these with control  $\beta$ -cells.

**Methods**

Tissue was obtained from six patients with CHI who underwent surgery for the treatment of hypoglycaemia. All patients were positive for mutations in the  $K_{ATP}$  channel gene *ABCC8*. Morphometric analysis and immuno-gold labelling of insulin (I-Au) was applied to frozen tissue sections of control ( $n=4$  cases) and CHI tissues (diffuse-CHI,  $n=3$ ; focal-CHI,  $n=3$ ). Data were acquired using Transmission Electron Microscopy from images stacks in each of the different groups; control  $n=60$  cells, diffuse-CHI  $n=58$  cells and focal-CHI  $n=61$  cells. Results

Three profiles of secretory granules were defined across all tissues; (i) mature granules with dense-core/crystalline insulin; (ii) immature secretory granules and (iii) secretory granules that were depleted of insulin (confirmed by I-Au labeling). We found that approximately 60% of secretory granules ( $n=3428$ ) were depleted of insulin in focal-CHI compared to around 10% of granules in diffuse- ( $n=2258$ ) and control  $\beta$ -cells ( $n=2577$ ). The percentages of immature granules were significantly lower in focal-CHI ( $5.7 \pm 1.7\%$ ) compared with diffuse CHI ( $45.5 \pm 8.7\%$ ) and control samples ( $31.6 \pm 3.7\%$ ). In contrast, control  $\beta$ -cells had a higher proportion of crystalline granules ( $62.9 \pm 3.1\%$ ) compared with focal- ( $36.6 \pm 3.5\%$ ) and diffuse-CHI ( $42.7 \pm 1.9\%$ ). We also found a higher incidence of multi-vesicular secretory granule structures in focal- ( $74.7 \pm 3.3\%$ ) compared to diffuse-CHI and control  $\beta$ -cells ( $39.5 \pm 6.8\%$  vs.  $27.8 \pm 5.6\%$ ).

**Conclusion**

Our data imply that  $\beta$ -cells in focal-CHI have a greater secretory capacity (increased number multi-vesicular secretory granules and depleted granules) than in diffuse disease, despite the fact that both conditions associate with *ABCC8* gene defects.

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**P55****Flash glucose monitoring in children with congenital hyperinsulinism; first report on accuracy and patient experience**

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**Introduction**

Recently, the factory calibrated FreeStyle Libre (FSL) flash glucose monitoring system has been introduced for use in patients with diabetes mellitus. We assessed the accuracy of FSL compared to the finger prick capillary blood glucose (CBG) over a 2 week period in patients with congenital hyperinsulinism (CHI) and assessed the parents' experience of using FSL.

**Methods**

About 346 episodes of CBG along with corresponding swipe FSL readings were available from 7 children with CHI (0.4–5 years). A detailed questionnaire was completed by the parents.

**Results**

The mean variation between the two methods was 0.55 mmol/l (SD  $\pm 0.9$ ), higher readings by FSL compared to CBG. The FSL sensor stayed in-situ for an average period of 13.5 days. There was a positive correlation between the two methods ( $r=0.73$ ). The FSL had a tendency to overestimate compared to CBG (bias = 0.55 mmol/l; 95% CI: 0.46 to 0.65). Only 72% of values were within the reference standard ( $\pm 0.83$  mmol/l) at glucose concentrations less than 5.6 mmol/l. The overall Mean Absolute Relative Difference (MARD) was 18%. 31 episodes of hypoglycaemia (CBG  $< 3.5$  mmol/l) were noted but FSL identified only 55% of these episodes. The Bland Altman plot showed the 95% limits of agreement between the 2 methods ranging from  $-1.23$  (95%CI:  $-1.39$  to  $-1.07$ ) to 2.35 (95%CI: 2.18 to 2.51) mmol/l. Majority of the parents found the glucose trend on FSL to be useful to detect and prevent hypoglycaemic episodes. All parents felt that FSL is a very easy and convenient method to measure the glucose level especially during sleep. A significant proportion of parents felt that FSL readings were not accurate and 50% of parents expressed interest to continue using FSL after the trial period.

**Conclusion**

Noticeable variability between the two methods of measuring the glucose was noted. Despite the ease of using the FSL system, concerns related to accuracy, especially at low glucose values do remain although parents find the glucose trend to be very useful. Further larger trials are needed in CHI patients before FSL is recommended as a routine alternative method for measuring glucose values.

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**P56****Doubtful efficacy of Sirolimus in the treatment of patients with severe congenital hyperinsulinism**

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**Introduction**

Congenital hyperinsulinism (CHI) is a disease of severe hypoglycaemia, often due to mutations in *ABCC8/KCNJ11*. Sirolimus, an mTOR inhibitor, has been reported to be successful in CHI patients, but the evidence is limited. We have aimed (i) to review the efficacy and safety profile of sirolimus, (ii) to assess the role of mTOR signalling pathways in CHI, (iii) to assess the impact of sirolimus in CHI pancreatic tissue.

**Methods**

Patients with CHI unresponsive to medical treatment were recruited (June 2014 to June 2016) with informed consent. Sirolimus efficacy was ascertained by cessation of intravenous dextrose and achievement of adequate fasting tolerance with sustainable euglycaemia. Patients were monitored for drug efficacy and side effects; treatment was withdrawn if persistent hypoglycaemia or serious side effects occurred. *In silico* analysis was used to assess the relationship between mTOR signaling pathways and CHI. Post-operative examination of pancreatic tissue was used to assess rates of cell proliferation using Ki67 expression.

**Results**

Four patients with severe CHI were included; 3 patients had homozygous *ABCC8* mutations and in one patient no mutations were identified. Sirolimus was effective in one patient with euglycaemia sustained following discharge from hospital. Two patients showed an initial response; however, treatment effect was reversed with increasing hypoglycaemia. In the patient without mutations, no response was observed. One patient had stomatitis, two patients developed exocrine pancreatic insufficiency and three patients had sepsis. Subtotal pancreatectomy was performed in 2 patients. Differential gene expression between CHI and age-matched control revealed that 1960 genes had significant changes ( $P < 0.01$ , paired *t*-test). However, mTOR gene expression was unchanged ( $P = < 0.98$ ) and there was borderline association of the mTOR signaling with CHI ( $P = < 0.03$ ). To verify this, we examined cell proliferation in pancreatic tissue from 2 children following continuous sirolimus treatment. We found incidence of proliferation showed no reduction following sirolimus, indeed it was increased by 7.3- ( $n=18,053$ ) and 2.6-fold ( $n=30,144$ ) over control values.

**Conclusion**

Sirolimus remains of doubtful efficacy in the treatment of severe CHI and can be complicated by side effects in young infants. mTOR inhibition is unlikely to cause clinically relevant loss of insulin effect in CHI.

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**P57****New histological characterisation of focal lesions and clinical implications**

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**Introduction**

Congenital Hyperinsulinism (CHI) is a heterogeneous condition caused by dysregulation of insulin secretion. Paternally inherited mutations in *ABCC8* or *KCNJ11* are associated with loss of the maternal 11p15 allele in focal CHI (CHI-F). CHI-F can be curative after selective lesionectomy. However, histological heterogeneity within the CHI-F lesions has not been previously reported. We aimed to examine the diversity in focal lesions and correlate with clinical phenotypes and outcomes.

**Methods**

About 20 subjects with CHI-F were included over a 12-year period. About 18F-DOPA PET-CT was used to localise lesions in patients with CHI-F, following mutation testing for *ABCC8/KCNJ11*. Immunohistochemistry, transmission electron microscopy and serial block face-scanning electron microscopy were used to further characterise the structural organisation within the lesions.

**Results**

In our group, 85% had paternal heterozygous mutations in *ABCC8*, and 15% in *KCNJ11*; one child had a de novo *ABCC8* mutation. About 18F-DOPA PET-CT confirmed and localised the focus before surgical lesionectomy. Sixty five percent of patients (13/20) were found to have a clearly demarcated and identifiable mass of insulin-expressing cells in the focal lesion, identified as Type 1 disease. Type 1 CHI-F lesions were encapsulated in a basement membrane that was composed of collagen fibre bundles organized into a loose orthogonal structure. In these patients, lesions were palpable at surgery and a focal lesionectomy was successful and resulted in curative outcomes. By contrast, in 35% of patients islet cell hyperplasia was not tightly encapsulated and not clearly demarcated from healthy tissue, identified as Type 2 disease. Type 2 CHI-F patients presented with symptoms earlier than Type 1 CHI-F ( $23 \pm 20$  days vs.  $55 \pm 17$  days), the surgical procedure was more complex and not completely curative in 50% of the patients. It was not possible to distinguish Type 2 CHI-F from Type 1 by 18F-DOPA uptake profiles, and there were no correlation between the subtypes of CHI-F and the genetic basis of disease.

**Conclusions**

CHI-F has an underlying heterogeneity in the organisation of focal lesions, unrelated to the genotype and not identifiable with 18F-DOPA-PET-CT. Classification into Types 1 and 2 has implications for surgical margin of resection and predicting disease outcomes.

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**P58****Assessing impact of the provision of accessible information to families with Congenital Hyperinsulinism (CHI)**

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**Introduction**

Parents of children with complex diseases require easily understandable information about their disease to improve health outcomes. Improved disease understanding will also aid shared decision making between clinicians and families. Congenital hyperinsulinism (CHI) is a rare and complex disease of hypoglycaemia associated with significant neurodevelopmental morbidity for which online video-sharing information resources are available. The utility of such information for parents of CHI patients has not been assessed.

**Aims**

1) To assess the effectiveness of three online (www.YouTube.com) videos in delivering CHI health information; 2) to evaluate impact of videos on parent confidence and anticipated future behaviour in caring for their child with CHI and 3) to consider opinions about the quality and format of the videos viewed.

**Methods**

A total of fifteen parents of CHI patients and fifteen non-clinician control subjects were invited to watch three online videos on genetics, hypoglycaemia and diazoxide treatment of patients with CHI. Prior knowledge about CHI or human biology was not assumed. The knowledge impact was assessed by six multiple choice questions (MCQs) before and after watching the videos. These questions were derived by a team of multidisciplinary professionals managing CHI patients. Feedback about quality and format of video was gathered through a 29 part modified e-health Impact Questionnaire.

**Results**

Overall, parents' ability to answer the MCQs improved after watching the videos in pooled analysis ( $P < 0.001$ , related samples McNemar test), although no improvement was noted for specific questions on hypoglycaemia, insulin actions and diazoxide side effects. No difference was noted between parents and controls either pre-video or post-video, thereby excluding selection bias. Feedback about quality and format had positive themes (intentional positive views in 57–100% for each question) suggesting parental trust and information value, although rapid pace of slide change and quantity of information were criticised. One parent of a child with hypoglycaemia induced brain injury found information about hypoglycaemia upsetting. The CHI videos promoted greater awareness and parental decision assertiveness.

**Conclusions**

Online accessible video based information is helpful for parents of children with CHI. Such information could improve family engagement to deliver improved care for healthier long-term outcomes for patients with CHI.

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**P59****Generalised lipodystrophy as a rare presentation of a hypothalamic tumour**

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**Introduction**

Generalised lipodystrophy is clinically characterised by lipoatrophy, hepatomegaly, hypertriglyceridemia, insulin resistance and acromegaloid features. It is recognised that diencephalic syndrome is a rare presentation of hypothalamic tumours in infants and young children. Children with this disorder have profound emaciation and generalised loss of subcutaneous fat, growth acceleration, hyperkinesia and euphoria. Hypothalamic tumours, particularly pilocytic astrocytomas have also been recently reported to be associated with generalised lipodystrophy, a clinical picture that may be very similar to the diencephalic syndrome.

**Case Report**

We present an 18 month old boy that was referred with significant failure to thrive from the age of 6 months and clinical features suggestive of generalised lipodystrophy. Despite having good appetite and a hyper caloric diet (1800 calories per day), his weight at presentation was  $-5.2$  SDS, height  $-2.1$  SDS and head circumference  $-2.2$  SDS. His examination showed generalised loss of subcutaneous fat with prominent musculature and subcutaneous veins, pale skin, triangular face and prominent forehead. He had no hepatosplenomegaly and his development and neurological examination were normal.

Investigations showed normal baseline pituitary function and normal metabolic profile with no dyslipidaemia or glucose intolerance. His liver ultrasound, however, demonstrated an 8 cm liver with diffuse fatty changes. He had a normal microarray and was negative for Russell-Silver syndrome. DNA sample was sent to the Institute of Metabolic Science in Cambridge to test for generalised congenital lipodystrophy. A brain MRI at the age of 2.5 years revealed a hypothalamic mass, currently awaiting histopathological diagnosis.

Our patient is distinct from those presenting with diencephalic syndrome because he did not have hyperkinesia or euphoria and there was evidence of fat deposition on the liver, despite loss of subcutaneous fat. Because of unexpected delays in performing the brain MRI, it is unclear if the onset of the lipodystrophy occurred prior to the development of the tumour, although unlikely in view of the tumour size.

**Conclusion**

Hypothalamic brain tumours should be considered in children with clinical features suggestive of generalised lipodystrophy, even without biochemical evidence metabolic abnormalities, normal pituitary function and normal neurological examination.

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**Obesity****P60****Association between waist circumference and family history of cardiovascular disease in a group of overweight/obese children and adolescents**

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**Introduction**

Central obesity may be the cause of cardiometabolic disorders in adults. In children visceral adiposity is also associated with cardiometabolic risk factors. Waist circumference (WC) is a good surrogate marker of central adiposity, simple to measure. Paediatric studies indicate that within a particular Body mass Index (BMI) category, children with large WC have higher cardiovascular risk than those with smaller WC.

**Aim**

To examine the relationship between WC and family history (FH) of cardiovascular disease (CVD) in a group of overweight/obese (ov/ob) children and adolescents.



**Methods**

children/adolescents aged 7–13 years (33 healthy controls matched for age and sex, 35 ov/ob) participated in the study. Anthropometry (weight, height, puberty staging, Body mass Index (BMI), WC) and physical examination were performed in all. FH of CVD taken. Statistical analysis was performed with IBM Statistics SPSS 20.0, the statistical significance was set at  $P < 0.05$ .

**Results**

Positive CVD FH was noted in 15/35 ov/ob children/adolescents (65.2%), only in 8/33 (34.8%) healthy controls. Significant effect of group was noted in WC, with WC mean value  $93 \pm 14.6$  cm in the ov/ob group,  $62.7 \pm 9.5$  cm in the control group respectively ( $P < 0.001$ ). Significant interaction was found between WC, CVD FH and group ( $P = 0.022$ ). In the ov/ob group statistically significant difference was noted between those with positive FH ( $98.7 \pm 16.8$  cm) and negative ( $88.5 \pm 11.1$  cm) respectively ( $P = 0.015$ ). Moreover, the ov/ob group differed significantly from the control group showing higher mean values in both negative ( $88.5 \pm 11.1$  cm vs  $63.8 \pm 9.6$  cm,  $P < 0.001$ ) and positive CVD FH ( $98.7 \pm 16.8$  cm vs  $59.3 \pm 8.8$  cm,  $P < 0.001$ ). Also, significant difference found in WC between ov/ob children/adolescents with positive CVD FH and those with negative (Mann-Whitney  $U = 84$ ,  $P = 0.042$ ). For those with positive FH the median WC value was increased (97 cm, 69.4–128.5) compared with those with negative (median WC 85.5 cm, 75–120), (table 1).

**Conclusion**

Increasing abdominal obesity is concerning in all European countries. In a recent greek study between children aged 6–12 years the WC mean values increased from  $60.8 \pm 7.1$  to  $65.0 \pm 7.7$  cm in a 2-year period. Preventive and treatment strategies are urgently needed to combat this obesity epidemic in all countries to reduce the associated CVD risk in adult life.

**Table 1** Descriptive statistics of WC and FH of CVD in the ov/ob group.

CVD FH (N)	Minimum	Maximum	Median	Mean $\pm$ SD
Positive (15)	69.4	128.5	97	$98.7 \pm 16.8$
Negative (19)	75	120	85.5	$88.5 \pm 11.1$

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**P61**

Abstract unavailable.

**Pituitary and growth****P62****Clinical characteristics of Cornelia de Lange Syndrome due to an HDAC8 mutation**Ingrid Wilkinson<sup>1</sup>, Nandu Thalange<sup>1</sup> & Peter Hammond<sup>2</sup><sup>1</sup>Norfolk and Norwich University Hospitals NHS Trust, Norwich, UK;<sup>2</sup>University of Oxford, Oxford, UK.

J was born at term (2.62 kg). She presented aged six months with severe faltering growth, (weight 5.1 kg, length 57.3 cm, OFC 39.0 cm). Investigations showed elevated prolactin (1838 mIU/l) and undetectable IGF1 but were otherwise normal. Her karyotype was 46XX. A brain MRI was normal. By 11 months of age she had evident developmental delay and dysmorphic features (triangular face; hypertelorism; synophrys; broad nasal root; short nose with rounded tip; carp like mouth; short neck and low anterior hairline) and bilateral conductive hearing loss. Aged 2 years she underwent an insulin tolerance test (peak GH 88.9 mU/l, Peak Cortisol 1196 nmol/l). Russell-Silver syndrome was initially considered, before a clinical diagnosis of Cornelia de Lange Syndrome (CdLS) was made. Her skeletal features were considered very characteristic of CdLS, however, her face was considerably less characteristic. 3D facial analysis suggested that she just fell into the CdLS spectrum. Aged 7y a de novo mutation in HDAC8 (Xq13.1) was found confirming CdLS.

CdLS is a dominantly inherited congenital malformation disorder. In ~60% of cases, NIPBL mutations are identified, with mutations in SMC1A (5%) and SMC3 (<1%) also recognised. Histone Deacetylase 8 (HDAC8) mutations were first identified as a cause of CdLS in 2012 (1). Reversible acetylation of histone is a key regulator of gene expression. Loss of HDAC8 activity results in increased SMC3 acetylation (SMC3-ac) and consequent abnormal gene expression.

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**P63****To treat, or not to treat? – Growth Hormone (GH) deficiency in a 12 year-old boy**Yoke Sin Hoh, Natasha Ip & Rajiv Goonetilleke  
Children's Unit, Hinchingsbrooke Hospital, Cambridgeshire Community Services, Huntingdon, UK.**Introduction**

We would like to highlight an interesting case of 12 year-old boy with GH deficiency and its diagnostic dilemma.

**Case report**

A 12 year-old boy was referred for growth failure. Over the last 3 years, his height and weight fell to the 2<sup>nd</sup> centile from the 25<sup>th</sup> and 9<sup>th</sup> centiles respectively. His poor growth was initially attributed to his Attention Deficit Hyperactive Disorder medication which was optimised with no effect. School reported his poor hygiene and concerning behaviour of hyperphagia and hoarding food. His family relationship was difficult and he was previously on the child protection (CP) register for neglect.

Clinically, he was thin (Body Mass Index [BMI]:  $15.6 \text{ kg/m}^2$ ; BMI Standard Deviation Score [SDS]:  $-2.4$ ) and pre-pubertal (Pubertal staging: PH1, G2). Serum assays showed no evidence of chronic illnesses, coeliac or hypothyroidism. He had low testosterone level ( $< 0.35 \text{ nmol/l}$ ) and his skeletal bone age was appropriate for his chronological age. Insulin tolerance test confirmed he was GH deficient (Peak GH level:  $4.5 \text{ ug/l}$ ; Peak Cortisol level:  $501 \text{ nmol/l}$ ). His MRI pituitary was normal. These tests confirmed he was GH deficient without primary pituitary gland abnormality. However, his behavioural and social concerns indicated physical and emotional neglect.

**Conclusion**

This created a diagnostic dilemma as there were findings in support of both a true GH deficiency as well as possible Psychosocial Short Stature (PSS). The clinical priority was to ensure the patient's safety therefore he was placed into residential care. GH treatment was never commenced. The patient's height and weight improved whilst in care (height velocity:  $16.9 \text{ cm/year}$ ) but fell when he returned home thereby indicating PSS. PSS is characterized by growth failure in association with emotional deprivation. These children have the characteristic features of reversible GH deficiency but do not respond to GH treatment. Instead, a change in social environment brings about catch-up growth.

GH profiling test was considered but was not necessary given the evidence supports the diagnosis of PSS. In this case, removing patient was imperative for his circumstance, however in less extreme social concerns, there could be a role of GH profiling to facilitate diagnosis.

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**P64**

Abstract unavailable.

## P65

**Novel compound heterozygous mutation in ASXL3 causing bainbridge-ropers syndrome and primary IGF1 deficiency: Expanding phenotype**

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**Introduction**

De novo truncating heterozygous mutations in the additional sex combs-like 3 (ASXL3) gene have been implicated to cause Bainbridge-Ropers syndrome (BRPS) characterised by severe developmental delay, feeding problems, short stature and characteristic facial features. We describe, for the first time, a patient with severe short stature secondary to IGF1 deficiency, severe learning difficulties and dysmorphic features due to novel compound heterozygous mutation in ASXL3.

**Patient and methods**

A 7-year-old boy had severe short stature (−3.5 SDS, MPH: −1.1 SDS), dysmorphic features, severe learning difficulties, and speech delay. He had downward slanting of eyes, low set ears, short neck, hypoplastic toe nails, shortening of metacarpals and ring finger, previous surgically repaired sagittal craniosynostosis and bilateral undescended testes. Peak growth hormone (GH) was 11.7 µg/l to arginine stimulation and bone age was delayed by 3 years. The rest of the pituitary function was normal. IGF1 was persistently low at 4.9 nmol/l (−3.1 SDS) with no increase on IGF1 generation test. A trial of high dose GH (50 µg/kg/day) was ineffective in improving height velocity. Subsequently, recombinant IGF1 therapy was commenced. CGH microarray did not reveal any copy number changes. Whole exome sequencing was performed on genomic DNA from patient's blood and both biological parents. Exons were captured by SureSelect XT Human All Exon V5 capture library. A Sequence library was constructed using the SureSelect XT Target Enrichment System and sequencing performed using the Illumina HiSeq2500.

**Results**

Two novel heterozygous ASXL3 mutations [p.(Arg989Gly), p.(Lys1026Asn)] were found in the patient, inherited from his unaffected mother and his unaffected father respectively. The missense mutations affect highly conserved amino acid residues across several species and in silico analysis predict the changes to be deleterious (SIFT), disease causing and probably damaging (MutationTaster, PolyPhen) on protein function.

**Conclusion**

We report, for the first time, a novel compound heterozygous mutation in ASXL3 causing BRPS along with IGF1 deficiency. ASXL3 is a putative Polycomb group (PcG) protein that is required to maintain the transcriptionally repressive state of homeotic genes throughout development. Further functional studies are undertaken to evaluate the mechanism(s) underlying the molecular interaction between ASXL3 and IGF1 pathways.

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## P66

Abstract unavailable.

## P67

**Trends in growth hormone prescription in the UK: Results from the 3 year National Growth Hormone Audit**

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**Introduction**

The National Growth Hormone (GH) audit was initiated in 2013 with funding from BSPED, to establish the ongoing trends in GH prescriptions in the UK and

facilitate future long term follow up studies through a central database. Here we have studied the trends in GH prescribing and the indications for treatment from 2013 to 2015.

**Method**

We examined data collected on a quarterly basis from centres across the UK on subjects less than 16 years of age, newly starting GH therapy.

**Results**

The number of reporting centres declined by 15% from 2013 to 2015 (79 to 67) with a mean of 904 new GH starters per year. Proportion of subjects starting GH (vs 0-16y population from 2011 Census, Office for National Statistics; % in UK) in constituent countries was England 86% (23.4 m; 84%), Scotland 9% (2.2 m; 8%), Northern Ireland 3% (0.9 m; 3%) and Wales 2% (1.3 m; 5%). General practitioners provided 60% of the ongoing prescriptions.

The most common indication for GH therapy was GH deficiency (56%), followed by Small for gestational age (16%) and Turner syndrome (9%) (Table 1). Off label prescriptions declined by 50% during the 3 year period. Of the total prescriptions, 64% were according to BNF recommended doses for specific indications.

**Conclusion**

The three year GH audit confirms that the majority of prescriptions are for licensed indications. The reasons for 36% prescriptions outside the recommended dose range remain to be explored. Ongoing challenges include maintaining a high return rate to capture optimum data and facilitate long term follow up studies.

**Table 1** Number of subjects (%) starting GH for each indication.

Year	GHD	Turner	PWS	CRI	SGA	SHOX	Off label	Total
2013	531 (55)	84 (9)	61 (6)	34 (4)	144 (15)	10 (1)	102 (10)	966
2014	531 (56)	100 (10)	53 (6)	23 (3)	148 (16)	20 (2)	69 (7)	944
2015	456 (57)	78 (10)	43 (5)	19 (2)	141 (18)	15 (2)	52 (6)	804

GHD – Growth Hormone deficiency, PWS – Prader Willi syndrome, CRI – Chronic renal insufficiency, SGA – Small for gestational age, SHOX – Short Stature Homeobox.

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## P68

**Normal final height in late presenting girls with Turner Syndrome (TS)**

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**Introduction**

The diagnosis of Turner Syndrome (TS) must be included in the differential diagnosis of all girls with short stature. Despite overall earlier diagnosis and treatment there remain patients with TS who present late with delayed puberty. Although growth hormone (GH) is known to increase final height (FH) in girls with TS, little evidence exists on treatment in late-presenting girls.

**Objective and hypothesis**

To assess the effect of late GH treatment along with delayed pubertal induction on FH of girls with TS.

**Methods**

Thirteen girls with TS presenting after 12 years of age were studied. Standard GH treatment was initiated immediately after diagnosis and 8/13 were also treated with the anabolic steroid oxandrolone. Oestrogen treatment was started at a mean of 1.75 years (SD: 0.77) after initiation of GH (minimum age 13 years). FH was calculated when the height velocity was ≤ 2 cm/year.

**Results**

Mean (SD) age was 14.37(1.7) years at GH start and 15.22(1.3) years at oestrogen replacement initiation. The mean (SD) FH-SDS using normal girls' growth charts [−0.89(0.70)], as well as TS-specific charts [1.12(0.63)] was statistically significantly higher compared to presentation height SDS (normal female growth charts [−2.62(0.56)] and TS charts [2.28(0.77)]) both  $P < 0.0001$ . The FH range was 151.2–165 cm ie. within the normal range for girls without TS. There was no statistically significant difference in FH-SDS between those patients who received oxandrolone and those who did not.

**Conclusions**

We have shown that despite late GH treatment in girls with TS presenting with delayed puberty, a normal final height can be achieved. Previous studies have shown that late pubertal induction improves final height, as well as oxandrolone treatment, factors that seem to have had a positive effect in our patients.

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**P69****Changes in Height and IGF-I SDS in the first year of GH treatment are related to BMI SDS**Victoria Price<sup>1</sup>, Jo Blair<sup>1</sup> & Dan Hawcutt<sup>1,2</sup><sup>1</sup>Hey Children's Hospital, Liverpool, UK, <sup>2</sup>University of Liverpool, Liverpool, UK.**Background**

During childhood, growth hormone (GH) doses are usually calculated using total body weight (TBW). This may result in inappropriately high doses in obese children where the intravascular compartment does not increase in proportion with the increase in weight, as the volume of distribution of GH is consistent with the majority of the drug being distributed in the total body water compartment.

**Methods**

Single centre, retrospective cohort study of patients treated with GH between 2010–13. Patients were stratified according to BMI SDS, and changes in height SDS and IGF-I SDS during the first year of treatment was compared between groups (1) in a mixed cohort of patients, and (2) a subgroup of GH deficient (GHD) patients.

**Results**

354 patients (133 female) received GH, of whom 213 (60.2%) had GHD. 52 patients (14.7%) were obese (BMI SDS > 1.75). The children within the lowest BMI-SDS category ( $\leq -1.75$ ) were shorter at the initiation of treatment than those children with higher BMI-SDS scores, in both the unselected and GHD cohorts ( $P < 0.0001$  for both). Baseline IGF-1 SDS did not differ between any of the BMI-SDS categories in either cohort. For both the unselected and GHD cohorts, gain in height SDS increased with increasing BMI SDS, until BMI exceeded 1.75SD ( $P < 0.05$  for both groups), and IGF-1 SDS increased significantly across all weight categories, with the highest values seen in the obese patients ( $P < 0.0001$  for both cohorts). IGF-1 SDS was  $> 2$  at the end of the first year of treatment in 31/354 (8.6%) patients overall, including 11/20 (55%) obese patients with GHD.

**Conclusions**

To our knowledge, these are the first data to link changes in height and IGF-I SDS in the first year of GH treatment with BMI. We speculate that our data illustrate a dose dependent effect of GH, as the most overweight children receive the highest doses, relative to the total body water compartment in which GH is distributed. The clinical significance of this observation is unknown, and robust clinical studies examining alternative dosing strategies using ideal or lean body weight should now be considered.

DOI: 10.1530/endoabs.45.P69

**Methods and Results**

We identified a novel hemizygous *EIF2S3* variant (c.1294C>T, p.P432S) in the three males and their heterozygous mothers. The variant was not present on control databases, including the ExAc Browser ( $> 90,000$  alleles). *EIF2S3* human embryonic expression analysis revealed strong expression in the ventral diencephalon, Rathke's pouch, the anterior and posterior pituitary, the retina, nasal epithelium and pancreatic islets of Langerhan at CS16, 19, 20, 23 and 8 weeks post-conception. We have generated a human *EIF2S3*-knockout pancreatic (I.1B4) cell line, using lentiviral shRNA cassettes. Data show a higher caspase activity with increased cell death in *EIF2S3*-knockout cells.

**Conclusion**

We report a novel *EIF2S3* mutation associated with X-linked hypopituitarism and glucose dysregulation. Data suggest a critical role for *EIF2S3* in both human pituitary development and insulin secretion. This is the first reported association of *EIF2S3* mutations with pancreatic and hypothalamo-pituitary dysfunction.

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**Thyroid****P71****Thyrotoxicosis: A rare paediatric endocrine manifestation of chromosome 2q37 deletion**

Ignatius Losa &amp; Nosheen Aman

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Albright hereditary osteodystrophy-like (AHO-like) syndrome is a rare syndrome characterized by features including distinctive dysmorphism, developmental delay and short stature. The 2q37 locus is the commonly deleted subtelomeric region. Individuals may have either pseudohypoparathyroidism (PHP), with end organ resistance to PTH and certain other cAMP dependent hormones, or pseudopseudohypoparathyroidism (PPHP) with normal hormone responsiveness. Autoimmune thyrotoxicosis has previously not been described in paediatric patients.

Patients with chromosome 2q37 deletion presenting with tiredness should undergo thyroid screening.

Carbimazole 5 mg oddaily

**P70****A mutation in eukaryotic translation initiation factor 2 subunit 3 (EIF2S3) associated with a novel syndrome of X-linked hypopituitarism and glucose dysregulation**Louise Gregory<sup>1</sup>, Carolina Ferreira<sup>1</sup>, Hywel Williams<sup>1</sup>, Sofia Rahman<sup>1</sup>, Kyriaki Alatzoglou<sup>1</sup>, Ritika Kapoor<sup>2</sup>, Peter Jones<sup>2</sup>, Khalid Hussain<sup>1</sup>, Charles Gaston-Massuet<sup>3</sup>, Waseem Qasim<sup>1</sup> & Mehul Dattani<sup>1</sup><sup>1</sup>UCL Institute of Child Health, London, UK; <sup>2</sup>Kings College Hospital, London, UK; <sup>3</sup>William Harvey Research Institute, London, UK.**Background**

*EIF2S3* (NM\_001415; Xp22.11) mutations have previously been reported in a single pedigree with microcephaly and developmental delay. The gene encodes the eukaryotic translation initiation factor 2 subunit 3 (eIF2 $\gamma$ ), the largest of three EIF2 subunits. EIF2 is a heterotrimeric GTP-binding protein, which initiates protein synthesis. It forms a ternary complex, mediating recruitment of initiator methionyl-tRNA to the 40S ribosomal subunit to scan the mRNA from the 5' end, to identify the AUG start codon for protein synthesis. To date, mutations in this gene have not been associated with hypopituitarism.

**Objective and hypotheses**

To identify the molecular basis for X-linked hypopituitarism by performing X chromosome exome sequencing, expression studies and functional analysis of novel variants.

**Patients**

Three males (twin brothers and their maternal cousin) presented with hyperinsulinaemic hypoglycaemia, GH and TSH deficiencies, and anterior pituitary hypoplasia. All three males were treated with rhGH, thyroxine and diazoxide. The latter was stopped in the twins at 7 years, one of whom manifested glucose dysregulation (2 hr glucose 8.4 mmol/l, insulin 22 mU/l in OGTT; late hypoglycaemia with BG 2.7 mmol/l and insulin 5.5 mU/l 5 hrs post-glucose load). His brother demonstrated late hypoglycaemia (BG 2.7 mmol/L, insulin 4.8 mU/l). The mothers (sisters) had resolved secondary amenorrhoea. Candidate gene screening for hypopituitarism and hyperinsulinism was negative.

	9/2/16	21/3/16	9/5/16	24/5/16	1/7/16
<b>ft4 (10–22 pmol/L)</b>	16.5	21.3	25.2	27	14.6
<b>TSH (0.5–4.9 mU/L)</b>	0.05	<0.01	<0.01	<0.01	<0.01
<b>TPO (0–60 iu/mL)</b>	304				
<b>Prolactin (59–619 mIU/L)</b>	166				
<b>FT3 (3.5–6.5 pmol/L)</b>				12.1	
<b>LH (1.5–13 iu/L)</b>		5.5			
<b>FSH (2.5–10 iu/L)</b>		9.6			
<b>TSH Rab (0.0–0.9 IU/L)</b>			1.5		

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**P72****Congenital hypothyroidism in vein of galen malformation patients**

Shirley Langham, Claire Toolis & Catherine Peters  
Great Ormond Street Hospital NHS Foundation Trust, London, UK.

**Introduction**

Vein of Galen (VoGM) is a rare intracerebral vascular anomaly which may be detected on antenatal imaging or present in the neonatal period with secondary cardiac failure. A potential association with congenital hypothyroidism was examined.

**Investigation**

Between the seven months of October 2015 and May 2016 six infants with VoGM were treated at our tertiary centre. Three (50%) were also referred through Congenital Hypothyroidism (CHT) Newborn Screening. These infants had borderline blood spot TSH concentrations ranging from 10–17 mU/l thus requiring a second screening card before referral to the CH service. Venous TSH concentrations ranged 17–44 mU/l (normal range <6). Two babies had low thyroxine hormone concentrations and all three required treatment with Levothyroxine.

All infants underwent technetium imaging and all had a normally located and shaped thyroid gland with avid tracer uptake, suggesting a diagnosis of CHT due to dysmorphogenesis. Initial starting doses of Levothyroxine were 25 micrograms daily (range between 8.6–10.5 mcg/kg/day). One infant required a dose reduction to 20 micrograms daily. Thyroid function normalised within 13–20 days of starting treatment. Of the three VoGM infants who were not referred through CH screening, one had normal thyroid function and the thyroid status of the two other infants is unknown.

Review of the CHT service records from 2006, identified three further infants with VoGM. Two of these infants required treatment with Levothyroxine. One infant died at a month of age and the second infant had a transient form of CHT and stopped treatment at 2 years of age.

**Conclusion**

This is the first report of an association between CHT and VoGM and would suggest that checking thyroid function in these infants would be advisable so that monitoring and early initiation of treatment with Levothyroxine can occur if indicated. An association between vascular malformations and hypothyroidism has been previously attributed to an excess of Type 3 diiodinase. It is possible that a similar process may occur in VoGM. Further investigation is warranted.

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**Introduction**

IIH is associated with hypo and hyperthyroidism. We report a case of IIH where the likely precipitant was the treatment for hypothyroidism itself, levothyroxine, and the challenges this presents.

**Case**

A 14-year-old girl was diagnosed with primary hypothyroidism following investigations for short stature (height 137 cm < 0.4<sup>th</sup> centile). Serum assay showed TSH 538 mU/l (0.55–4.78 mU/l), T4 0.68 pmol/l, (1.7–22.7 pmol/l), negative anti-thyroid antibodies. Thyroid ultrasound showed a small gland. Levothyroxine 50 micrograms once daily was started.

Four days after initiation of treatment she developed headaches. She represented one month later with blurred vision in the right eye. Serum assay showed TSH 22.64 mU/l, T4 12.4 pmol/l, thyroid peroxidase antibody 117 iu/ml. Fundoscopy revealed bilateral papilloedema, cotton wool spots and splinter haemorrhages. The blind spot was enlarged. MRI showed a small pituitary and magnetic resonance venography was normal.

Lumbar puncture was performed; the opening pressure was 40 cm H<sub>2</sub>O the closing 15 cm H<sub>2</sub>O, IIH was diagnosed. She was started on acetazolamide, her symptoms resolved within two weeks.

**Conclusion**

The literature reveals eleven case reports where IIH occurred with levothyroxine initiation. Of those six had a normal T4 at the time of IIH diagnosis.

The mechanism by which levothyroxine causes IIH is unclear. Hypothyroid patients have a reduced ability to excrete free water. We also know there is an association between hypothyroidism and hyponatraemia.

Levothyroxine normalises tissue composition and excess water is excreted. Could an excessive diuresis occur, along with normalisation of the hyponatremic state; leading to altered CSF dynamics and predispose to IIH? Our patient was profoundly hypothyroid; could the alterations in CSF dynamics be more marked in this patient? Perhaps the risk of IIH could be minimised by more gradual introduction of levothyroxine.

The presumed precipitant of IIH, levothyroxine, could not be stopped without the patient becoming hypothyroid. There was no evidence available for substituting T4 for T3 in this scenario. Indeed T3 can increase venous pressure, a proposed mechanism in the development of IIH. In this case giving acetazolamide resulted in an improvement in symptoms. However optic nerve fenestration preserves vision in resistant cases.

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**P73****Levothyroxine therapy associated with idiopathic intracranial hypertension (IIH)**

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