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CME Training Day Abstracts
CME1

**Congenital adrenal hyperplasia - antenatal and neonatal management**

Nils P Krone
Academic Unit of Child Health, Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK.

Congenital adrenal hyperplasia (CAH) comprises a family of inherited autosomal recessive disorders of steroidogenesis, characterized by deficiency of cortisol and an accumulation of substrate precursors. CAH is most commonly caused by 21-hydroxylase deficiency, which causes virilisations of the external genitalia in females. In addition, deficiency of 11-hydroxylase and P450 oxidoreductase are also associated with virilisation of the external genitalia in females. Prenatal treatment of pregnant mothers can avoid or reduce this virilisation. However, several concerns have been raised in recent years including the potential of future impact on psychological development and metabolic health in individuals exposed to dexamethasone in prenatal life. Furthermore, ethical concerns have been raised as three out four female fetuses will be exposed to dexamethasone, whilst being unaffected and not having any treatment benefit. Postnatally, all patients with require urgent detection to avoid salt wasting and metabolic deterioration. Whilst in most Western countries, this is facilitated by newborn screening, clinical care in the UK relies on the clinical diagnosis by health care professionals. Acute management requires a structured diagnostic work-up, the replacement of glucocorticoids and most often mineralocorticoids as well as sodium chloride. In addition, support of the parents needs to play an integral part of care provision during this early phase of treatment. This presentation will discuss recent developments on prenatal diagnosis, provide an overview on prenatal dexamethasone treatment and give a summary on postnatal diagnostic work-up and management.

DOI: 10.1530/endoabs.51.CME1

CME2

**Hypoglycemic disorders in Neonates & Children**

Senthil Senniappan
Liverpool.

Glucose is essential for cerebral metabolism. Knowledge of the homeostatic mechanisms that maintain blood glucose concentrations within a tight range is the key for diagnosis and appropriate management of hypoglycemia. Neonatal hypoglycemia can be transient and is commonly observed in at-risk infants. A wide range of rare endocrine and metabolic disorders can present with neonatal hypoglycemia, of which congenital hyperinsulinism (CHI) is responsible for the most severe form of hypoglycemia. The early recognition, diagnosis and immediate management of CHI is important as delay in the diagnosis and inappropriate management can lead to hypoglycaemic brain injury. CHI is a heterogeneous condition in terms of clinical presentation, histology and molecular genetics. CHI is characterised by inappropriate and unregulated insulin secretion from pancreatic β-cells in the presence of a low blood glucose concentration. The causes, pathophysiology, investigations and management of CHI will be discussed.

DOI: 10.1530/endoabs.51.CME2

CME3

**Glucocorticoid therapy and adrenal suppression**

Peter Hindmarsh
London.

Glucocorticoids form the mainstay of many treatment modalities in paediatrics ranging from short term use in asthma to longer term use as anti-inflammatory agents in nephrotic syndrome and rheumatoid disorders. Long term use although effective brings with it the problems of adrenal suppression. When considering weaning a patient from glucocorticoid use consideration needs to be given to the type of glucocorticoid used, duration of treatment, dosage used and current disease activity. The speed of weaning is determined mainly by disease activity and risk of relapse. Essentially if treatment is less than 3 weeks duration glucocorticoid therapy can be stopped without weaning. If greater than 3 weeks or where there have been multiple short courses over a 12 month period then a weaning schedule is needed. Dosing can be reduced by 25% every 1–2 weeks depending on the underlying disease. Once the dose is down to an equivalent of 12 mg/m² per day the glucocorticoid can be switched to hydrocortisone and the dose reduced by 2.5 mg per week until just below the normal daily production amount of 7 mg/m² day. There is a hierarchy of hypothalamo-pituitary-adrenal recovery starting with restitution of the normal circadian rhythm followed by the stress response. This can be assessed by 24 hour profile work and synacthen stimulation. Other options for assessing recovery will be discussed. Until full recovery of both the circadian rhythm and the response to synacthen stimulation the patient should follow an emergency care plan.

DOI: 10.1530/endoabs.51.CME3

CME4

**Thyrotoxicosis – diagnosis and management**

Tim Cheetham
Newcastle.

Key discussion points

- Make sure you know what it is that you are treating – is this Graves’ hyperthyroidism (with associated TSH receptor antibodies) or simply a brief, hyperthyroid phase of autoimmune thyroid disease (without TSH receptor antibodies) that will settle down spontaneously?
- Ideally obtain the result of the thyroid receptor antibody titre pre intervention with carbimazole.
- Unrecognised Graves’ can have a profound impact on educational attainment. Time with unrecognised Graves’ can compromise an individual’s ability to learn to a major degree.
- All treatment modalities – carbimazole, radioidine (RI) and surgery – have their advantages and disadvantages. Tailoring therapy to the individual according to factors such as age, goitre size and future plans is important.
- ‘Block and replace’ antithyroid drug therapy may be appropriate in some instances despite the increased likelihood of adverse events.
- Some patients with Graves’ will not only remit but will also become hypothyroid.
- Life on long-term thyroid hormone replacement post-surgery or post-RI is not perfect – we need new treatments for Graves’ hyperthyroidism that increase the likelihood of long-term remission.

DOI: 10.1530/endoabs.51.CME4

CME5

**An approach to investigation and management of hypo and hypercalcemia**

Raja Padidela
Manchester.

Hypocalcemia is defined as serum calcium (Ca) level below the lower limit of the normal range of 2.2–2.7 mmol/L. It may arise because of inadequate Ca supply (dietary deficiency, Vitamin D deficiency or resistance), impaired parathyroid hormone secretion or resistance (pseudohypoparathyroidism). Hypomagnesemia may lead to hypocalcemia due to impaired parathyroid hormone secretion and/or end organ resistance, and hence it is important to promptly recognize and treat it concomitantly. Neonates can present with jitteriness, irritability, apnoea, and generalized or focal convulsions. In older child mild hypocalcemia is associated with numbness and tingling sensation while severe hypocalcemia can cause muscle cramps, tetanic carpopedal spasm, laryngospasm with stridor, and convulsions. Hypercalcemia develops when the rate of Ca entry into the extracellular fluid exceeds the kidneys’ capacity for its excretion. Mechanisms include increased absorption of Ca from the gastrointestinal tract, increased release of Ca from the skeleton or decreased excretion of Ca from the kidneys. Symptoms of hypercalcemia in infants are often nonspecific and include feeding difficulties, vomitting, constipation, failure to thrive, irritability and hypotonia. Older children may present with anorexia, nonspecific abdominal pain, muscle weakness and neuropsychiatric symptoms. Polydipsia and polyuria may lead to dehydration and fever. Chronic hypercalcemia and accompanying hypercalciuria may predispose to nephrocalcinosis, nephro lithiasis and, if left untreated, to renal...
impairment. Measurement of bone profile, parathyroid hormone, magnesium, 25 OHD, 1,25 (OH)2 D (sample to be stored) and urine calcium creatinine ratio measurement helps in identifying a cause for hypo and hypercalcemia. In addition, renal ultrasound scan may be required for assessment of nephrocalcinosis. Depending on aetiology, hypocalcemia is managed by increasing Ca intake (IV for acute severe hypocalcemia), Vitamin D or analogues of active Vitamin D (hypoparathyroidism and pseudohypoparathyroidism) and rarely parathyroid hormone injection/infusion. The principles of management of hypercalcemia include hydration and sodium diuresis, reduction of gastrointestinal Ca absorption, inhibition of bone resorption and dialysis.

DOI: 10.1530/endoabs.51.CME5

CME6
Precocious puberty and its variants
Gary Butler
London.

Precocious pubertal development is generally defined as the clinical manifestation of secondary sex characteristics above the 99.6th centile for age. In the UK this corresponds to 8 years in girls and 9 years in boys. The UK growth charts divide at these ages to remind us that a child who plots on the left sided panel and who has pubertal signs is precocious and warrants medical review. The vertical puberty lines have reminders of precocity (and delay). Stage lines on the RCPCH 2-20 year specialist childhood and puberty close monitoring growth chart can determine the centile at entering each of the Tanner stages and menarche and also aid in monitoring the pace of pubertal development. Sometimes the pace can be over-rapid and thus warrant investigation itself. In a tall, early pubertal developing child, the upper 99.6th centile line and its left sided boundary can help decide whether the growth and pubertal progress is precocious. Some children, especially girls with dark hair may present with precocious pubarche. Differentiating this from serious adrenal disorders is usually straightforward on follow up. True early thelarche may not be of concern in toddlers and in tall early maturers. The differential process from pathological precocious puberty will be discussed. The absence of benefit of over-treating early normal developers may be associated with a risk of PCOS. However severe behavioural disturbance may be an indication to treat. Rapid onset and progress through puberty can be seen in children with central disorders both congenital or acquired, and those born SGA. This requires careful tracking and intervening earlier rather than later with a GnRH analogue may produce a significant gain in pubertal height and prevent the loss due to premature epiphyseal fusion.

DOI: 10.1530/endoabs.51.CME6

CME7
Insulin pumps and CGMS – what’s new?
Neil Wright
Sheffield.

Continuous Glucose Monitoring and Flash Glucose Sensing are exciting new technologies popular with many patients and their parents who are keen to have access to such technologies. However such technologies are costly and it is important that clinicians identify patients who are most likely to benefit and ensure that families have appropriate training in order to optimise their use. The aims of this overview are firstly to review the evidence underpinning CGMS and to discuss the magnitude of potential gains in terms of improving HbA1C, reducing hypoglycaemia and reducing anxiety in particular regarding hypoglycaemia. Secondly the relevant NICE guidance, ACDC guidelines and regulatory framework around their implementation and withdrawal if ineffective will be discussed. Finally the practical application of these technologies will be examined with particular emphasis on patient training and education packages and on the utilisation of more advanced features such as rate of change indicators in order to optimise the potential clinical benefit on glycaemic control and on hypoglycaemia within diabetes clinics.

DOI: 10.1530/endoabs.51.CME7
Main Symposia
Endocrine Track 1: Symposium 1

$S1.1$
Newborn screening for congenital hypothyroidism: performance and outcomes of the UK programme.

Rachel Knowles
London.

Introduction
Early detection of congenital hypothyroidism (CHT), and treatment with oral thyroxine, supports the critical period of early brain development, improves growth and prevents the metabolic effects of adult hypothyroidism. Screening for CHT, involving an assay for thyroid-stimulating hormone (TSH), has been included in the UK newborn blood spot screening programme since 1981. Since the introduction of screening, the number of CHT cases has increased, although the reasons for this are unclear. There has been limited evaluation of the performance of the current UK programme.

Methods
UK-wide active surveillance to estimate the current incidence of CHT in infancy and to evaluate performance of the newborn screening programme. Surveillance was conducted through the British Paediatric Surveillance Unit and newborn screening laboratories from 2011 to 2012 to identify children aged <5 years who were investigated after a presumptive-positive screening result or clinical presentation. Children were followed for 3 years to confirm CHT diagnosis and clinical management. Differences in the TSH assay cut-off used by English laboratories provided an opportunity to explore the optimal screening test cut-off.

Results
Six hundred and twenty nine newborns (58.3% girls) were reported after presumptive-positive screen and an additional 21 children (52.4% girls) after clinical presentation. 508 children commenced thyroxine but this was discontinued in 76 (15%) children. 432 (85%) remained on treatment at three years. Incidence of CHT was 5.3 (95%CI 4.8, 5.8) per 10,000 live-births. Screening programme sensitivity, specificity and positive predictive value were 96.76%, 99.97% and 66.88% respectively. Evaluation at different TSH cut-offs suggested that the optimal cut-off was likely to be lower than the recommended standard.

Discussion / Conclusion
Performance of the UK screening programme for CHT is good, however standardisation of screen test cut-offs is advisable and re-evaluation of the recommended cut-off is warranted. Clinical follow-up is essential to avoid unnecessary continuation of therapy, and ascertain longer-term outcomes.

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$S1.3$
Subclinical hypothyroidism – lessons from clinical studies in adults
Salman Razvi
Newcastle.

Subclinical hypothyroidism (SCH) is a relatively common endocrine condition characterised by raised serum thyrotropin (TSH) levels in the presence of normal circulating thyroid hormones. It is generally recognised that SCH – especially if it is sustained - is a mild form of hypothyroidism but whether it should be treated or not is a matter of a long-standing debate amongst both paediatric as well as adult endocrinologists. In adults, there are conflicting data on the long-term outcomes of SCH with some studies suggesting adverse metabolic, cardiovascular, pregnancy-related and quality of life outcomes. On the other hand, there is emerging evidence to suggest that SCH may not be detrimental to health (or may even be beneficial) in the very elderly. Clinical trials of treatment of SCH have mostly shown modest benefit in reduction of cardiovascular risk factors: mainly dyslipidaemia, but little or no improvement in other areas. Therefore, current evidence does not support the view that all patients with SCH should be treated. However, there may be certain groups of individuals that may gain from treatment in adult populations. This overview will identify such groups that may be at risk of the adverse effects of SCH and could potentially benefit from treatment. Furthermore, how the lessons learnt from adult SCH populations could be applied to younger groups will be discussed.

DOI: 10.1530/endoabs.51.S1.3

Endocrine Track 1: Symposium 2

$S2.1$
Abstract unavailable.

$S2.2$
APS1 – an expanding disease spectrum
Catherine Owen
Newcastle.

Autoimmune Polyglandular Syndrome (APS1), also known as Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED), is a rare but frequently debilitating disorder, usually presenting in childhood and adolescence; it is typically caused by homozygous AIRE mutations. The cardinal manifestations are chronic mucocutaneous candidiasis, autoimmune hypoparathyroidism and autoimmune adrenal insufficiency; the development of any two of these three classic features leads to the diagnosis. There are many associated minor manifestations and these may be the main presenting features. It is becoming increasingly apparent that the involvement of non-endocrine tissues can play a significant role in the morbidity and mortality associated with this condition. This presentation, with the aid of cases, will consider:

- The variability of the early clinical picture and the difficulties that this poses when making a diagnosis of APS1.
- The underlying immune deficit in APS1 and the immune markers that can facilitate the diagnostic process.
- The diverse clinical picture that we have observed in local patients and the management challenges associated with the non-endocrine organ-specific manifestations.
- The need for input from multiple different paediatric specialties due to this widening clinical picture and the role of a specialised APS1 clinic.

$S1.2$
Congenital hypothyroidism – lessons from a tertiary service
Catherine Peters
London.

Congenital hypothyroidism (CH) occurs due to dyogenesis or dyshormonogenesis of the thyroid gland. Newborn screening for CH was introduced in the UK over 30 years ago and has almost eliminated the severe intellectual deficits caused by the deficiency of thyroxine to the developing brain. The recognised incidence of CH increased immediately post introduction of screening due to the improved detection and diagnosis of cases. However, further increases in the incidence of CH have been reported internationally and this is variably suggested to be due to a combination of lower screening detection thresholds, changes in population demographics and iodine status. Using data from over 1700 infants who have been referred to a single centre with positive CH screening results, lessons have been learnt in terms of the impact of changing screening TSH thresholds, underlying the physiology and genetics of CH and outcome data. In this cohort, we demonstrated that the group of infants classified as Asian/ British Asian and Chinese by the UK Office of National Statistics have higher TSH cut points than the group of infants classified as white. This Asian group is also over-represented in the cohort referred from the CH screening laboratory compared to the background population. In addition, there is a high incidence of genetic mutations in the DUOX2 pathway for infants with borderline screening results. These mutations are reported most frequently in populations from the Asian subcontinent. They may be associated with transient CH. Using data from this cohort, we have studied audiology outcomes. These suggest that there is an increase in hearing loss in infants with CH, and this is not detected by newborn hearing screening. In summary, 30 years after the introduction of newborn CH screening, there are still many unanswered questions regarding the physiology, genetics and outcomes of infants with CH.

DOI: 10.1530/endoabs.51.S1.2
• Recent reports of heterozygous mutations in AIRE exerting a dominant negative effect, leading to patients who have a less severe form of APS1, developing at a later age and with better outcomes, raising the possibility that AIRE mutations may be more widespread in patients with autoimmunity than previously thought.

• Potential strategies that may optimise the management of these patients and delay or prevent the onset of further autoimmunity.

Key learning point: APS1 is not just an endocrine disease and almost any tissue can be affected. Vigilance is therefore needed for prompt diagnosis and outcomes can only be improved if a range of specialists are involved in the management of these highly complex patients.

DOI: 10.1530/endoabs.51.S2.2

Diabetes Track 1: Symposium 3
S3.1
Nephropathy – What have we learned from AdDIT?
David Dunger
Cambridge.

Introduction
The Adolescent type 1 Diabetes cardio-renal Intervention Trial (AdDIT) is a collaboration across 32 sites in Canada, Australia and the United Kingdom exploring the early detection and prevention of complications in adolescents with type 1 diabetes.

Methods
Over 4,000 young people aged 10–16 years were screened to identify 450 high risk (based on urinary albumin excretion) for a randomised controlled trial (RCT) of statins and ACE inhibitors and 400 low risk subjects for an observational study over 2–4 years.

Results
The results of the RCT, which will be published in 2017 will be reported together with recent analysis of the combined AdDIT cohort of 850 subjects.

Discussion / Conclusion
Implications for early risk stratification and later strategies for prevention of complications will be discussed.

DOI: 10.1530/endoabs.51.S3.1

S3.2
Insulin Pump Therapy: What is the Evidence?
Jo Blair
Liverpool.

Introduction
Intensive insulin treatment regimens, multiple daily injections (MDI) and continuous subcutaneous insulin infusions (CSII) are used widely in the NHS, despite a lack of evidence that more expensive treatment with CSII is superior to MDI. In this presentation, data from previous observational and interventional studies will be reviewed. The findings of the SCIPi study (SubCutaneous Insulin: Pumps or Injections?), which compared the effectiveness, safety, quality of life (QoL) and incremental cost per quality-adjusted life-year (QALY) gained of CSII to MDI, will then be discussed.

Methods
SCIPi was a pragmatic, randomised controlled trial with 1:1 web-based block randomisation of newly diagnosed patients, stratified by age and centre. CSII or MDI was initiated within 14 days of diagnosis. Primary outcome: HbA1c 12 months after diagnosis.

Results
Two hundred and ninety three participants median age 9.8 years (0.7 to 16.0) were randomised (CSII:149, MDI:144). HbA1c was comparable between groups: age adjusted least-squares mean CSII: 60.9 mmol/mol (95% CI 58.5 to 63.3) MDI 58.5 mmol/mol (95% CI 56.1 to 60.9). Severe hypoglycaemia and diabetic ketoacidosis was reported in six and two participants randomised to CSII respectively, and two and zero participants randomised to MDI. 68 adverse events (14 serious) were reported during CSII treatment and 25 (8 serious) during MDI treatment. Growth outcomes did not differ. Insulin use was 0.1 units/kilogram /day higher with CSII (95%CI 0.0 to 0.2, P=0.01). QoL reported by parents, but not participants, was slightly higher for those randomised to CSII. CSII was more expensive than MDI: £1,863 (95% CI £1,620 to £2,137) with no additional QALY gains, −0.006 (95% CI −0.031 to 0.018).

Conclusions
No clinical benefit of CSII over MDI was identified. CSII is not a cost-effective treatment in patients representative of the study population. Further research should focus on determining the perceived benefits of CSII and developing validated tools to measure them.

DOI: 10.1530/endoabs.51.S3.2

Diabetes Track 1: Symposium 4
S4.1
Abstract unavailable.

S4.2
Severe Insulin Resistance: A Practical Approach
Rachel Williams
Cambridge.

Severe insulin resistance (SIR) is an umbrella term which encompasses a number of clinical conditions, all of them rare. This talk will use a case based approach to demonstrate a practical approach to the investigation and management of severe insulin resistance and will include severe insulin resistance secondary to insulin signalling defects and to different forms of lipodystrophy. The aim of the talk will be to provide clinicians with a useful framework to approach the clinical diagnosis and give guidance regarding appropriate investigations. Key Learning Points:

i) What is the definition of severe insulin resistance?

ii) What are the clinical features of the different forms of severe insulin resistance?

iii) What investigations should be done?

iv) What are the available treatments?

DOI: 10.1530/endoabs.51.S4.2

S4.3
Diabetes and technology. Current state of the art and future prospects
Carlo L Acerini
Department of Paediatrics, University Senior Lecturer, University of Cambridge, Cambridge, UK.

Advances in diabetes technology, particularly the introduction of continuous subcutaneous insulin infusion (CSII) pumps and of subcutaneous glucose sensing devices, have transformed the Type 1 diabetes (T1D) management landscape over the last 20 years. These devices have become more commonplace in our clinical practice, yet the evidence base that they have contributed to the modest improvements in glycaemic control in children and young people with T1D over these last two decades is far from certain. Data from a limited number of observational studies and small clinical trials of CSII therapy and of subcutaneous continuous glucose monitoring (CGM), used either alone or in combination (sensor augmented pump therapy), suggest that they are most effective at improving quality of life and in reducing the frequency of severe hypoglycaemia. Furthermore, meta-analysis of studies comparing ‘standard’ treatment approaches such as multiple daily injection (MDI) therapy and self-monitoring of blood glucose via finger pricks (SMBG) with CSII and CGM do not suggest that the latter result in sustained better glycaemic control over the short / medium term, and long term data are lacking. Observations from ‘real world’ data obtained from prospective, national diabetes registries are also at best equivocal. Integrating CSII and CGM technologies using control algorithms are likely to be more effective at maintaining blood glucose levels within the normal range. Low glucose suspend (LGS) and ‘predictive’ LGS set-ups are now commercially available and are the first steps towards developing fully ‘closed loop’ (artificial pancreas (AP)) systems, of which several AP systems are currently undergoing home based clinical trials. Although the role of current diabetes technologies in paediatric diabetes care are well established, ongoing research within this population is required not only to establish their clinical effectiveness and safety but, critically, also their acceptability, equity of access and cost-effectiveness for our patients and for our healthcare system.

DOI: 10.1530/endoabs.51.S4.3
Diabetes Professionals

Sessions
Diabetes professional day: Session 1

DP1.1

Abstract unavailable.

DP1.2

Things I have tried to aid engagement with Young People
Jason Gane
Newcastle.

Clinicians know that adolescence is a very difficult time to support young people in managing their diabetes. Studies, including the DCCT, consistently show that the average HbA1c of this age group is significantly higher than in any other age group. This talk aims to explore the possible reasons for this consistent finding and highlight how normal adolescent development can explain much of this variation. By understanding the young peoples’ needs, management plans can be developed to support them. There are a number of tools available from interview techniques to new technologies that can assist the clinician in supporting young people. Clinical experience of some of these modalities will be presented.

DOI: 10.1530/endoabs.51.DP1.2

DP1.3

Sex, contraception and pregnancy
Debbie Matthews
Newcastle.

Discussion/Conclusion
Sexual & reproductive health are important areas to be considered in the care of young people with Type 1 diabetes remembering that risk-taking behaviour is more common in those with chronic conditions. Education and advice about sexual health & contraception should be provided taking into account any background cultural and religious differences. Adolescent girls with diabetes should be aware of the importance of a planned pregnancy and that ovulation is preserved in the presence of poor glycaemic control. A number of methods of contraception are suitable for use in YP with diabetes including the combined oral contraceptive pill. Despite considerable progress, studies from the UK reveal poor outcomes for women with diabetes in pregnancy including a two-fold increased risk of congenital malformation, a five-fold increased risk of stillbirth and a three-fold increase in perinatal mortality rates and caesarean delivery compared with the background population. Improved outcomes may be achieved by intensive glycaemic control both before and during pregnancy.

DOI: 10.1530/endoabs.51.DP1.3

Diabetes professional day: Session 2

DP2.1

How to transition – Lessons from a longitudinal study
Allan Colver
Newcastle.

NIHR funded a 5 year Programme Grant for Applied Research to explore how to promote the subjective wellbeing and health of young people with long term conditions by generating evidence to enable NHS Commissioners and Trusts to facilitate the successful transition of young people from child to adult health care, thereby improving health and social outcomes. It completed in September 2017. I shall cover some background to transition, then summarise the purpose of the Programme and the methods of it work packages. I shall then report the main results and implications of the Research programme. One of the work packages was a longitudinal study. We had annual contact over 4 years with a cohort of 374 young people, aged over 14 and pre-transfer on entry to the study. Each had one of three conditions: Diabetes mellitus as an exemplar of a chronic illness; Cerebral palsy as an exemplar of a complex physical impairment; Autism and associated mental health problem as an exemplar of a complex mental health and neurodevelopmental problem. I shall draw out similarities and differences between these three groups with respect to the outcomes and process measures that we captured.

DOI: 10.1530/endoabs.51.DP2.1

DP2.2

Aids to correct genetic diagnosis in MODY: being smarter with laboratory medicine
Timothy McDonald
Exeter.

Rarely does the diagnosis of diabetes go beyond the broad classification of type 1 or type 2 diabetes. This is usually based on simple clinical criteria such as BMI, age of diagnosis and presence of ketosis. We know that approximately 15% of patients are wrongly diagnosed and therefore receive suboptimal treatment. In addition, rarer monogenic forms of diabetes are present in at least 3% of patients in the paediatric clinic and are often misdiagnosed as type 1 or type 2 diabetes. The correct diagnosis in this group is important as knowing the genetic cause indicates the most appropriate treatment. In this lecture we will explore the traditional and new technologies we have available to us to improve diagnosis in diabetes and how we can combine blood tests with clinical probability models to maximise diagnostic accuracy.

DOI: 10.1530/endoabs.51.DP2.2

Diabetes professional day: Session 3

DP3.1

Type 1 Kidz – Does peer support & education really help?
Chloe Brown

Introduction
Type 1 Kidz is a project, facilitated by Investing in Children CiC, which offers regular group sessions to children and young people living with Type 1 Diabetes and their families across North East England. The aim is to support children and young people to share experiences and stories and learn together to improve their short and long term outcomes. This is supported by a Professional Steering Group.

Methods
Monthly or quarterly group sessions for children and young people are held across six regions. The children and young people create the agenda for the sessions and the discussions are led by Young Facilitators.

Results
Children and young people report being more confident in managing their diabetes and there is a wealth of feedback and case studies to support this. More clinical data and case studies are currently being collected and analysed and these will hopefully be available to share in the presentation.

Discussion / Conclusion
Using a unique rights-based approach the project puts the needs and wants of children and young people at the forefront of everything it does. The project has expanded considerably over the past 3 years and over 150 children and young people have engaged. It has previously won a Bright Ideas Award and two Quality in Care Awards.

DOI: 10.1530/endoabs.51.DP3.1

DP3.2

Diabetes and eating disorders
Ginny Birrell
Middlesbrough.

Introduction
The incidence of both type 1 diabetes and eating disorders in young people is increasing. The combination of these disorders requires a multidisciplinary approach to management.

Endocrine Abstracts (2017) Vol 51
Methods
Background information of these disorders will be provided with a structured approach to recognition and assessment

Discussion/Conclusion
Having an inquisitive mind to the possibility of eating disorders in patients with Type 1 diabetes will lead to earlier and improved recognition. Use of junior marsipan as an assessment tool for severity will aid decision making. A joint MDT approach is required across diabetes team and eating disorder teams for successful management.

DOI: 10.1530/endoabs.51.DP3.2

DP3.3
Obesity, diabetes and metabolic syndrome
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The prevalence of Obesity is increasing worldwide. This is due to a deterioration in dietary habits and lack of physical exercise in a genetically predisposed population. Obesity can commence in childhood and be progressive. Early detection, population wide education regarding prevention and early intervention is extremely important. The management of obesity must include an individualized evaluation and suitable, achievable plan. Obesity can be progressive through adolescence and contribute to overall prevalence. While Prevention is key, effective treatment must also be available. Exercise and lifestyle changes are paramount but difficult to achieve. Medical weight management is limited by the availability of biochemical compounds which positively affect weight reduction. Surgical options for weight management are effective but underutilized. Paediatric and adult physicians must play a key role in prevention, medical management and supporting surgical intervention. They must therefore equip themselves to tackle this issue.

DOI: 10.1530/endoabs.51.DP3.3

Diabetes professional day: Session 4
DP4

Abstract unavailable.
Endocrine Nurse Session
EN1.1
Skeletal dysplasias-diagnosis, management and prospects for future therapies
Michael Wright
Newcastle.

The skeletal dysplasias or genetic skeletal disorders (GSDs) are a heterogeneous group of over 450 conditions associated with varying degrees of disproportionate short stature. The diagnosis of these conditions has relied on a combination of clinical and radiographic assessment. The original classifications of the GSDs was based on x-ray imaging, but Spranger and others predicted that there would be ‘families’ of GSDs with the same underlying molecular basis. The advent of molecular testing for these conditions has confirmed this hypothesis with the delineation of a large number of different spectra of conditions associated with sequence variants in genes e.g. the FGFR3 gene, type II collagen gene and the gene encoding COMP. Conversely this type of analysis has uncovered genetic heterogeneity in what were initially thought to be single phenotypes e.g. multiple epiphyseal dysplasia. Molecular analysis using multigene panels and clinical exomes has, as a result, become more common and in some centres routine. The interpretation of results from these multigene analyses requires great caution to ensure that background genetic variation is not interpreted as pathogenicity. Treatment of patients with GSDs has traditionally been focused on appropriate input from physiotherapists and occupational therapists with orthopaedic, neurosurgical and ENT intervention required in a significant proportion of children and adults. Pharmacotherapies in this group of conditions are best illustrated by the use of bisphosphonates in patients with osteogenesis imperfecta. More recently potential treatments have been developed which target key elements of the molecular pathways involved in the pathogenesis of these conditions. We and others have suggested that it may be possible to repurpose existing therapeutic agents based on improved understanding of molecular pathology of these conditions and recognition of previously unknown effects of existing drugs. We will describe some of our current work in this area.
DOI: 10.1530/endoabs.51.EN1.1

EN1.2
Neuroscience, neuroendocrinology and the psychology of obesity: Should you ‘go with your gut’ or is it ‘mind over matter’?
Caroline Steele
Leeds.

Although ‘simple’ nutritional obesity is increasingly prevalent in the population some other types, such as those secondary to underlying medical conditions, remain relatively rare. These childhood disorders associated with obesity (such as hypothyroidism, Cushing’s syndrome, hypothalamic obesity, leptin deficiency, Prader-Willi Syndrome and melanocortin-4 receptor mutations) will be reviewed and consideration given to which patients should be investigated for these conditions. Research studies of patients with obesity secondary to some of these underlying medical conditions have used investigative techniques such as functional neuroimaging and eating behaviour studies, and have explored variations in the hormones involved with the regulation of appetite and food intake which may underlie the development of obesity in these conditions. A brief overview of these techniques and their findings in relation to these disorders will be discussed and their use in investigating the underlying pathophysiology of ‘simple’ nutritional obesity considered. As the importance of the central nervous system in initiating and maintaining obesity is becoming increasingly clear, techniques involving neuroscience, neuroendocrinology and psychology have been identified by the Medical Research Council (MRC) as one of their scientific areas of obesity research priority. The use of these varied investigative techniques recognises that obesity is a ‘complex physiological and socioeconomic issue, spanning many disciplines’. By understanding the underlying mechanisms of obesity in those with underlying medical conditions, this helps to guide researchers investigating ‘simple obesity’ and aid in the goal of eventually developing effective interventions to prevent and treat these conditions.
DOI: 10.1530/endoabs.51.EN1.2

EN1.3
Long term endocrine and metabolic consequences in survivors of childhood leukaemia
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London.

Leukaemia is the most common childhood cancer with an excellent 5-year survival rate of >80%, but many survivors face long-term health consequences. Low risk patients who were treated with chemotherapy-only are at risk of obesity and the metabolic syndrome. Endocrine and cardiometabolic abnormalities are common in high risk patients who required adjunct cranial irradiation and/or haematopoietic stem cell transplantation (HSCT) with without total body irradiation (TBI). Growth failure is reported in 20–80% of childhood HSCT survivors with mean 1-2 s.d. loss to genetic target height. Gonadal failure may present with pubertal problems/infertility, and severity is associated with the type and dosage of conditioning therapy. Females are more often affected than males and almost all who had fractionated TBI>12 years old will develop ovarian failure. Some males progress through puberty spontaneously with virilisation, but have small testes as Leydig cells are more radiation resistant than Sertoli cells. Thyroid disorders can present as subclinical/primary hypothyroidism, or autoimmune hypothyroidism. TBI is associated with increased risk of thyroid malignancy, hence regular monitoring is essential and further investigations should be instigated if indicated. Cardiometabolic abnormalities such as diabetes mellitus, hypertension and dyslipidaemia are increasingly recognised in HSCT survivors without raised body mass index. Impaired glucose tolerance is reported in 26–33% and diabetes mellitus in 9.5–17%. The aetiology of diabetes is often a combination of reduced beta-cell reserve and insulin resistance, but can also be autoimmune. Fasting glucose and HbA1c are unreliable in identifying survivors with diabetes and oral glucose tolerance tests are recommended. The presentations of diabetes are variable and treatment must be individualised. There is conflicting reports on bone health in survivors of HSCT with likely greater reduction in bone mineral density with increasing age than general population. Further research into the rehabilitation of survivors is required to reduce long term morbidity and early mortality.
DOI: 10.1530/endoabs.51.EN1.3
Meet the Expert Session
The diagnosis of hypogonadism in a young person represents reduced sex steroid production and subfertility. Optimising sex steroid replacement both in terms of preparation and dose occurs after pubertal induction. Clinical practice has changed in the UK in respect to females. The management of subclinical hypogonadism and benefits of testosterone replacement in male cancer survivors and Klinefelter syndrome remain unclear. The endocrinologist needs to navigate carefully the concerns of parents in relation to impact on behaviour and concerns about personal hygiene in young people with learning difficulties while ensuring every attempt is made to establish them on bone protective sex steroid replacement. Counselling young people with respect to their options for fertility and risks associated with pregnancy is an important aspect of transitional care. While hypogonadism is frequently lifelong there are groups of patients in whom resumption of gonadal function can occur either permanently or temporarily. This possibility needs to be discussed along with contraception if unwanted pregnancy is to be avoided. It also provides a window of opportunity for fertility preservation. Reevaluation of gonadal function is therefore recommended. Through cases these aspects of hypogonadism will be explored.

DOI: 10.1530/endoabs.51.MTE1
Oral Communications
Oral Communications 1

OC1.1 Dexamethasone for the treatment of 11-beta-hydroxysteroid-dehydrogenase Type 2 deficiency treatment in an adolescent
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11-beta-hydroxysteroid-dehydrogenase type 2 deficiency (11bHSD2) or syndrome of apparent mineralocorticoid excess is an autosomal recessive condition that characteristically presents with hypokalaemia and hypertension. In this condition, cortisol is not inactivated to cortisone and thus the excess cortisol cross reacts with the mineralocorticoid receptors in the kidney leading to hypertension, hypokalaemia and suppressed plasma renin activity (PRA) and aldosterone levels. The diagnosis and treatment options in a 15 year old girl were reviewed and adjusted. She was born at 37+5 weeks gestation to Pakistani parents with a low birth weight of 1.54 kg. At 2 years of age, hypokalaemia was noted during routine investigations. Given the family history of 11bHSD2 she had a urine steroid profile which showed a high urinary cortisol/cortisone ratio suggestive of 11bHSD, along with a suppressed PRA (0.4 pmol/ml per hr) and aldosterone (<55 pmol/l). Treatment was commenced on spironolactone, amiloride, amiodipine and oral potassium to control the blood pressure and hypokalaemia.

At 13 years she represented to endocrine services with a height of 0.19 SDS, weight —1.53 SDS, and BMI —2.44 SDS. She has bilateral hearing loss and dry cracked skin on the heels. Further investigations revealed nephrolcalcinosis and elevated ambulatory blood pressures (daytime and nighttime averages of 128/83 and 125/72 respectively). Thus she would be at risk of end stage renal disease and these individuals may require a renal transplant. Treatment was then changed to low dose dexamethasone 0.5 mg at night suppress the endogenous cortisol in the kidney and thus aiming for measurable PRA and aldosterone levels. This resulted in improved electrolyte control and successful stopping of other medications and weaning of potassium supplements. Remarkably it also improved her life long dry cracked heels. Education about steroid stress dosing for illness was provided. Repeat ambulatory blood pressure will dictate whether she is a candidate for the addition of a mineralocorticoid receptor antagonist. Despite the elevated cortisol levels, individuals with 11bHSD deficiency typically have a low birth weight, and low BMI along with hypokalaemia and hypertension. This is an important and treatable cause for hypertension and consideration should be given to instituting dexamethasone to suppress the endogenous steroids.

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OC1.2 Neonatal hypoglycaemia: missed opportunities for detecting hyperinsulinism
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Background
Timely diagnosis and management of neonatal hypoglycaemia is important due to associated short and long-term sequelae including neurodevelopmental delay. Hyperinsulinism should be distinguished from other causes of hypoglycaemia as management and acceptable glycaemic parameters may be different.

Aims
To characterize admissions with hypoglycaemia and assess the use of hypoglycaemia screen to detect hyperinsulinism.

Methods
Retrospective case note review of infants admitted to a tertiary neonatal unit between 1st January 2011 to 31st December 2014 with a primary diagnosis of hypoglycaemia.

Results
One hundred and two consecutive cases were reviewed (5.1–8.5% of total annual NICU admissions). Median gestational age was 37.4 weeks (range = 33.4–42.1), 64% of cases > 37 weeks gestation. Median birthweight = 2710.5 g (range = 1600–4830 g). 88% of cases were classified as ‘infants at risk of hypoglycaemia’ by hospital guidelines. 76% had no history of maternal diabetes, 13% had mothers with gestational diabetes, 7% had mothers with type 1 diabetes and 4% had mothers with type 2 diabetes. 19% had evidence of neonatal sepsis, 27% had a maternal preeclampsia and 100% had an Apгар score > 9 at 10 minutes. 83% had no hypoglycaemia screen. Cases with a glucose infusion rate (GIR) > 8 mg/kg per min, 63% had no hypoglycaemia screen and > 10 mg/kg per min, 33% had no hypoglycaemia screen. Twelve cases (12% of total) had biochemical evidence of hyperinsulinism, with 1/12 having a history of maternal diabetes (Type 2). Comparing those with hyperinsulinism with those with either normal hypoglycaemia or no screen taken; there was significantly longer duration of IV fluids (140.40s vs. 59hours, p=0.003) and hospital stay (12.5 days vs 6 days, p=0.003) but no significant difference in birthweight (2425 g vs 2580 g, p=0.76), time to stable glucose (27 hours vs 19 hours, p=0.26) and GIR (10.25 mg/kg per min vs 6.0 mg/kg per min, p=0.12).

Conclusion
Hypoglycaemia is a common reason for admission to the neonatal unit. There were missed opportunities for a hypoglycaemia screen, especially in those with high GIR. Those with hyperinsulinism take longer to discontinue IV fluids and stay longer in hospital.

DOI: 10.1530/endoabs.51.OC1.2

Oral Communications 2

OC2.1 Discordant TSH measurements in an euthyroid child due to a homologous TSHbeta subunit gene variant with variable immunoactivity
Eva van Walree1, A Emilje H. Hendriks2, Carla Moran1, Adeline K Nicholas1, Greta Lyons1, Anne McGowan1, David Halsall1, Sue Oddys1, V Krishna Chatterjee1 & Nadia Schoenmakers1
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Introduction
Thyroid function tests are frequently undertaken in children with non-specific symptoms suggestive of thyroid dysfunction. Infrequently, susceptibility of automated thyroid hormone assays to interference may generate misleading results, with the potential for inappropriate diagnosis and treatment. We report an unusual case with apparent subclinical hyperthyroidism, due to negative interference in particular TSH assay platforms, with an underlying genetic basis. Case report
An 8 year old boy presenting with tiredness exhibited undetectable TSH levels (< 0.03; (Reference Range, RR 0.35–5.5 mU/l)), but normal thyroid hormone measurements (FT4 14.4; (RR 10–19.8 pmol/l), FT3, 6.6; (RR 4–7.5 pmol/l) prompting further endocrine investigation. He had been born at term to non-consanguineous South Indian parents, following IVF treatment. He was clinically euthyroid and growing along the 91st centile. Following an episode of non-autoimmune thyroiditis his mother was euthyroid; and his father and sibling were well. Further evaluation of his thyroid function tests revealed undetectable TSH levels in two assays (Centaur and Immulite 2000, both manufactured by Siemens), but normal TSH in three other platforms (Wallac Delfia, Roche Elecsys and Abbot Architect, Table 1). FT3 and FT4 were consistently normal, and the discordancy of TSH measurements suggested assay interference. TSH is a heterodimeric glycoprotein comprising alpha and beta subunits encoded by separate genes. Sequencing of TSHB revealed a homologous, Arginine to Glycine aminoacid change (R75G) which has been identified previously.

Conclusions
Unlike loss-of-function TSHB mutations mediating central hypothyroidism, in silico modelling predicts that R75G mutant TSHB generates a bioactive TSH heterodimer. However, Arginine-75 is part of an epitope recognised by antibodies used in some immunoassays, explaining loss of TSH immunoactivity in such platforms. The high allele frequency of R75G TSHB in South Asian populations (1.2%, Exac), mandates that discordant, subnormal TSH readings in patients of this ethnicity should be reanalyzed using an alternate TSH assay known to cross react with this variant or prompt TSHB sequencing for this substitution.

Table 1

<table>
<thead>
<tr>
<th>Centaur</th>
<th>Immulite 2000</th>
<th>Wallac Delfia</th>
<th>Roche Elecsys</th>
<th>Abbot Architect</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (mU/l)</td>
<td>&lt;0.03 (35.5–5.5)</td>
<td>&lt;0.03 (5.4–4.4)</td>
<td>0.93 (0.4–4.4)</td>
<td>2.67 (0.27–4.2)</td>
</tr>
<tr>
<td>FT3 (pmol/l)</td>
<td>15.4 (10–13.8)</td>
<td>14.7 (13.9–22)</td>
<td>14.6 (9–20)</td>
<td>15.4 (10–22)</td>
</tr>
</tbody>
</table>

DOI: 10.1530/endoabs.51.OC2.1
OC2.2 Evolving primary adrenal insufficiency masked by adrenal suppression from long-term steroid treatment
Pooja Vasista & Savitha Shenoy
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Introduction
Adrenal suppression secondary to long-term steroid therapy is a known risk and this can mask the evolution of primary adrenal insufficiency.

Case report
A 6 years old girl with background of recurrent oral ulcers (probable mucocutaneous Behcet’s), Alpha-1-Antitrypsin deficiency, Bronchiectasis, on long-term oral Prednisolone treatment, was noted to have hyponatraemia (Na = 122 mmol/l) and hyperkalaemia (K = 6.6 mmol/l) during an inter-current illness and referred to the local Endocrine team. Clinically, she was noted to have Cushingoid features with significant growth concerns. Investigations confirmed Adrenal Insufficiency likely secondary to adrenal suppression due to long-term Prednisolone (Hydrocortisone (HC) equivalent dose of 30 mg/m2 per day).

Follow-up MDT discussion, it was agreed to change Prednisolone to HC with FC replacement doses and remains well.

Table summarising the results:

<table>
<thead>
<tr>
<th>Nov-16</th>
<th>Mar-17</th>
<th>Jun-17</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC Dose (mg/m2 per d)</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>Sodium (mmol/l)</td>
<td>129</td>
<td>129</td>
</tr>
<tr>
<td>Potassium (mmol/l)</td>
<td>6.6</td>
<td>6.1</td>
</tr>
<tr>
<td>Renin (mIU/l)</td>
<td>538</td>
<td>sample insufficient</td>
</tr>
<tr>
<td>Aldosterone (pmol/l)</td>
<td>95</td>
<td>&lt;55</td>
</tr>
<tr>
<td>ACTH (ng/l)</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

Low dose synacthen test
- 0 min (nmol/l) 250
- 20 min (nmol/l) 205
- 30 min (nmol/l) 219

Adrenal antibody Negative
USG abdomen Normal
Management Weaning HC FC commenced Continue FC and HC

Discussion
This case highlights that evolving primary adrenal insufficiency can be masked by adrenal suppression from long-term steroid treatment. Need for mineralocorticoid supplement whilst on HC in a case treated for adrenal suppression was the first clue which alerted of the possibility of primary adrenal insufficiency as the underlying diagnosis.

DOI: 10.1530/endoabs.51 OC2.2

OC3.2 A novel syndrome of nephrogenic syndrome of inappropriate antidiuresis, precocious puberty, parathyroid insensitivity associated with a novel GNAS mutation, p.F376V
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Introduction
Mutations in GNAS, affecting the alpha subunit of heterotrimeric G proteins, are implicated in several endocrinopathies. We report a patient with features of both receptor activation and inactivation in association with a novel de novo heterozygous somatic mutation.

Case report
Asymptomatic hyponatraemia (Na 117-123) was identified in a male neonate, and treated with sodium supplementation and fludrocortisone. Biochemical data were consistent with nephrogenic syndrome of inappropriate antidiuresis (NSIAD), and this was confirmed on Tolvaptan challenge. Medication was stopped, and sodium concentrations regulated by fluid restriction. A skeletal survey showed appearances suggestive of increased PTH activation with an elevated PTH and a normal calcium. By the age of 2 years, he developed rapidly advancing gonadotrophin-independent precocious puberty. Commencement of spironolactone and anastrozole led to recurrent hyponatraemia and he was therefore commenced on bicalutamide and letrozole. Sanger sequencing revealed a de novo GNAS mutation (c.1126T>G; p.Phe376Val) on the maternally inherited allele. Whole exome sequencing did not identify any further mutations which could provide an alternative explanation for the constellation of features seen in our patient. We hypothesise that this specific mutation in GNAS, which has not been previously described, causes activation of the G protein receptors GnRH and AVP2, leading to the combination of NSIAD and gonadotrophin-independent precocious puberty. As the maternal allele is expressed in the proximal tubules, we also suggest that this mutation leads to a paradoxical inhibition of the PTH response, leading to an increased circulating concentration of PTH causing the skeletal features.

Conclusion
We describe a previously undescribed condition in association with a novel germline mutation in GNAS, leading to a complex pattern of tissue-specific activation/inactivation. The unique spectrum of endocrinopathies could offer new insights into G-protein function.

DOI: 10.1530/endoabs.51 OC3.2

OC3.1 Oral Communications 3

OC3.1 Manifestation of hormone resistance depends on the type of inheritance in Albright’s Hereditary Osteodystrophy
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Introduction
Albright’s Hereditary Osteodystrophy (AHO, Pseudohyoparathyroidism type 1a) is inherited in an autosomal dominant manner. End-organ resistance is seen, primarily affecting parathyroid hormone (PTH) and thyroid hormones (TSH). The manifestation of hormone resistance, in particular resistance to PTH, depends on whether the mutated allele is inherited maternally or paternally.

Cases
A 4 year old male child was incidentally found to have hypocalcaemia (Serum Calcium: 1.72 mmol/l) with normal ALP as part of screening blood tests for speech difficulties. Further investigations identified raised PTH (72.2 pmol/l) with normal Vitamin D (42 nmol/l) and normal Urine Ca:Creatinine ratio. He was noted to be short compared to parents’ heights, had short stubby fingers, small, hard subcutaneous swellings on the right wrist and chest wall suggestive of subcutaneous calcification. Wrist X-ray revealed short 4th and 5th metacarpals and soft tissue calcification over the volar aspect of the 1st MCP joint. Diagnosis of AHO was considered which was confirmed by Genetics test (GNAS Gene changes). He was commenced on One Alpha and Oral Calcium. His 7 year old sister had undergone operation in infancy for removal of a swelling on the chest wall which had revealed calcification on biopsy. She underwent assessment and was noted to be short, had short stubby fingers and firm, small, subcutaneous swellings on her right heel, wrist and thigh. Blood tests confirmed hypocalcaemia (Serum Calcium: 1.62 mmol/l), raised PTH (91.4 pmol/l) with normal Vitamin D and urine Ca:Creatinine ratio. Diagnosis of AHO confirmed and treatment commenced. Family were referred to the genetics team who confirmed several family members on maternal side of the family had AHO (mother, mother’s twin sister, maternal uncle and maternal grandfather) with no evidence of hormone resistance.

Conclusion
Full expression of the gene (AHO – hormone resistance) occurs in maternally inherited cases (the two children) and partial expression (AHO alone) occurs when the gene is inherited from the father (mother and her siblings inherited from their father). This differential effect of the gene suggests the involvement of genomic imprinting of the GNAS1 gene in the expression of this disorder.

DOI: 10.1530/endoabs.51 OC3.1
Patients with self-limited delayed puberty harbour mutations in multiple genes controlling GnRH neuronal development

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Objectives
Abnormal pubertal timing affects >4% of adolescents and is associated with adverse health outcomes. Up to 80% of variation in the timing of pubertal onset is genetically determined. Self-limited delayed puberty (DP) segregates in an autosomal dominant pattern, but in the majority the neuroendocrine pathology and genetic regulation remain unclear. Miss-regulation of the embryonic migration of GnRH neurons has been implicated in the pathogenesis of DP (Howard et al 2016). We hypothesised that new candidates for the genetic basis of DP could be identified using expression data on genes up- or down-regulated during GnRH neuronal migration.

Methods
We performed whole exome sequencing (WES) in 160 members of 67 families from our self-limited DP patient cohort, and filtered the data for genes with rare, predicted deleterious variants that segregated with trait within families. These data were firstly examined for overlap with gene expression data from microarray analysis of GnRH/GFP primary rat neurons at E14, E17 and E20. Secondly the data were compared to a microarray analysis of genes differentially expressed in GN1 (immature and migratory) and GT1-7 (mature and non-migratory) immortalised GnRH neurons.

Results
After WES, 7350 genes contained rare, predicted deleterious variants that passed quality control. Microarray analysis identified 677 genes with significant (fold change > 2) up- or down-regulation during the time period of embryonic GnRH neuronal migration, and 102 differently expressed between GN11 and GT1-7 cells. 265 genes identified as significantly up- or down-regulated during GnRH-GFP primary rat neurons at E14 and at E20, and 33 genes reaching statistical significance for differential expression between GN11 and GT1-7 cells, were also identified as potentially pathogenic in self-limited DP patients. These include the G-protein coupled receptor LGR4, the neuronal growth regulator NEGR1 and several other neuronal chemokines or axonal guidance molecules.

Conclusions
This analysis has yielded several interesting new rare, potentially pathogenic variants in genes implicated in GnRH neuronal migration and development in 12 families from our cohort. Whilst these candidates need to be functionally validated, these data provides further evidence for the importance of GnRH neuronal migration in the timing of puberty onset.

DOI: 10.1530/endoabs.51.OC4.1

OC4.2
Cumulative radiation exposure from imaging and associated lifetime cancer risk in children with osteogenesis imperfecta

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Background and objectives
Children with Osteogenesis Imperfecta (OI) require frequent imaging for fractures and surveillance of bone mineral density. Radiation exposure in childhood carries the highest risk of cancer. Here, we estimate the cumulative effective radiation dose (E) and lifetime cancer risk (LAR) from imaging in children with OI. We also explore the hypothesis that the rate of fracture positive imaging for investigation of injuries is related to family history of OI.

Methods
We reviewed all imaging (X-ray, computed tomography [CT] & bone densitometry [DXA]) conducted from 2003 to 2016 in children with OI (0–19 years) with a minimum observation period of 5 years, at a tertiary paediatric centre. E was estimated for each image using age-dependent local reference data. LAR was calculated using cumulative E with organ, sex and age specific risk coefficients. Patients were then categorized by cancer risk.

Results
We present results from 106 children (50% females, 5747 images) with mild (n = 74), moderate (n = 22) and severe (n = 10) OI. The median (range) observation period was 11.7 years (5.2–15.6). The number of images taken per year for mild OI was 3.1 (1.9–5), moderate 5.4 (2.7–8.2) and severe 9.8 (5.9–22.9). CT accounted for 0.8% of total imaging episodes but contributed 66% of total E. Cumulative E and LAR differed significantly between mild and moderate OI (P = 0.006), and mild and severe (P = 0.001). The median LAR of cancer was 8.8 cases per 100,000 exposed patients (0.8–403), which increased with OI severity. Of the patients with a moderate or severe OI all had undergone CT scans and 88% had scoliosis or vertebral fractures. Family history of OI did not impact cumulative E, LAR or rate of fracture positive imaging, which was 60%.

Conclusions
When compared to baseline LAR (50%) the additional cancer risk in our OI cohort, from imaging, was small (0.0088%). Those with vertebral fractures, scoliosis or severe OI carried the highest risk of cancer, and in this group the LAR reached 0.4%. We recommend replacing spiral x-rays with vertebral fracture assessments on DXA (7.5 times less radiation), and exercising caution with CT imaging to further minimise cancer risk.

DOI: 10.1530/endoabs.51.OC4.2

OC4.3
Novel FOXA2 mutation causes hyperinsulinism, hypopituitarism with craniofacial dysmorphism and endometrioid-derived organ abnormalities

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1Alder Hey Children’s NHS Foundation Trust, Liverpool, UK; 2University of Liverpool, Liverpool, UK; 3Centre for Endocrinology, William Harvey Research Institute, London, UK; 4Queen Mary University of London, London, UK; 5NIHR Alder Hey Clinical Research Facility for Experimental Medicine, Liverpool, UK.

Background
Congenital hypopituitarism (CH) is characterised by the deficiency of one or more pituitary hormones and can present alone or in association with complex disorders. Congenital hyperinsulinism (CHI) is a disorder of unregulated insulin secretion despite hypoglycaemia that can occur in isolation or as part of a syndrome. The underlying genetic etiology causing the complex phenotype of CH and CHI is unknown.

Patient and Methods
A female baby born to non-consanguineous Caucasian parents at 42 weeks gestation with a birth weight of 4.185 kg (+1.72SDS) was noted to have high glucose requirement and a hypoglycaemia screen confirmed CHI. 18F-DOPA PET-CT suggested diffuse pancreatic lesion. She also developed TSH, ACTH and GH deficiencies. MRI brain showed a hypoplastic anterior pituitary, absent posterior pituitary, thin pituitary stalk and corpus callosum. Genetic analysis was negative for ABC88, KCN11, HNF4A and GCK mutations. She has solitary median maxillary incisor, congenital nasal pyriform aperture stenosis, pulmonary stenosis, renal cystic dysplasia, severe gastroesophageal reflux requiring jejunostomy, persistent oxygen requirement and hepatic portal bridging fibrosis. Whole exome sequencing was performed and the identified variant was confirmed by Sanger sequencing. Further functional studies were performed to demonstrate the pathogenicity of the variant.

Results
A de novo heterozygous mutation in FOXA2 (c.505T>C; p.S169P) was identified which is at a highly conserved DNA binding domain, not present in control databases and predicted to be deleterious to the protein function. We demonstrated strong expression of Foxa2 mRNA in the developing hypothalamus, pituitary, pancreas, lungs and oesophagus of mouse embryos using in situ hybridization. Expression profiling on human embryos by immunohistochernistry showed strong Foxa2 expression in the neural tube, third ventricle, dienephochel and pancreas. Transient transfection of HEK293T cells with WT (Wild type) hFOXA2 and mutant hFOXA2 showed impairment in transcriptional reporter activity by mutant hFOXA2. Further analyses using western blot assays showed that hFOXA2 p.S169P variant is pathogenic resulting in lower expression levels when compared with WT hFOXA2.

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Germline mutations in BRAF and other components of the RAS/MAPK pathway are found in RASopathies, whose features include short stature and pupetal delay. The underlying mechanism of endocrinopathies in RASopathies has not been fully elucidated. We report four BRAF mutations (two of which are novel) in four children with congenital hypopituitarism and RASopathy features. To demonstrate the functional role of the variants we performed phosphoproteomic analyses using mass spectrometry and identified that they significantly increase levels of phosphorylated ERK demonstrating that the BRAF genetic variants are pathogenic activating mutations. To further demonstrate the role of activated RAS/MAPK pathway in hypopituitarism, we used a murine transgenic approach to express the activating BRAFV600E mutation using a pituitary-specific Cre reporter line, Prop1:Cre. Genotypes of offspring from Prop1:Cre × BrafV600E;Prop1:Cre genetic crosses showed a significant deviation from the expected Mendelian ratio, indicating embryonic lethality. BrafV600E/
Methods and results
CaSR mutations were P.Thr282Asn, not previously described, and the previously described p.Ala843Glu, p.Tyr829Cys, p.Phe821Leu. Patients presented with hypocalcaemic seizures or tetany in the first few weeks of life. Additional features were bilateral cataracts, hypomagnesaemia, Barter type V. One patient had nephrocalcinosis before CSPI. Age at start of CSPI was 3 weeks, 6 weeks, 6 months, 6 years and 20 years. Medtronic and Omnipod patch pumps were used for two patients. Treatment was started in an inpatient setting. Duration of treatment is currently 1–3 years. PTH requirement was 0.21, 0.13, 0.15, 0.5 and 3 mcg/kg per day. Four patients required Magnesium supplementation. All patients received Cholecalciferol. Calcium concentration stabilised and patients continue to require weekly or bi-weekly blood tests. Number of admissions significantly reduced during CSPI. Seizures stopped in all patients on CSPI. Current calcium concentrations range from 1.75 to 2.15 mmol/l. Current urine Calcium/creatin ratio range from 1.2 to 2.5 mol/mol. Nephrocalcinosis has remained stable. One patient stopped pump treatment temporarily due to instable calcium concentrations.

Conclusion
We describe continuous subcutaneous PTH infusion as a suitable treatment for ADH that cannot be controlled conventionally. We also describe a new CaSR mutation resulting in ADH and cataracts, which is also a feature of the mouse model for ADH. Cataracts have since been found in some patients with ADH. Longer follow up is required to assess whether continuous sc PTH treatment delays the progression of nephrocalcinosis.

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OC4.7
Adverse effects of delayed induction of puberty in girls Turner syndrome: Turner Syndrome Life Course Project
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Background
The Turner Syndrome Life Course Project, UCLH, has collected data on 810 women with TS, attending clinic for 20 years and has accumulated over 8000 clinic visits. We present an analysis of the effects of timing and type of exogenous oestrogen on health outcomes in adults.

Methods
A cross-sectional analysis of 475 subjects with primary amenorrhoea with accurate age of pubertal induction data was performed using correlation coefficients controlling for age. A second univariate analysis inclusive of accurate age of pubertal induction data was performed using correlation coefficients controlling for age. A second univariate analysis inclusive of accurate age of pubertal induction data was performed using correlation coefficients controlling for age.

Results
Results Median (90th centiles) age of pubertal induction was 14 years. Oestrogen start age and transdermal 17β estradiol were not associated with hip and spine T-score (Z = 3.02, P = 0.001). Differences in medical endpoints were not significant between transdermal estradiol users and oral oestrogen users (Z = 1.98, P = 0.05).

Conclusions
Given the propensity of women with TS to develop hypertension ethinylestradiol is contraindicated.

DOB: 10.1530/endoabs.51.OC4.7

OC4.8
Impact of risk factors for Fetal Growth Restriction (FGR) on intrauterine growth and birthweight
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Background
Abnormal uterine artery Doppler (UA) at 23 weeks is considered to be a risk factor for FGR. However, the incidence of being born small for gestational age (SGA) in those with abnormal Doppler is not defined.

Aims
1. To determine the incidence of birthweight <2nd centile (BW <C2nd) in pregnancies at high risk of FGR.
2. To determine the effect of specific antenatal FGR risk factors on fetal growth trajectory and birthweight.

Methods
Data were obtained from women seen in a clinic for those at high risk of FGR. Entry criteria were low first trimester PAPP-a or second trimester raised inhibin +/- AFP. Pregnancies were categorised according to FGR risk subgroup; small placenta (<10 cm) and abnormal 23 week UA (defined by pulsatility index >1.3MoM, resistance index >0.7MoM +/− noting on one or both waveforms (group A), small placenta & normal UA (B), normal placenta & abnormal UA (C), normal placenta & normal UA (D). Estimated fetal weight and birthweight centiles were calculated, customised for maternal height, weight, ethnicity, gestation and sex.

Results
226 pregnancies that resulted in livebirths >34 weeks gestation were analysed (A: 16; B: 18; C: 40 and D: 152) of which, 20 (9%) were SGA births. The proportion of babies with BW < C2nd was highest in group A (4/16, 25%), compared with group B (1/17, 6%), C (9/40, 23%) and D (6/152, 4%). ANOVA and Student’s t-test of fetal growth trajectories between 23 weeks and birth showed differences between FGR risk groups in Δ weight (A = 2.10 kg, B = 2.73, C = 2.42, D = 2.66, P = 0.001). Mean birthweight (A = 2.64 kg, B = 3.33, C = 3.02, D = 3.26, P < 0.01) and mean birthweight centiles (A = 15.80th, B = 36.60th, C = 28.30th, D = 37.90th, P = 0.008) were also significantly different.

Conclusions
In pregnancies considered to be at higher risk of FGR, 9% were born SGA, rising to 25% for those with a small placenta and abnormal UA. Serum markers combined with UA and to a lesser extent, placental size can be used to identify adverse growth trajectory and small size at birth.

DOB: 10.1530/endoabs.51.OC4.8

Oral Communications 5
OC5.1
New insights into the preoperative localisation of corticotroph adenomas in paediatric Cushing's disease (CD)
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Introduction
Selective transphenoidal microadenoectomy (TTSS) is the first-line treatment of paediatric Cushing’s disease (CD). Corticotroph adenomas in children are often small and difficult to visualize. We aimed to assess the utility of pituitary MRI and bilateral inferior petrosal sinus sampling (BIPSS) in confirming the diagnosis of CD and the localisation of the adenoma. We also report our early experience of STEALTH MRI (volumetric T1 weighted, contrast-enhanced scan).

Methods
Fifty one paediatric CD patients have been managed by our centre since 1982. In 40 children (21 M mean age 12.9 years (5.6–17.8), we had data for BIPSS, pituitary MRI and TSS findings (nine did not have BIPSS, two had surgery elsewhere). An inferior petrosal sinus to peripheral (IPS/P) plasma ACTH ratio before CRH > 2.0, or peak IPS/P ratio after CRH > 3.0 were considered diagnostic for central ACTH secretion. An inter-petrosal sinus gradient (IPS/IPG) after CRH of > 1.4 was considered positive for ACTH lateralisation. 39 had pituitary MRI and one patient had a CT scan. Four patients (4F, aged 11.2–16.0 year) had pre-operative STEALTH MRI recently introduced for surgical planning.
Results
BIPSS correctly identified central ACTH production in 37/40 (93%) and the adenoma position in 27/40 (68%) cases. Conventional MRI scanning identified a pituitary lesion in 18/40 (45%) cases and there was concordance of the positions of the adenoma with operative findings during TSS in only 15/40 (38%) children. Following TSS, 31/40 (78%) children were in remission (0900 serum cortisol < 50 nmol/l). BIPSS and MRI demonstrated the correct adenoma position in 22/31 (71%) and 15/31 (48%) respectively, four patients had additional STEALTH MRI scans (3/4 had inconclusive conventional MRI/BIPSS findings). In all four patients, STEALTH MRI correctly identified the position of the adenoma and all are in post-operative remission.

Discussion
BIPSS is safe and well tolerated in children when performed by an experienced radiologist. BIPSS achieves a high diagnosis rate of central ACTH production in paediatric CD although evidence of adenoma position is less accurate. Microadenoma visualisation rate with conventional MRI scanning is low, however steath MRI may emerge as a new improved technique for pituitary imaging in paediatric CD.

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OC5.2
The clinical and molecular spectrum associated with obesity-associated GNAS1 mutations
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Heterozygous mutations in GNAS1, which encodes the Gnas protein involved in multiple signalling pathways, are classically associated with Albright’s Hereditary Osteodysplasia (AHO). GNAS1 is one of few genetic loci that undergo allelic-specific methylation resulting in the parent-specific expression of at least four different transcripts. The classic constellation of phenotypic features includes short stature, round face, brachydactyly, obesity, dental hypoplasia and subcutaneous calcifications. These features have been reported with both paternally and maternally inherited mutations. Additionally, maternally inherited mutations can result in resistance to parathyroid hormone, thyroid stimulating hormone, growth hormone releasing hormone and gonadotrophins. Here we describe the identification of 24 patients with GNAS1 mutations from the whole exome and targeted resequencing of 5000 patients with severe early onset obesity. We describe the clinical spectrum in mutation carriers which includes hyperphagia as well as low basal metabolic rate, short stature in some but not all children and mild learning difficulties. These clinical characteristics may in part be explained by the ability of mutant forms of GNAS to impair receptor-dependent and receptor independent signalling by GPCRs such as MC4R, Beta-2 and Beta-3R. We conclude that mutations in GNAS1 present with a highly variable phenotype. Our ascertaining by studying a large number of children with severe obesity, has revealed a degree of clinical variability that is greater than reported. This may have contributed to under-diagnosis of patients who lack the classic phenotypic features. Broader recognition of the spectrum of features seen in GNAS1 mutations could aid diagnosis and patient care.

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OC5.3
Novel evidence implies ALADIN, the triple A syndrome gene product is involved in mitochondrial physiology
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Triple A syndrome (AAAS), a rare and debilitating autosomal recessive disorder. It is characterised by adrenal failure, alacrima and achalasia. > 70% patients develop a neurodegeneration. The AAAS gene encodes ALADIN, a nuclear pore complex (NPC) protein necessary for the selective nuclear import of DNA protective molecules and is important for cellular redox homeostasis. ALADIN’s role is not fully characterised: its discovery at the centrosome and the endoplasmic reticulum suggests a role outside the NPC. ALADIN deficiency has been linked to disruption of mitochondrial stressogenic enzymes and increased mitochondrial superoxide species. We hypothesised that AAAS is a consequence of mitochondrial dysfunction.

Aim
To examine whether ALADIN has a role in mitochondrial physiology
Methods
A stable knockdown (KD) of AAAS-gene expression using synthetic shRNA lentiviral transduction was established in a neuroblastoma cell line (SHSY5Y) to model AAAS (AAAS-KD). Western blotting confirmed an 80% reduction of ALADIN expression. Microarray (Quagen, PAHS-065) was used to profile the expression of 84 genes related to oxidative stress in AAAS-KD and wild-type (WT) SHSY5Y cells. Immunoﬂuorescence was used to detect ALADIN using a rabbit polyclonal anti-ALADIN antibody (Proteintech Europe). MitoTracker identiﬁed the mitochondria. Confoal microscopy identiﬁed the subcellular localisation of ALADIN relative to mitochondria. ALADIN deplete AAAS-KD SHSY5Y cells established any non-specific staining. Mitochondrial volume was measured by 3D reconstruction of the ﬂuorescent images, using Imaris.

Results
Microarray revealed that reduced levels of ALADIN altered the expression of 8 genes in oxidative stress pathways (ACAT, SOD1, PXDN, PRDX6, HSPA1A, GPX3, CCS, and ALB). Confocal imaging demonstrated ALADIN co-localisation with the mitochondria in WT SHSY5Y cells. Additionally, mitochondrial volume was increased in AAAS-KD (n=5) compared to WT cells (n=6): mean 73.29 μm3, SEM ± 21.44 vs mean 54.82 μm3, SEM ± 7.681 (P=0.122), respectively.

Discussion
In this model, ALADIN deficiency impacts the transcription of genes involved in oxidative stress pathways. ALADIN appears to co-localise with mitochondrial marker MitoTracker. ALADIN deficiency is associated with an increase in mitochondrial volume. This supports the further exploration of ALADIN’s role in mitochondrial physiology.

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OC5.4
Characterisation of skeletal developmental in mouse models of Duchenne Muscular Dystrophy
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Short stature and osteoporosis are common in DMD. Glucocorticoids slow disease progression but are associated with further growth retardation and skeletal fragility. The muscular dystrophy x-linked (mdx) mouse is the most commonly used animal model of DMD. However, the phenotype is relatively mild and few medications that have shown therapeutic benefit in the mdx have translated clinically. The utrophin heterozygous mdx mice might be more appropriate but their growth and bone phenotype have not been investigated. We tested the hypothesis that: Mouse models of DMD (mdx and mdx:utr) have an intrinsic abnormality of linear growth and skeletal development. A cross-sectional study of 49 mice sacrificed at 3.5 and 7 weeks was performed. Mdx/mdx:utr mice were obtained from Jax, alongside C57Bl/10 controls(WT). Growth was assessed twice weekly, forelimb grip strength testing performed, CK measured and histopathology assessed using H+E tibialis anterior sections. Tibiae were scanned using SkyScan microtomography and 3-point bending undertaken.

Muscle
WT mice had the greatest normalised grip strength at all ages. Mdx:utr had higher mean grip strength at 7 weeks than mdx mice. CK assay results indicated significantly higher serum values from mdx (P<0.02) and mdx:utr (P<0.002), versus WT. Muscle histology was consistent with these observations.

Growth
No significant difference in bodyweight gain between groups at any age and no difference in tail length by 7 weeks. Gain in body length was 0.3 mm less/day compared to WT (n=5) compared to WT mice culled at 7 weeks, but Micro- CT of tibial length revealed no genotype difference.

Bone
No significant differences in trabecular bone parameters between groups at any age, except for structural model index (greater in 3-week WT mice, P<0.04). Cortical bone parameters and bone mechanical properties similar at all ages. There are very limited strategies available to treat short stature and osteoporosis in DMD. We have demonstrated that young mdx and mdx:utr mice exhibit muscle weakness, but don’t show a bone or growth phenotype and therefore have clear limitations. Finding a more suitable pre-clinical mouse model is therefore essential.

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OC5.5 Uterine development: the effect of induction of puberty with oestrogen in primary Amenorrhoea
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Introduction
The uterus develops during puberty and increases not only in length but also in width and depth, to achieve a mature shape. Pubertal induction with exogenous oestradiol aims to mimic this. Research to date shows variable results for the attainment of an adult uterine configuration in females with hypogonadism. Suboptimal uterine development is hypothesised to be a contributing factor for adverse reproductive outcomes in females with hypogonadism undergoing egg donation IVF.

Methods
This is a single centre, retrospective, cross sectional study of females who underwent pubertal induction. Nulliparous females with a history of hypogonadism and pubertal induction, attending University College London Hospital, were recruited. A pelvic ultrasound was performed by a single observer and uterine dimensions and clinical data were recorded. The reference group consisted of 28 nulliparous women attending with male factor subfertility with a normal pelvis on ultrasonography.

Results
Fifty-six females with hypogonadism were recruited; nine with Gonadotrophin Deficiency, 19 with Premature Ovarian Insufficiency and 28 with Turner Syndrome. The mean age of those with hypogonadism at the time of ultrasound scan was 13.2 years compared to 33.5 years for the reference group. Those with hypogonadism presented at an average age of 12.7 years and started oestradiol therapy at a mean age of 15.1 years. Females with hypogonadism achieved menarche significantly later than those with spontaneous puberty (16.6 years vs 13.2 years; P < 0.05). Those with hypogonadism achieved significantly reduced total length, anterior posterior (AP), transverse and uterine volume measurements compared to the reference group (length 67.3 mm vs 73.1 mm; P = < 0.05, AP 24.3 mm vs 30.4 mm; P = < 0.05, transverse 36.03 mm vs 41.6 mm; P = < 0.05, volume 35.0 ml vs 48.9 ml; P = < 0.05)

Conclusion
Despite standard Oestradiol therapy, those with hypogonadism achieved significantly smaller uteri compared to the reference group. Not only was the uterine length suboptimal but also the AP and transverse measurements, suggesting an immature shape. Inadequate uterine development may contribute to negative fertility and pregnancy outcomes and therefore, understanding which factors influence uterine size in this cohort, will be paramount to optimise pubertal induction treatment.

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OC5.6 Phenotypic spectrum and response to recombinant human IGF1(rhIGF-1) therapy in patients with homozygous intrinsic pseudoxon (69Y)GH receptor mutations
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Objectives
Patients with homozygous 69Y mutations have GH insensitivity (GHI). We previously described spectrum of clinical and biochemical phenotypes of 11 69Y patients (David et al. JCEM 2007;92:655) and now report 9 additional patients. Response to rhIGF-1 therapy has not previously been assessed.

Methods
20 69Y patients (12 M, 11 families, mean age 4.0±2.2 year) were diagnosed genetically in our centre. Continuous parametric variables were compared using student t-test or ANOVA with Bonferroni correction for multiple comparisons. Results
10(20/50%) patients had facial features of GHI, 19(20/95%) from consanguineous families and 18/20(90%) of Pakistani origin. At diagnosis, mean height SDS = –4.1±0.95 (–5.9 to –1.7), mean IGF-1SDS = –2.8±1.4 (–6.8 to –1.0), IGFBP-3 SDS = –3.0±2.1(–8.9 to –0.6), mean basal and peak GH levels 11.9 and 32.9 mcg/l respectively. 12/20 had IGF-1 generation test (IGFGT), 11(12/92%) showed no response (IGF-1 rise < 15 ng/ml), 1 responded (132 to 255 ng/ml); 17/20(85%); 11M) received rhIGF-1. Complete data was available for 15/17. Mean age at rhIGF-1 initiation was 9.0±2.7 years (5 pubertal at rhIGF-1 initiation and received GnRH analogue concomitantly). Mean duration of rhIGF-1 was 5.3±2.5 years. Mean baseline HV 4.6±1.1 cm/y increased to 7.4±1.8 cm/y (P =<0.001) demonstrating a linear rate of growth between year 1 HV and sex, age at rhIGF-1 initiation, baseline height SDS or baseline IGF-1SDS. Mean cumulative change in height SDS at end of treatment was 1.4±2.6 (0.4 to 2.0); 11/15 patients (10 naive to rhIGF-I) completed linear growth; mean final height (FH) was –4.0±1.5 SDS (–5.7 to –1.8). In 4/15 (all naive to rhIGF-I), height SDS at latest assessment (LH) was –2.9±0.3 SDS (–3.2 to –2.6) compared to pre-treatment –4.1±0.5 SDS (–4.6 to –3.6) (P =<0.02). In 3 untreated patients, FH was –3.5 and –5.0 and LH was –4.4 SDS. Difference between target height (TH) SDS and FH/LH SDS was less than that of TH SDS and pretreatment height SDS (2.3±0.3 vs 3.2±0.8; P =<0.001).
Conclusion
The homozygous pseudoxenon GHR mutation caused both classical and mild GHI phenotypes, even within the same family. The majority of patients did not incorporate rhIGF-1 during an IGFGT. rhIGF-1 treatment improved height outcomes that of TH SDS and pretreatment height SDS (2.3±0.3 vs 3.2±0.8; P =<0.001).

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OC5.7 The Phenotyping of Overgrowth (POD) Study: a novel ‘no win, no fee’ model for translating research findings into clinical diagnoses
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Introduction
Rare genetic overgrowth disorders are a group of conditions characterised by height and/or head circumference >2 s.d. above the mean for age and sex, learning disability, congenital anomalies, and in some cases childhood tumours.

POD is a national cohort study that includes a next generation sequencing (NGS) panel of overgrowth genes. We present a new model for clinical confirmation of pathogenic variants identified by this research panel. Clinicians requesting diagnostic testing for patients meeting the eligibility criteria are charged only if (1) a pathogenic variant is identified and (2) the variant is confirmed by the West Midlands Regional Genetics Laboratory. If no pathogenic variants are identified, no charge is incurred. POD is a pilot project for assessing the cost effectiveness of this strategy.

Methods
An OpenClinica electronic data capture system was used to collect Human Phenotype Ontology (HPO) coded clinical data. The custom NGS panel was designed using Agilent SureDesign software and Agilent SureSelect QT X Target Enrichment was used for library preparation prior to sequencing on the Illumina MiSeq. Bioinformatic analysis was performed using Agilent SureCall software. Pathogenic variants were confirmed by Sanger sequencing in the service laboratory before results were fed back to clinicians.

Results
Twenty-eight individuals with undiagnosed overgrowth disorders were tested on the panel of 20 genes and pathogenic variants identified and confirmed in two participants. One participant was diagnosed with Malan syndrome due to a de novo missense variant in NFX1 and a second patient was diagnosed with Tatton-Brown-Rahman syndrome due to a de novo nonsense mutation in DNMT3A.

Conclusions
Panel testing of overgrowth genes in the research setting translates into improvements in clinical care by identifying previously unknown diagnoses. We believe the novel ‘no win, no fee’ model will be attractive to clinicians, increase equity of access to genetic testing and reduce time spent on the ‘diagnostic odyssey’. We anticipate that diagnosis rates for rare genetic overgrowth disorders will improve with national recruitment to POD through paediatric endocrinology clinics and the implementation of an updated panel of 44 overgrowth genes.

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OC5.8
Central hypothyroidism with extrathyroidal features due to a partial X-chromosome deletion involving the TBL1X locus
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Introduction
Isolated congenital central hypothyroidism (CeCH) is a rare entity associated with mutations in IGSF1, TSHB, TRH or the coding region of TBL1X. We describe a female with CeCH and extrathyroidal features due to a partial X-chromosomal deletion involving TBL1X and other genes. Further studies showed markedly reduced TBL1X expression in patient-derived leukocytes and enabled linkage of particular clinical phenotypes to specific genes.

Case
A 29 year old female was diagnosed with isolated CeCH at age 13 years with T3 8.3 pmol/l (reference range, RR 9–20), TSH 2.5 mU/l (RR 0.4–4) and normal TSH response to TRH (0 mins: TSH 0.6 mU/l; 20 mins: 10 mU/l). In addition, she exhibited mesomelic short stature (height –4.5 S.D.) and a wide carrying angle, undulant deformity and relative macrocephaly (OCF +4.5 S.D.). Significant developmental delay and a diagnosis of autism had necessitated special schooling.

Results
Allozyme SNP 6.0 array delineated a de novo heterozygous 9.5 Mb deletion of the short arm of the X chromosome from band p22.2, including 16 genes in the pseudoautosomal region (PAR1), which escapes X chromosome inactivation: PLCXD1, GTPBP6, PPF23B, SHOX, CPL2F1, CSF2RA, IGLB, SCL25A6, ASMTL, P2RY8, AKAP7A, ASMT, DHRX, ZBED1, CD99, XG. The following non-PAR genes were encompassed by our patient’s deletion: GYG2, ARSD, ARSE, ARSH, ARSF, MXRA5, PRXR, NLGN4X, VAX3, PDAL, STS, VBX, PNPLA4, VCA2, VAX5, ANOS1, FAM94, FAM96 and the proximal exons of TBL1X. However, X-chromosomal inactivation (XCI) was almost completely skewed (95:5) and significantly decreased TBL1X mRNA levels in patient-derived leukocytes supported preferential inactivation of the normal X chromosome.

Conclusions
This is the first case of CeCH with partial TBL1X deletion and potentially minimal TBL1X expression. Haploinsufficiency of SHOX in the PAR region (Leri-Weil dyschondrosteosis) and deficiency of NLGN4X in the non-PAR region (autism, intellectual disability) explain extrathyroidal phenotypes.

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OC5.9
Adult height in patients with testotoxicosis
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Background
Familial male-limited precocious puberty (FMPP) or ‘testotoxicosis’ is a rare form of gonadotrophin-independent precocious puberty. There is a paucity of data on final adult height in these patients and no consensus on what constitutes appropriate treatment. Our aim was to assess the management and final height of patients with FMPP under our care as well as those reported in the literature.

Methods
Growth data were obtained from notes of four local patients with FMPP. We then undertook a literature search (June 2017) to extract data on reported cases of FMPP where final height data were available using Ovid Medline and PubMed. The keywords ‘testotoxicosis’ or ‘familial male-limited precocious puberty’ or ‘familial male precocious puberty’ or ‘male-limited gonadotropin-independent precocious puberty’ were used. Treatment and height data were extracted from published cases and UK 90 population data used to calculate s.d. scores.

Results
Final height data were available on 25 men with FMPP of whom 21 were treated with agents that impair steroidogenesis (ketoconazole; n = 12), anti-androgens (cyproterone, spironolactone, medroxyprogesterone, flutamide; n = 11), aromatase inhibitors (AI-Letrozole, Anastrozole, Testolactone; n = 4), GnRH analogues (n = 6) and growth hormone (n = 2). The final height SDS of patients ranged from –3.8 to +1.52 with a median of –1.5 S.D., which was not significantly different to the mid-parental target of –0.6 S.D. (P = 0.11). Seven patients (28%) were short with a height more than 2 S.D. below the mean, all receiving anti-androgen ± ketoconazole. Eight patients (32%) had a final height above the mid-parental target, three of whom received an AI. The median height s.d. of the four untreated patients was –0.03 and of the four receiving an AI was +0.5 s.d. All eight of these patients had a height within normal limits.

Conclusions
Treatment with a third generation aromatase inhibitor is associated with a positive height outcome but untreated FMPP is not always associated with a height below parental target. The impact of the various interventions is complicated by ‘polypharmacy’, variation in treatment duration and a likely difference in underlying clinical phenotype. Clinicians need to be cautious when counselling families about the potential impact of medication on final adult height.

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OC6.1
Freestyle flash glucose monitoring and structured education improve HbA1c and quality of life in children with Type 1 diabetes mellitus
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Background
The Freestyle Flash glucose monitoring (Flash GM) is a new technology suitable for children and adolescents with Type 1 Diabetes Mellitus (T1DM). Clinical accuracy, safety and user acceptability of the Flash GM has been demonstrated in a recent study. In 2017 the UK Association of children’s diabetes clinicians (ACDC) launched national guidelines for training healthcare professionals in delivering Flash GM to children with T1DM.

Objective
To evaluate patient glycaemic control and quality of life (QoL) scores following the use of the Flash GM with provision of education and support on the use of the Flash GM.

Methods
Fifty-three children with T1DM were started on Freestyle Flash GM for a minimum of 3 months. Patients and parents were provided with key education and support on the use of the Flash GM using the ADCD guidelines prior to starting the Flash GM and on fortnightly bases. The Peds QL 3.2 diabetes questionnaire was used to assess the QoL scores of patients and parents before and after the use of the Flash GM.

Results
Fifty-three children (34 boys and 19 girls) with a mean age at diagnosis of 7.8 years and a mean diabetes duration of 4.4 years were evaluated. The mean HbA1c 3 months after starting the Flash GM showed significant improvement when compared with mean HbA1c values at 12.6 and 3 months before starting the Flash GM (HbA1c 59.17 mmol/mol vs 62.23 mmol/mol, P value 0.009; 59.29 mmol/mol vs 62.14 mmol/mol, P value 0.009; 58.72 mmol/mol vs 65.34 mmol/mol P value 0.009 respectively). The Peds QL 3.2 scores demonstrated significant improvement in patients QoL following the use of Flash GM (P value 0.01).

Conclusion
Our findings provide promising support for the use of the Flash GM in children with T1DM. Flash GM technology associated with appropriate Flash GM education at the initiation of the technology and regular support from healthcare professionals improves overall glycaemic control and QoL in children with T1DM.

DOI: 10.1530/endoabs.51.OC6.1

OC6.2
School holidays: are they also a holiday from diabetes control?
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Introduction
To maintain an average HbA1c of less than 48 mmol/mol requires good diabetes control throughout the year. School holidays take on average 13 weeks (25%) of the year in the UK, therefore good control in holidays as well as term-time is
paramount. Little work has been done in this area but it has been suggested diabetes control may be worse during holidays. This study aimed to retrospectively compare diabetes control between term time and the school holidays.

Methodology
All school aged children with type 1 diabetes, being managed by our centre and attending school within the Sheffield catchment area were entered into the study. Demographic data from the hospital records was recorded. DIASEND download data routinely obtained at each clinic appointment was reviewed for the duration of the summer and Christmas holidays during the 2015–2016 school year. DIASEND data for the same period after each holiday was also collected.

Results
One hundred and twenty children (median age 11 years, 43% pump users) had data available for analysis. Daily mean blood glucose was significantly higher for both the Christmas and summer holidays (10.6 and 11.0 mmol/l respectively) compared to the term-time (10.1 and 10.1 mmol/l P<0.01). During the Christmas holiday children did fewer blood tests per day (5.4 vs 5.9, P<0.01), with more readings above target (53% vs 47% P<0.01). During the summer holidays children did a similar number of tests to the term time (5.3 vs 5.4 P=0.5) but still had significantly more results above the target range (50% vs 46% P<0.01). Those using insulin pumps had no difference in the average daily insulin used or the number of boluses given between term-time and either holiday.

Conclusion
Diabetes control in children and young people with type one diabetes appears to worsen during the school holidays. A 0.5 mmol/l difference in mean blood glucose equates to approximately a 4 mmol/mol difference in HbA1c. This highlights the need for education to equip patients and their families to adjust insulin regimes for changes in routine.

DOI: 10.1530/endoabs.51.OC6.2

OC6.3
Bite size educational programme in clinic
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Introduction
Ongoing structured education for children and young people with type 1 diabetes and their families is considered essential by ISPAD (2014) and NICE (2015), because there is a lot of education and skills that need to be reinforced.

In 2016 the majority of the self-management education was provided at our trust by diabetes self-management education (DSME) sessions, which are two hour sessions designed to improve self-management. This format of education is comprehensive in nature, however, only 6% of the 350 families attended in 2016. Patient feedback consistently reported attending extra hospital appointments as a major barrier.

It was agreed by the team in late 2016 to try a complementary educational approach with the aim of reaching a larger number of families. The suggested complementary approach is a bite size 5-10 minute education session delivered during clinic waiting time, covering a different topic every 3 months. The intended design is to allow self-assessment of knowledge, identify gaps, and finally to fill the gaps with interactive education.

Method
From January 2017 to March 2017 in the adolescent clinic, the first bite size topic was piloted. The session aim was to improve knowledge regarding Hba1c, including what is the Hba1c test measuring and the importance of using average blood glucose to predict HbA1c, and 55% felt confident they would check average blood glucose in the next 2 weeks.

Conclusion
This audit has ascertained in clinic bite size education reached over two thirds of the cohort, which was a massive improvement on 6% achieved by DSME in 2016. Also diabetes knowledge can be improved in ten minutes of interactive education. Further validation of this approach for the whole cohort is our next step.

DOI: 10.1530/endoabs.51.OC6.3

OC7.1
JUMP: Maternal family history of diabetes and non-white ethnicity adversely affects beta cell response in young people with Type 2 Diabetes
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Background
Type 2 diabetes (T2D) in children and adults continues to rise. The relative contribution of pancreatic beta cell failure is not established. We aimed to analyse beta cell function in a subgroup of the UK T2D (JUMP) cohort.

Methods
Participants were recruited at 58 hospital centres across England and Wales (n=204). Patients were 5–18 years, diagnosed with T2D (ADA criteria) and a BMI SDS> +1.0. At baseline, demographics, clinical and medical history, biochemistry and anthropometric data were collected (n = 168). A subgroup of the cohort underwent standard short OGTT (n=39) with glucose, C-peptide and insulin levels taken at 0 and 30 minutes for calculation of HOMA-IR, HOMA-%S, HOMA-%B, Insulinogenic Index (IGI) and Disposition index (DI) using the Web-based HOMA calculator (https://www.dtu.ox.ac.uk/homacalculator). Modelling was applied to the linear regression analyses adjusting for demographics, growth or disease status.

Results
Previously baseline demographics of the JUMP cohort have been reported (BSPED 2015). There is a predominance of females (73.8%), mean age at diagnosis of 13.2 years and mean BMI SDS +2.85. The majority of CYP were non-white (57.8%). Subgroup analysis of the short OGTT data showed no significant difference versus the overall cohort (White population 60%, age at diagnosis 12.9 years, BMI SDS at diagnosis +2.9). Family history (most significantly in diabetics in mothers versus fathers, P<0.05) was strongly associated with reduced DI. This was consistent also with IGI and HOMA-%S.

Conclusions
The JUMP cohort represents a UK national prospective cohort study of CYP with Type 2 Diabetes. Non-white ethnicity, longer duration of disease have been reported in association with reduced DI (and inadequate beta cell compensation in response to reduced insulin sensitivity). Our novel finding is that a maternal FH of diabetes significantly increases the risk of a low DI. Further follow-up will establish whether this is a risk factor for earlier development of complications.

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OC7.2
Use of human pluripotent stem cells to model monogenic diabetes
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Heterozygous mutations in the transcription factor, hepatocyte nuclear factor 1 beta (HNF1B), result in multisystem disease including diabetes due to beta-cell dysfunction and pancreatic hypoplasia. However, the mechanisms that underlie development of diabetes in HNF1B mutation carriers are still not fully understood due to lack of an appropriate animal model system. Human pluripotent stem cells (PSCs), which are capable of self-renewal and can differentiate into any cell type, are ideally suited to model human developmental diseases. The aim of this project was to develop a human PSC based model system to determine the molecular mechanisms by which HNF1B mutations cause pancreatic hypoplasia and diabetes.

HNF1B mutant PSC lines were produced using CRISPR-Cas9 genome editing. Isogenic HNF1B wild-type and homozygous and heterozygous mutant cell lines were then directed to differentiate along the pancreatic lineage. Cells were phenotyped at each stage to check for expression of pancreatic markers using immunohistochemistry, flow cytometry and qPCR. The normal expression pattern of HNF1B in human pancreas development was analysed and showed
upregulation of HNF1B at the foregut stage, and during pancreas specification. Homozygous knockout of HNF1B resulted in failure of foregut and pancreatic progenitor development, while heterozygous knockout of HNF1B resulted in impaired insulin secretion upon glucose stimulation. RNA-sequencing analysis identified that the majority of top downregulated transcription factors and pathways in mutant compared with wild-type cells at the pancreatic progenitor stage, were those associated with pancreatic development. Cell proliferation assays showed a significant decrease in the proliferation rate in HNF1B heterozygous and homozygous mutant cells compared with wild-type cells at the foregut stage, however, there was no change in the apoptosis rate.

HNF1B haploinsufficiency may therefore impair the expansion and maintenance of pancreatic progenitor cells in vivo during human pancreas development, resulting in reduced beta cell numbers at birth and diabetes later in life. This in vitro model provides further insights into the molecular mechanisms by which HNF1B regulates human pancreas development and function, as well as potentially identifying new genes and pathways that contribute to diabetes pathogenesis and providing novel therapeutic targets.

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**OC7.4**

Effect of a reduced fluid replacement regimen on resolution of diabetic ketoacidosis in children: comparison of BSPED 2015 and 2009 guidelines

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Background

A substantially reduced fluid replacement regimen was introduced in the ‘New’ BSPED (2015) compared to ‘Old’ BSPED (2009) guideline for DKA management in children. However, effects of varying fluid replacement regimens are limited and we explored this by comparing outcomes of the two guidelines on the resolution of DKA.

Methods

In a retrospective audit of consecutively admitted patients (age < 18 years) to two hospitals in Barts NHS trust with DKA between Jan-2014 and March-2017, we evaluated the resolution time of DKA defined by recovery of acidosis (pH > 7.30), ketosis (blood ketones < 1.0 mmol/l) or bicarbonate (> 18.0 mmol/l) levels. Biochemical parameters before, the nearest to 6 and 12 hours into treatment and at resolution were collected. Effective osmolality was calculated using formula: (2xSodium) + glucose. 

Results

Of 82 patients admitted data were available for 44 (transferred (n = 12), data unavailable (n = 26)). Twenty and 24 patients were managed by the ‘New’ and ‘Old’ guidelines respectively. The median age was 10.1 years (interquartile range, 6.4-15.1), 28 patients (63.6%) were newly-diagnosed and 15 (34.1%) had severe DKA (pH < 7.1). Age, DKA severity and proportion of newly-diagnosed patients were similar in both groups. The fluid administration rates were substantially lower (24.0(24.0-39.1) vs 55.0(45.0-69.0)ml/hour, P < 0.001), in the ‘New’ guideline, but frequency of fluid boluses was similar (40% vs 50%, P = 0.44). The resolution of DKA evaluated by pH (‘New’ vs ‘Old’), 14.8(7.9-19.2) vs 15.7(7.8-24.7) hours, P = 0.72) or ketosis (21.2(12.3-29.8) vs 20.3(12.5-35.6) hours, P = 0.59) or bicarbonate levels (15.8(10.4-27.8) vs 20.7(11.9-25.6) hours, P = 0.63) were similar. The levels of sodium, potassium, chloride and bicarbonate, pH and effective serum osmolality before, at 6 and 12 hours and resolution, and hypoglycaemia rates were similar. However, the time to decline of glucose levels to 14 mmol/l tended to be lower (4.28(3.41-6.83) vs 6.15(4.29-10.17) hours, P = 0.11) and was significantly lower (3.86(3.25-5.43) vs 5.48(5.0-9.75), P = 0.018) in mild DKA in the ‘New’ guideline. No patients developed cerebral oedema.

Conclusions

We found that ~ 50% reduction in fluid replacement in DKA was not associated with significant changes in resolution time, electrolyte levels or osmolality. However, hyperglycaemia was corrected faster in the ‘New’ guideline. Larger studies are important to evaluate the effects on cerebral oedema.

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**OC7.7**

Level of WFS1 protein expression correlates with clinical progression of optic atrophy in Wolfram syndrome patients

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Introduction

Wolfram Syndrome (DIDMOAD) is an autosomal recessive disease caused by mutations in WFS1 gene, resulting in childhood onset diabetes mellitus and optic atrophy. There have been limited functional assays for WFS1 genetic variants. 'partial WFS1 expression' were either asymptomatic, colour blind or impaired insulin requirement between groups.

Results

There was no statistically significant difference in the glycated haemoglobin or osmolality and hypoglycaemia rates were similar. However, hyperglycaemia was corrected faster in the ‘New’ guideline. Larger studies are important to evaluate the effects on cerebral oedema.

Conclusions

We found that ~ 50% reduction in fluid replacement in DKA was not associated with significant changes in resolution time, electrolyte levels or osmolality. However, hyperglycaemia was corrected faster in the ‘New’ guideline. Larger studies are important to evaluate the effects on cerebral oedema.

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**OC7.5**

Service satisfaction, mental wellbeing and clinical progression in young people with diabetes in transition from child to adult services

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Introduction

Transition from child to adult healthcare is a period of vulnerability for young people with diabetes. We hypothesised that patient satisfaction with services and patient wellbeing would be positively associated with a satisfactory clinical progression.

Methods

We included data from 150 young people recruited in 2012 to a longitudinal study of transition (http://research.ncl.ac.uk/transition). Young people’s satisfaction with services (‘Mind the Gap’) and patient mental wellbeing (Warwick and Edinburgh Mental Well being instrument or WEMWBS) were assessed at baseline and annually for 3 years in 5 diabetes units in England; 108/150 (72%) remained in the study to the final visit. Following collaborator discussion and literature review, a composite measure of satisfactory clinical outcome was constructed according to change in HbA1c (<= 7% increase in HbA1c from baseline), episodes of diabetic ketoacidosis (none), attendance at clinic (> 75%) and attendance at annual retinal screening appointments (100%).
The median age of young people at study entry was 16.0 years (IQR 1.27). The HbA1c at baseline was comparable to the National Paediatric Diabetes audit 2011/12. Young people’s HbA1c increased from a median of 69 mmol/l, year 1, to 75 mmol/l, year 4. The WEMWBS score was comparable to study populations at study entry and was stable over the study duration. The Mind the Gap score was also stable throughout. By study end, 32 individuals had satisfactory clinical outcome and 76 a suboptimal outcome. The two groups were comparable in terms of age, duration of diabetes, and baseline HbA1c. There were no differences in median satisfaction with services and WEMWBS scores in either group.

Conclusion

Mental well-being in young people with diabetes is similar to the population as a whole and did not change during transition. Two thirds of the study population had a sub-optimal clinical progression after transition which was not related to wellbeing or satisfaction scores.

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OC7.6

Single-centre experience of bariatric surgery in adolescents with significant obesity

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Childhood obesity is a serious public health challenge. Bariatric surgery is gaining popularity as a treatment modality for severely obese adolescents. Backgrounds

To report the safety and 1 year outcome data on morbidly obese adolescents that underwent bariatric surgery at a tertiary hospital in the UK.

Methods

A retrospective review of patients (mean preoperative BMI 50.4 kg/m²; mean BMI SDS +4.2) who underwent bariatric surgery from 2011 to 2017 was performed. Comorbidities included hypertension, insulin resistance, obstructive sleep apnoea, limited mobility and psychosocial issues. Weight loss as measured by percent excess weight loss (%EWL) at 1 year post-operatively, resolution of hypertension post-operatively. Mean HOMA improved from 7.4 to 3.0 at 12 months.

Results

Bariatric surgery (three gastric bands and fifteen sleeve gastrectomies) was performed in eighteen patients (M=5, F=13). Mean percentage weight loss, as a percentage of total body weight at 6 (n=17) and 12 (n=13) months, was 21.0 and 24.5%, respectively. Mean BMI at 12 months post-procedure was 36.5 kg/m² - a mean fall of 14.3 kg/m² (median 14.5). Mean BMI SDS fell from +4.2 to +3.5 at 6 month and +3.0 at 12 months.

There were no post-operative surgical complications. Resolution of diabetes occurred in the single patient diagnosed with T2DM (HbA1c dropped from 8.9 to 5.2% at the end of year). All five patients diagnosed with hypertension had resolution of hypertension post-operatively. Mean HOMA improved from 7.4 to 2.4 at the end of year (n=6). Mean vitamin D levels pre-operatively were low at 29.2 nmol/l and improved at 6 months to 50.8 nmol/l (n=6) with supplementation. Two patients developed anaemia 1 year post-operatively associated with significant weight loss.

Conclusions

Bariatric surgery is effective and safe treatment modality of severely obese adolescents in the short term. Further studies are required to investigate the long-term effects of bariatric surgery in adolescents. Follow-up into adulthood is recommended.

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OC7.7

Role of Degludec in improving diabetes outcomes in young people - An observational study from Young Diabetes Connections (YDC) Network, London

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Introduction

YDC is a partnership of four hospital trusts: Kings College Hospital, Princess Royal University Hospital, Lewisham University Hospital and Evelina London Children’s Hospital, caring for a total of 492 children and young people with diabetes. Most young people are on conventional long acting insulin (Levemir and Glargine), but increasingly, poorly controlled patients (HbA1C > 100 mmol/mol) with high admission rates are being switched to insulin Degludec due to prolonged duration of action and improved injection experience.

Objective

To assess the impact of conversion to Degludec on HbA1C, A&E and inpatient admissions with Diabetic Ketoacidosis (DKA), and clinic absences in young people with diabetes.

Methods and design

A retrospective observational study was done across four sites from October 2014 to April 2017 on the advice of the joint formulary committee who approved Degludec for paediatric use. Data was collected from case notes and clinic letters. Demographic variables, monthly data on A&E admissions, DKA admissions, and Clinic DNAs (Did Not Attend)/rescheduling in the year pre-and post-starting Degludec and HbA1C at 3.6 and 12 months were collected.

Results

Forty-eight patients (46-Type1,2-Type 2, M:F=25:23, mean age 15.3years (range 11–19) with poor control (mean HbA1C 105 mmol/mol) were included. Follow up on Degludec ranged from under 3 months to 2years. There was a statistically significant drop in monthly inpatient admissions with DKA (n =48, mean 0.06 pre and 0.03 post Degludec, P=0.027) after Degludec was started. There was a marginal decrease in monthly A&E admissions which was statistically non-significant. Mean HbA1C dropped from the start (n =48, mean 105 mmol/mol) to 3 months (n =25 mean 104.58 mmol/mol) and 1 year (n=15 mean 101 mmol/mol) after starting Degludec, with a mean of 107 mmol/mol (n=32) at 6 months. This was statistically not significant. There was no drop in monthly clinic DNAs.

Conclusions

The results show a significant drop in DKA admissions and a drop in HbA1C at 3 months and 1 year. It would be important to verify these changes with bigger numbers such as using data from across our South East Coast and London Diabetes Network.

DO: 10.1530/endoabs.51.OC7.7

OC7.8

Out of hours telephone advice service improves emergency department attendances for diabetes related complications

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Introduction

We sought to the impact of an out of hours telephone advice service for children and young people with diabetes mellitus on Emergency Department attendance rates.

Methods

In July 2014 we commenced a collaborative service for 240 patients with diabetes across two Paediatric diabetes centres- Croydon University Hospital (CUH) and St George’s University Hospital, London. Paediatric diabetes specialist nurses and consultants in Paediatric diabetes joined a shared rota. All patients, their families and hospital staff were given a single point of contact telephone number for their local Paediatric diabetes service. Outside of normal working hours (Monday–Friday, 9 am–5 pm) this phone number is diverted to the mobile phone of the member of staff on call. Each staff member is on call 1 week at a time and commits to giving immediate advice or returning a call within one hour. Data on ED attendance rates was only available for one centre (CUH).
Results
No adverse clinical incidents have been recorded in association with the service since it started. The mean number of Emergency department attendances at CUH for diabetes related complications (DKA, hypoglycaemia, unstable diabetes or intercurrent illness) between 2007 and 2013 was 43. This dropped in each of the 3 years since commencing the telephone advice service to only 14 attendances in 2016.

Conclusions
We conclude that the out of hours telephone advice service is clinically safe and reduces the burden on Emergency Department attendances.

DOI: 10.1530/endoabs.51.OC7.8

OC8.1
Hydrocortisone tablets: human factors in manipulation and their impact on dosing accuracy
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Introduction
Exposure to deficient/excess glucocorticoids can lead to long-term health problems in patients with adrenal insufficiency. An age-appropriate low dose hydrocortisone formulation is not available therefore manipulation a 10 mg tablet is required with potential for inaccurate dosing.

Aims
To assess the variability in manipulation procedures recommended by healthcare professionals and undertaken by parents/carers. To quantify the dose-variability in the manipulated product based on the method of preparation.

Methods
Parents (HC/UC1) of children with adrenal insufficiency from across the UK completed a survey assessing the methods used to manipulate hydrocortisone 10 mg tablets. Naïve participants undertook manipulation of a 10 mg tablet (Auden-Mackenzie vs Amapharm brand) to make a 2.5 mg dose either by quartering the tablet or by crushing, dispersing in 10 ml and withdrawing 2.5 ml. Drug content was analysed.

Results
One hundred and twenty five parents completed the questionnaire. 25.6% of parents did not or do not remember receiving training on preparing hydrocortisone tablets. Variability in dosing was observed based on both brand and method of manipulation.

Conclusion
This is the first study that compares the methods used by parents/carers to the advice provided by healthcare practitioners.

Table 1
Methods of hydrocortisone administration recommended by paediatric endocrine doctors and nurses

<table>
<thead>
<tr>
<th>Method of hydrocortisone administration</th>
<th>Patient age range 5–15 months</th>
<th>Patient age range 1–4 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole tablet (10 mg)</td>
<td>Nurse (n = 28)</td>
<td>Doctor (n = 32)</td>
</tr>
<tr>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Whole tablet in water</td>
<td>50</td>
<td>31.1</td>
</tr>
<tr>
<td>Cut tablet</td>
<td>65</td>
<td>40.6</td>
</tr>
<tr>
<td>Crushed tablet</td>
<td>70</td>
<td>40.8</td>
</tr>
</tbody>
</table>

The presence of score-lines on Auden-Mackenzie tablets did not improve the accuracy of quartering tablets compared to a non-scored brand (Amapharm). In a significant proportion of patients the manipulation of tablets is likely to result in inaccurate dosing and to impact on patient morbidity.

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OC8.2
Assessment of adrenal function and recovery of HPA axis in children with chronic asthma assessed by LDST
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Background
Biochemical evidence of adrenal insufficiency (AI) is reported commonly during inhaled corticosteroid (ICS) treatment for asthma. The significance of mildly abnormal results is uncertain. For this reason we adopt a stratified approach to the management of patients with impaired cortisol responses to the low dose short Synacthen test (LDSTT): Patients with peak cortisol 350–499 nmol/l (‘sub-optimal’) receive hydrocortisone 20 mg/m² per day during sick days only, patients with peak cortisol 100 nmol/l or peak cortisol >500 nmol/l are considered normal. Recovery of adrenal function during this treatment regimen has yet to be reported.

Aims
To describe recovery of adrenal function in children with AI treated according to this protocol.

Design
Retrospective observational study.

Methods
The results of LDSTTs, performed between 2008 and 2016 in selected children with asthma, taking high dose ICS or with symptoms of AI, were studied.

Results
Two hundred and thirty eight tests in 113 (74 M) children, age 10.4 (3.3–14.8) years, 2.1 (0.2–7.7) tests/child. Duration of follow up: 2.2 (0.2–7.7) years. Abnormal baseline test: N=17 (12 M), 15%, age 8.6 years (3.3–16.5), ICS dose (beclomethasone equivalent) 800 mcg/day (200–1000). Repeat tests: N=17, normal in 11 (65%), suboptimal in seven (41%), abnormal in four (24%). Suboptimal baseline test: Suboptimal: N=54 (37 M), 48%, age 10.9 years (4.7–15.6), ICS dose 800 mcg/day (200–1000) Repeat tests: N=50 (93%), normal in 36 (72%), suboptimal in 11 (22%), abnormal in three (6%). Normal baseline test: N=92 (25 M), 37%, age 10.4 years (3.8–14.8), ICS dose 500 mcg/day (100–1000) Repeat tests: N=6 (14%), normal in three (50%), suboptimal in two (33%) abnormal in one (17%). Basal and peak cortisol levels increased by >15% (2x inter-assay coefficient of variation) in 33/73 (45%) and 42/73 (57%) subjects respectively, and decreased by >15% in 14/73 (19%) and 7/73 (10%) respectively. A statistically non-significant fall in height SDS (baseline –0.2 (−1.7 to +2.5), follow up –0.7 (−1.9 to +2.9)), of uncertain clinical significance was observed in patients treated with daily hydrocortisone only. BMI SDS did not change in any diagnostic group.

Conclusion
Recovery of adrenal function is common during this treatment regimen.

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Parent reported outcomes in conditions affecting sex development

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Background
There are gaps in our understanding of the impact of conditions that affect sex development, such as DSD and CAH, on the parent and patient.

Aims
The project aimed to explore whether patient reported outcomes (PRO), assessed by standardised questionnaires, could be integrated within routine paediatric endocrine clinic visits.

Methods
Previous validated questionnaires were used to develop a parent Self-Report questionnaire containing eight domains (40 items) for caregivers of children <7 years. Domains were derived from a validated DSD-specific measure and a brief screening measure for adult depression and anxiety. A parallel parent Proxy-Report questionnaire containing eight domains (30 items) and assessing the child’s adaptation was also developed. Each subscale was scored as the raw score and presented as a standard deviation score (SDS) relative to a DSD or healthy population depending on subscale. Parents of 31 children were approached and 24 (12 - conditions affecting sex development, 12 - other endocrine conditions) completed the forms. 27 parents completed the parent Self-Report questionnaire and 15 parents the Proxy-Report.

Results
Both questionnaires were found to be acceptable for routine use in clinic and took less than 10 minutes to complete. On the parent Self-Report scale, the median (range) SDS score for ‘Future Concerns’ was $-0.35$ ($-1.87, 1.04$) and $1.04$ ($-2.00, 1.73$) for mothers of children with conditions affecting sex development compared to other endocrine conditions, respectively ($P=0.02$). ‘Talking to Others’, ‘Stigma’ and ‘Surgery’ also had a lower score in parents of children with a condition affecting sex development but these were not significantly different from the other group. Although both groups of parents had mainly positive SDS on the Proxy-Report, parents of these children tended to score lower than those of children with other endocrine conditions on the majority of the subscales.

Conclusions
Parents of children with conditions affecting sex development reported greater levels of stress, particularly relating to future concerns. These questionnaires can be used as a routine health care evaluation and their use may allow greater targeting of support as well as the development of clinical benchmarks.

DOI: 10.1530/endoabs.51.OC8.3
Poster Presentations
**Thyroid P001**

**Relationship between the level of trace elements and growth in school children group of 6 to 12 ages with goitre**

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The aim of the study was to determine level of trace elements and whether it is related to the growth in children with goitre. The study was performed in children of ages 6-12 years. Goitre staging was performed according to the WHO criteria. A total of 86 cases, 55 with goitre and 31 as control group, were included in the study. When parameters were compared in cases with and without iodine deficiency, TSH and FT3 levels were determined significantly higher in cases with iodine deficiency. TT3, FT4 and TT4 values were in normal ranges and there were no significant differences between the two groups. In cases with iodine deficiency, selenium (Se) level was detected as low, zinc (Zn) level was high but there was no significant difference between manganese (Mn), iron (Fe) and copper (Cu) levels. When parameters were compared in cases with and without goitre, no difference was detected in TT3, TT4 and FT4 values while TSH and FT3 values were significantly higher in cases with goitre. Serum selenium level was detected lower in cases with goitre but no statistically significant differences were detected in the levels of other trace elements between the two groups. It was also observed that height standard deviation score (height SDS) and body weight standard deviation score (weight SDS) of cases with goitre were negatively affected in cases with an advanced stage of goitre. Statistically significant positive correlation was found between height SDS and serum Zn, Se, Cu, Fe and ferritin. Zn was found to be the most influential trace element for height SDS. A negative correlation was found between height SDS, weight SDS and Mn. A positive statistically significant correlation was found between weight SDS and Se, Zn, Fe and Cu levels. Se was observed to be the most influential trace element for weight SDS. Trace elements have an important role for height and weight gain. Importance of nutrition, trace element intake and iodized salt usage should be explained to families.

DOI: 10.1530/endoabs.51.P001

**P002**

**Radioactive Iodine therapy for the management of hyperthyroidism in children and adolescents**

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**Background**

Radioactive iodine therapy (RAI) is established as a safe and effective treatment for adults with Grave’s disease. As thyrotoxicosis in children is rare, it is difficult to obtain high quality evidence about the safety and efficacy of RAI. We present data from our centre between 2007 and 2017.

**Methods**

20 paediatric patients with hyperthyroidism (16F), median age 15.7 years (range 10.8–19.3) had RAI in our centre either one or two doses. Median follow-up for all patients was 1.4 years (0–9 years).

**Results**

All patients received an initial median iodine-131 (1-131) dose of 607 MBq (419–804 MBq). The primary indications were: definitive treatment following antithyroid drug treatment (ATD) (16/20; 80%), intolerance/sensitiveness to ATD (2/20; 10%), poor compliance to ATD (1/20; 5%) and acute psychosis secondary to thyrotoxicosis (1/20; 5%). Following one dose of I-131, 15/20 (75%) patients achieved hypothyroidism in median 7 months (range 1–19 months) following RAI. Two (10%) were lost to follow up data is difficult to obtain due to the rarity of hyperthyroidism in paediatric patients but can be achieved by collaboration between centres. DOI: 10.1530/endoabs.51.P002

**P003**

**Long-term follow-up of Grave’s disease in Adolescents: a 10 year study from a single UK tertiary centre**

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**Introduction**

Anti-thyroid medications are the first line therapy for children and young people with Grave’s disease (GD). Some studies have shown remission rates up to 40-50%; however long-term follow up studies have reported much lower remission rates in children compared to adults.

**Aim**

To review the long-term follow up and management of adolescents with Grave’s disease in a single tertiary centre in the UK.

**Methods**

This is a retrospective study of 37 patients with Grave’s disease who attended the tertiary endocrine outpatient clinic between 2007 and 2017. Patients who were excluded consisted of Hashimoto’s thyrotoxicosis, unclear diagnosis of Grave’s disease and patients with incomplete data on the system.

**Results**

37 patients [M:F, 3:9:1] with Grave’s disease were included with a mean age of 12.16 years (≤ 3.5). In the sample studied, 27 (73%) received ‘block and replace’ therapy (carbamazole and thyroxine) whilst 1 (29%) received carbimazole only (titration regimen). The average duration of treatment for ‘block and replace’ was 30 months (range 3–62). The average duration of treatment for carbimazole only was 21.8 months (range 2–36). Out of the 27 patients who received ‘block and replace’ therapy, 11 patients were still receiving ongoing treatment at the time of data collection. 14 patients had a trial ‘off medication’ and the average duration of remission was 9.4 months (range 0.25–21). Out of the 7 patients who received carbimazole only, 5 of them had a trial ‘off medication’ and the average duration of remission was 10.3 months (range 2–24). In the ‘block and replace’ group, only 1 out of 14 (7.1%) patients achieved remission. For carbimazole only group, one patient (out of 5, 20%) achieved remission.

**Conclusion**

Majority of children tend to relapse after anti-thyroid medications and require definitive treatment in the long term. Larger prospective studies are essential to understand the predictive factors for long term remission which would allow clinicians to develop criteria for medical vs surgery/radioiodine therapy.

DOI: 10.1530/endoabs.51.P003

**P004**

**Double Trouble in a case of iatrogenic induced hyperthyroidism**

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**Background**

Two twin sisters with infantile epilepsy developed biochemical hyperthyroidism after commencement of Topiramate, which resolved post cessation. This case-report describes the events and has found limited evidence in the literature.

**Case presentation**

MCDA twins, 9 months of age, were admitted with seizure activity. Additionally twin 2 had neurocutaneous melanosis and a viral respiratory illness. Medications on admission were: Levetiracetam, Vigabatrin, Pyridoxine, Thiamine and Biotin. Both twins were commenced on Topiramate: 1 mg/kg per day in divided doses to optimize seizure control; no radiation or iodine exposure occurred within this time-period. Two days later thyroid levels were incidentally checked; both were biochemically hyperthyroid; but asymptomatic. Results showed: Twin 1 TSH: 0.11 mIU/l (0.27–4.2), FT4: 50.8 pmol/l (10–23) with FT3: 8 pmol/l (3.1–6.8)
and twin 2 TSH: 0.10 miu/l, FT4: 42 pmol/l with FT3: 6.8 pmol/l. Notably twin 1 was tested a month prior (Pre-Topiramate) and had raised TSH levels (8.94 miu/l), with normal FT4 (18.7 pmol/l); twin 2 had a normal TSH (1.94 miu/l) checked 3 days prior to commencing Topiramate.

Outcome

Following this, Topiramate was stopped and alternative medication started. One week post cessation, thyroid function had normalised. Twin 1 TSH: 0.71 miu/l, FT4: 13.2 pmol/l and twin 2 TSH: 3.8 miu/l and FT4: 12.3 pmol/l. It was considered unethical to re-challenge them with Topiramate.

Discussion

No peer-reviewed reports and one case report about hyperthyroidism secondary to Topiramate were found. Topiramate causes weight loss, although purported mechanism(s) aren’t fully known. Equally, there are numerous patients on Topiramate who haven’t developed deranged thyroid function. Further consideration is needed to elucidate the underlying cause; be it: drug interaction, metabolism related or other. Biotin is known to cause assay interference resulting in elevated FT4 and suppressed TSH. Although as both Twins were on Biotin throughout, including post cessation of Topiramate and normalisation of thyroid function, it doesn’t appear to be the underlying cause here.

Learning Points

Low threshold to check thyroid function tests post starting Topiramate, even when patients are asymptomatic and awareness of possible drug/assay interactions resulting in thyroid dysfunction.

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P005

Follicular thyroid carcinoma due to a heterozygous gain of function mutation in thyrotropin receptor (TSHR)

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Introduction

Activating mutations in thyrotropin receptor (TSHR) have been previously described in the context of non-autoimmune hyperthyroidism (familial or sporadic) and thyroid adenomas. We describe, for the first time, a mutation in TSHR contributing to follicular thyroid carcinoma (FTC) in an adolescent girl.

Case

A 12-year-old girl presented with a right-sided neck swelling, increasing in size over the previous four weeks. Clinical examination revealed a firm, non-tender right sided thyroid nodule with no features of hypo or hyperthyroidism. An ultrasound scan of the thyroid showed a well circumscribed heterogeneous highly vascular mass, measuring 21×17×17 mm, arising from the right lobe. Thyroid function tests showed a suppressed TSH (<0.03 mIU/l), normal FT4 [10.1 pmol/l, normal range 9–11] and raised FT3 [9.1 pmol/l, 3.6–6.4]. TPO and TRAB antibodies were negative. A right hemithyroidectomy was performed and the histology of the sample revealed follicular carcinoma with mild to moderate nuclear pleomorphism and evidence of both capsular and vascular invasion (pT1b). A total thyroidectomy was subsequently performed with no histological evidence of residual carcinoma. Sanger sequencing of DNA extracted from the solid tumour tissue revealed a missense somatic mutation (c.1703T>C, p.Ile568Thr) in TSHR. Levothyroxine was commenced post-operatively with normalisation of the thyroid function [TSH 1.7, FT4 9.9 pmol/l]. Corrected calcium [2.38–2.48 mmol/l, normal range 2.15–2.74 mmol/l] and PTH [5.9 pmol/l, normal range 1.16–6.9 pmol/l] were stable during the post-operative period.

Conclusion

Papillary thyroid carcinomas constitute the most common thyroid malignancy in childhood while FTC is exceedingly rare. Follicular carcinoma due to TSHR mutation suggests an underlying, yet to be explored, molecular pathway leading to the development of malignancy. The case is also unique in that the clinic presentation of FTC as a toxic thyroid nodule has not been previously reported in children.

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Bone

P007

Early hypocalcaemia in neonates associated with vitamin D deficiency

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Neonatal hypocalcaemia (NH) is a well described phenomena with values of 2–2.25 mmol/l seen at 24 h of age after the cessation of transfer of transplancental calcium. Levels then increase to normal by 2 weeks of life. Calcium levels below 2.0 mmol/l in infants > 1.5 kg is considered to be pathological hypocalcaemia. The role of vitamin D in NH is unclear and not well studied in both neonate and mother.

Aim

To present the features of neonates with hypocalcaemia focussing on their vitamin D concentration along with maternal levels in a large district general hospital.

Method

A retrospective study of all admissions (notes and investigations) to Whiston Hospital neonatal unit over a 6 month period September 2016–February 2017, to identify neonates with hypocalcaemia (Adjusted calcium <2.0 mmol/l), their vitamin D levels and risk factors for NH.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gestation (weeks)</th>
<th>Weight (kg)</th>
<th>Calcium (mmol/l)</th>
<th>Phos- phate (mmol/l)</th>
<th>Magnesium (mmol/l)</th>
<th>ALP (IU/L)</th>
<th>Vitamin D (nmol/l)</th>
<th>PTH (pmol/l)</th>
<th>Maternal Calcium (mmol/l)</th>
<th>Maternal Vitamin D (nmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>2.14</td>
<td>1.66</td>
<td>2.03</td>
<td>1.69</td>
<td>305</td>
<td>24</td>
<td>19.2</td>
<td>2.25</td>
<td>15</td>
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<tr>
<td>2</td>
<td>35</td>
<td>2.28</td>
<td>1.64</td>
<td>2.06</td>
<td>1.78</td>
<td>254</td>
<td>29</td>
<td>2.45</td>
<td>n.a.</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>35</td>
<td>2.28</td>
<td>1.64</td>
<td>2.06</td>
<td>2.55</td>
<td>246</td>
<td>24</td>
<td>17.2</td>
<td>2.31</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>32</td>
<td>1.75</td>
<td>1.75</td>
<td>n.a.</td>
<td>n.a.</td>
<td>224</td>
<td>27</td>
<td>2.5</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>35</td>
<td>2.06</td>
<td>1.99</td>
<td>2.13</td>
<td>1.69</td>
<td>307</td>
<td>29</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

n.a., not available.
Results
Five patients were identified. All were born prematurely but in the third trimester. All neonates were deficient in vitamin D (<30 nmol/l) with one infant severely deficient (<20 nmol/l). Three of the mothers were severely deficient. No neonates had associated hypomagnesemia.PTH was appropriately elevated. None of the mothers had gestational diabetes and there was no history of birth asphyxia.

Conclusion
In this short case series of premature babies, low neonatal vitamin D appears to be associated with NH with no other risk factors present. There was also associated maternal Vitamin D deficiency, which could have resulted in low neonatal calcium and vitamin D.

DOI: 10.1530/endoabs.51.P007

P008
Antenatal diagnosis in osteogenesis imperfecta needs more than a genotyping
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Osteogenesis imperfecta (OI) is a disorder that affects bone material properties, mass and architecture, with resultant bone fragility. Most (85–90%) affected individuals have a mutation in one of the two genes encoding type I collagen (COL1A1/2), although mutations in 16 other genes have been identified that result in congenital bone fragility. Mother A presented in her sixth pregnancy, after having four previous first trimester miscarriages and one own infant. Early antenatal scans showed bowed lower limb bones and poor growth. Amniotic fluid cells showed a COL1A1 defect, reported by the NE Thames Regional Genetics Laboratory as consistent with severe or lethal OI. The baby was deemed to be too severely affected to be entered into an impending fetal mesenchymal stem cell transplant study (BOOSTH4). Parents were offered, and refused, termination. At 34 weeks the ultrasound showed a very small fetus with mild bowing of the lower limbs. Because of the risk attributable to severe growth retardation, the decision to deliver electively at 37 weeks was made. Baby A was born in good condition weighing 1.23 kg and requiring no resuscitation. Expressed breast milk (EBM) feeds started straight away. Newborn and infant physical exam showed diastasis of the skull sutures, bowed lower limb but not upper limb segments, and bilaterally undescended testes. Baby A plotted below 0.4th centile in weight and head circumference. Multidisciplinary team approach was taken, including physiotherapists, speech and language, dietician, neonatologists, metabolic bone physiologists, and the baby is growing very slowly, tracking away from 0.4th centile and has had one bronchiolitis episode at day 40. This case highlights important issues in the approach to genetic diagnosis and antenatal interventions. Specifically, genetic testing does not give the full picture in OI and experience is required to provide an accurate interpretation. In addition, clear definition of the pre-treatment state of the fetus is needed to provide assurance regarding the effect of any antenatal intervention.

DOI: 10.1530/endoabs.51.P008

P009
A cause of severe hypercalcaemia: overdose or hypersensitivity to vitamin D?
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Background
Hypercalcaemia is caused by many different conditions. Vitamin D intoxication with severe hypercalcaemia is rare in the neonatal and infancy period. Here we described a 4-month-old male with severe hypercalcaemia secondary to taking oral 600/000 units of vitamin D. He was diagnosed vitamin D 24-hydroxylase gene (CYP24A1) mutation after evaluation.

Case presentation
He was admitted to our hospital with high serum calcium level (23 mg/dl). Serum vitamin D level was >250 ng/ml, parathyroid hormone level was 1.7 pg/ml. The treatment consisted of intravenous rehydration with treatment of hypercalcaemia (diuretics and corticosteroids) at the beginning. Because serum calcium level decreased slowly, pamidronate treatment was added. Serum calcium returned to the normal range within 12 days, with weight gain progressively over the following weeks. Abdominal ultrasound objectified renal nephrocalcinosis.

Conclusion
Mutations in the CYP24A1 gene cause reduced serum 24,25(OH) 2 D 3 to 25(OH)D 3 ratio, elevated serum 1,25 dihydroxyvitamin D (1,25(OH)2 D 3), hypercalcaemia, hypercalciuria and nephrocalcinosis. This case might accepted vitamin D intoxication because of high vitamin D intake. But severe hypercalcaemia should be remarkable for CYP24A1 gene mutation.

DOI: 10.1530/endoabs.51.P009

Adrenal
P010
An unusual presentation of congenital lipoid adrenal hyperplasia and novel STAR mutation in two siblings
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1University Hospital Southampton, Southampton, UK; 2Salisbury NHS Foundation Trust, Salisbury, UK; 3Queen Mary University of London, London, UK; 4University College London, London, UK.

Introduction
Congenital lipoid adrenal hyperplasia (CLAH) is rare and caused by mutations in the steroidogenic acute regulatory (STAR) gene, which is involved in a key step in the synthesis of pregnenolone from cholesterol. Cases typically present in the first days of life with severe adrenal crisis, salt wasting and severely disrupted androgen secretion which may result in sex reversal in 46, XY individuals.

Case report
We present a 21-month-old female and her younger brother. She first presented to her local hospital with tonsillitis, initial blood sugar was 1.6 mmol/l, serum sodium 126 mmol/l and a random cortisol of 69 nmol/l (full biochemistry at presentation is described in table below). She was born at term and was otherwise well apart from two previous admissions with tonsillitis and hypoglycaemia. The younger sibling presented at 22 months of age with increased skin pigmentation. Genetic testing revealed no mutations in NR0B1 (DAX1), MC2R or MRAP genes, initial genetics for other causes of isolated adrenal insufficiency were negative. Later re-testing showed the siblings to have compound heterozygous STAR mutations p.G221S and p.G201D, the former previously reported and the latter a novel mutation.

<table>
<thead>
<tr>
<th>Sibling 1</th>
<th>Sibling 2</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation</td>
<td>22 months</td>
<td>21 months</td>
</tr>
<tr>
<td>Karyotype/Phenotype</td>
<td>XX - female</td>
<td>XY - male</td>
</tr>
<tr>
<td>Na+ at presentation</td>
<td>126</td>
<td>135</td>
</tr>
<tr>
<td>K+ at presentation</td>
<td>4.2</td>
<td>5.8</td>
</tr>
<tr>
<td>Glucose</td>
<td>2.0</td>
<td>3.8</td>
</tr>
<tr>
<td>ACTH</td>
<td>5246</td>
<td>1715</td>
</tr>
<tr>
<td>Synacthen test (cortisol in nmol/l)</td>
<td>56-57-55</td>
<td>295-323-311</td>
</tr>
<tr>
<td>Renin</td>
<td>250.2</td>
<td>&gt; 1728</td>
</tr>
<tr>
<td>Aldosterone</td>
<td>54</td>
<td>104</td>
</tr>
<tr>
<td>17-OHP</td>
<td>&lt; 1 nmol/l</td>
<td>&lt; 1 nmol/l</td>
</tr>
<tr>
<td>Very long chain fatty acids</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>7-Dehydrocholesterol</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Conclusions
A diagnosis of CLAH should be considered even in children presenting with primary adrenal insufficiency (PAI) presenting outside the neonatal period. When the aetiology of PAI is uncertain in an index case, prompt investigation of siblings for evidence of evolving PAI should be considered. Our cases highlight a novel STAR mutation, p.G201D, and the advantage of newer sequencing methods that permit concomitant sequencing of more than one gene.

DOI: 10.1530/endoabs.51.P010
A case report of functioning adrenal cortical tumor in a female child
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Androgen-producing tumours of the adrenal are extremely rare. The androgen effects and malignancy potential can be detrimental in children. Adrenal adenomas are usually small, whereas carcinomas are larger and aggressive. We present the challenges in managing a female toddler with a large androgen secreting adrenal adenoma. A 22 month old 46,XX girl presented with features of hyperandrogenism but not of glucocorticoid or mineralocorticoid excess: tall stature, facial and pubic hair, clitoromegaly, deepening of voice, muscular appearance and major behavioural changes from age 9 months. At presentation, her height and weight were 94.5 cm (at 97th centile) and 18.25 kg (above 90th centile) respectively. Initial androgens levels were: DHEA-Sulphate 22.8 μmol/L, Androstenedione > 50.0 nmol/L, Testosterone 23.4 nmol/L, Free Androgen Index 48.8. 8am renin and cortisol were normal, and ACTH undetectable. Tumour markers (Carcinembryonic Antigen, Beta-HCG, Alpha fetoprotein) were negative. Bone age was advanced between 3 and 4 years. Ultrasound abdomen revealed a well-defined round mass in the right adrenal. MRI revealed a large solid mass 4.6 × 3.6 (axial)/4.4 cm (CC) with no cystic, necrotic, or haemorrhagic component. There was no tumour rupture, invasion into the kidney, liver or adjacent vessels. She underwent right adrenalectomy. Complete macroscopic clearance was achieved despite the tumour being friable and haemorrhagic. Histological findings were consistent with a localised adrenal adenoma (based on adjacent vessels. She underwent right adrenalectomy. Complete macroscopic component. There was no tumour rupture, invasion into the kidney, liver or adjacent vessels. She underwent right adrenalectomy. Complete macroscopic clearance was achieved despite the tumour being friable and haemorrhagic. Histological findings were consistent with a localised adrenal adenoma (based on adjacent vessels). AmJ Surg Path 2003; 27:867–881). Post-op androgen levels were low: DHEA-Sulphate <0.5, Androstenedione <1 and testosterone <0.5. Standard dose Synacthen test showed suboptimal Cortisol (93 and 195 nmol/L at 0 and 30 min) and the need for hydrocortisone replacement. Although the tumour was large relative to the child and surgical resection unusually challenging, clinical and histological findings were suggestive of an adrenal adenoma. While this carries a good outcome, some effects of prolonged androgen exposure in early life might be irreversible and will required ongoing management.

DOI: 10.1530/endoabs.51.P011

Could this be Adrenal Crisis in Retrospect? – Acute Cardiovascular Collapse in a 9-Year-Old Girl
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1Paediatrics, Cork University Hospital, Cork, Ireland; 2Emergency Medicine, Cork University Hospital, Cork, Ireland.

Introduction
Adrenal crisis is a life-threatening condition and an absolute medical emergency, requiring prompt diagnosis and treatment to prevent grave morbidity and mortality. We describe a case that posed significant diagnostic dilemma due to inaccuracy of history and clinical findings.

Case Report
A 9-year-old girl presented acutely with loss of consciousness, GCS of 5/15. This was preceded by a 3-day history of abdominal pain, vomiting and diarrrhoea. She had PDA repair at 18 months of age. Examination findings demonstrated cardiovascular collapse. She was peripherally shut down, tachycardic with unrecordable blood pressure. Investigations showed severe metabolic acidosis (pH6.97, lactate 8.6 mmol/l, base excess – 19.4). Serum glucose level was 8.6 mmol/l, sodium 131 mmol/l, potassium 4.3 mmol/l. She received 40 ml/kg of 0.9% saline. Fluid resuscitation improved her clinical and biochemical status. She was subsequently managed for gastroenteritis and pneumonia (evident on chest radiograph). Inflammatory markers and blood cultures were negative. Further work up revealed borderline Synacthen test baseline Cortisol: 274 nmol/L, 30 min: 395 nmol/L, 60 min: 479 nmol/L with ACTH level of 5.6 pmol/L. She failed her insulin tolerance test in terms of cortisol response (basal glucose: 4.4 mmol/L, cortisol: 166 nmol/L, 15 min glucose: 1.3 nmol/L, cortisol: 168 nmol/L). Other endocrine panel were unremarkable. Magnetic resonance imaging of pituitary was normal. She had a good outcome after 1 week hospital stay. She was commenced on oral hydrocortisone at 10 mg/m2 per day and fludrocortisone at 100 μg/day. Adrenal insufficiency medcic alert bracelet and emergency card were given. Subsequent outpatient reviews showed resolution of gastrointestinal symptoms and lethargy.

Conclusion
This case buttresses the point that it does not always tick the boxes. Adrenal insufficiency should be strongly considered in all cases of cardiovascular collapse in Emergency Paediatrics even in the absence of classical biochemical findings.

DOI: 10.1530/endoabs.51.P012

Two neonates with foetal adrenal haemorrhage in a tertiary care centre
Anu Sharma & Elissa Smit
University Hospital of Wales, Cardiff, UK.

Introduction
Foetal adrenal haemorrhage is relatively rare with a reported incidence of 0.2% in neonates. We share our experience of two neonates who were diagnosed to have adrenal haemorrhage in our centre over last 5 years. We also carried out a retrospective review of literature on existing evidence regarding diagnosis and evaluation of neonates with adrenal haemorrhage.

Methodology
Two neonates with confirmed adrenal haemorrhage were identified from radiology and foetal medicine data-base. Their case notes were reviewed. An extensive literature review was carried out on PubMed, Cochrane database using keywords ‘foetus’/‘neonate’ AND ‘Adrenal haemorrhage’.

Case 1
A month scan was carried out antenatally in view of 2-vessel cord which incidentally detected a left adrenal haemorrhage. The neonate was delivered by uncomplicated vaginal delivery. The newborn examination was normal. A post-natal abdominal ultrasound showed bulky left adrenal gland although it was smaller than previous scan. A repeat ultrasound at 3-months, showed gradual resolution of adrenal haemorrhage.

Case 2
An adrenal haemorrhage was noted incidentally on an antenatal scan. There was no history of sepsis, prolonged labour or traumatic birth. The neonate was born by normal vaginal delivery and newborn examination was unremarkable. Serial ultrasound abdomen showed gradual resolution of adrenal haemorrhage.

Review of literature and discussion
Adrenal haemorrhage is relatively common in neonates with reported incidence of 0.2% in neonates although in our experience only 2 neonates were radiologically diagnosed to have adrenal haemorrhage over last 5-years. It is likely that many adrenal haemorrhages remain unrecognised and therefore under-reported. Prematurity, prolonged labour, sepsis and hypoxia are predisposing factors for adrenal haemorrhage although both of our patients were diagnosed incidentally. Foetal adrenal haemorrhage also needs to be considered in neonates presenting with persistent jaundice. Neuroblastoma remains an important differential diagnosis especially in neonates with suspected unilateral adrenal haemorrhage. Clinical presentation and presence of predisposing factors and serial Doppler ultrasound changes help distinguish unilateral adrenal haemorrhage from neuroblastoma which is usually associated with poor prognosis and aggressive clinical course. Most of the adrenal haemorrhages are self-resolving and do not require long term adrenal hormone replacement.

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Cortisol or NOT
Nehal Thanawala & Gomathi Marganabanthu
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Baseline cortisol values may not necessarily rule out Addison’s disease. We report a case with vague symptomatology, normal cortisol baseline values with high index of suspicion and positive low dose synacthen test which lead up to the diagnosis. Young boy age 9 presented with low serum sodium levels and intermittent concern with abdominal symptoms, exhaustion and altered behaviour. He had normal baseline pituitary function including cortisol of 223 that decreased to 156 (133-537 nmol/l) over the next month. Serum and urine osmolality were normal. Kidney function screen was normal. Gas had a borderline low bicarbonate around 15–19 and Kidney ultrasound scan was unremarkable.

Endocrine Abstracts (2017) Vol 51
Gonadal, DSD and reproduction

**P015**

Consensus for UK principles of management of adolescents and infants with Disorders of Sex Development (DSD)

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1University of Manchester, Manchester, UK; 2University Hospitals Bristol Foundation Trust, Bristol, UK; 3University of Bristol, Bristol, UK; 4Royal Manchester Children’s Hospital, Manchester, UK.

Disorders of sex development (DSD) are a group of conditions caused by atypical development of chromosomal, gonadal or anatomical sex which pose complex, long-term diagnostic, investigatory and management challenges requiring expert teams and close collaboration with families and peer groups. The lack of nationally agreed clinical standards for the management of DSD has been recognised by the British Society of Paediatric Endocrinology and Diabetes, and these are now in development but with limited support of evidence-based literature, hence the use of Delphi Consensus methodology to develop key principles of management.

**Method**

Using the DELPHI survey method over a 6 week period, we sought to reach consensus for 14 statements concerning Principles of Management devised by the BSPED DSD specialist interest group (SIG) with peer group review. An online survey was sent to DSD multidisciplinary team (MDT) professionals and support groups across the UK in two rounds (R1 and R2). Each statement had 4 fixed responses and free text comment. Statements reaching 70% agreement met consensus. All free text comments were reviewed. R1 respondents were invited to participate in R2 for amended statements not meeting consensus.

**Results**

89 contacts were invited to participate in R1. 70 responses were received with 45 (51%) initial responses and 24 additional responses through survey forwarding by DSD MDTs. 12 (85%) statements reached consensus in R1. In R2, 51 (73%) responses were received for amended statements and consensus was reached on all remaining statements. Particular issues highlighted were timescales to diagnosis and referral due to geographical service distributions, agreement on key members of the DSD MDT and psychology provision and availability of peer reviewed literature for patient information.

**Conclusions**

The DELPHI process demonstrated a successful and effective method in achieving expert consensus for Principles of Management for DSD, a complex condition with limited evidence-base. Despite geographical service landscapes, standards/principles set through national consensus will drive forward improved patient care and service provision.

On behalf of the British Society of Paediatric Endocrinology and Diabetes (BSPED) DSD Special Interest Group (SIG) and Clinical Committee.

DOI: 10.1530/endobs.51.P015

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**P016**

Using salivary testosterone measurements to assess androgen deficiency in adults with Duchenne muscular dystrophy (DMD)

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1Great North Children’s Hospital, Newcastle upon Tyne, UK; 2Newcastle University, Newcastle upon Tyne, UK; 3John Walton Muscular Disease Research Centre, Newcastle University, Newcastle upon Tyne, UK; 4Roslin Institute, Edinburgh University, Edinburgh, UK; 5John Walton Muscular Dystrophy Research Centre, Newcastle University, Newcastle upon Tyne, UK.

**Background**

Many adolescents and young adults with DMD receive long-term glucocorticoids (GC), a well-recognised cause of hypogonadotrophic hypogonadism. Pubertal induction is routinely offered to DMD adolescents in our centre but few individuals remain on supplementation into adulthood and it is unclear whether these men have age-appropriate endogenous testosterone production. Salivary testosterone (SalT) measurement is available but has not been used to assess androgen status in this setting.

**Objectives**

To assess SalT levels in men with DMD without the need for them to attend hospital and to compare androgen status with current/previous testosterone and GC usage.

**Design, setting and participants**

All adults with DMD were sent a Sal-T sampling kit and a short questionnaire covering GC/testosterone usage and Tanner self-assessment. Approval was not required by the local Research Ethics Committee as this was a service development initiative. SalT levels were measured by LC-MS/MS in South Manchester University Hospital (adult male reference range: 70–340 pmol/l).

**Results**

56% of patients submitted a sample (26/75). Eighteen are currently available for analysis. Three were insufficient, 1 corresponded to a prepubertal boy, 1 was lost and 3 are pending. 9/18 were treated with GC (mean equivalent dose ~25 mg prednisolone). Eleven patients never received exogenous testosterone. One patient has started induction, six are post induction of whom three remain on testosterone. Median SalT was higher in those off-GC (255 vs 126 pmol/l). In the GC-treated group who had undergone induction, SalT was highest in those currently receiving testosterone (231 vs 126 pmol/l). Levels were lowest in those never exposed to testosterone (median: 77 pmol/l). 13/18 self-reported Tanner stages IV-V. 2 patients never exposed to testosterone reported Tanner I-II.

**Conclusions**

GC therapy is associated with lower SalT concentrations in adults with DMD. There is evidence of some endogenous testosterone production following pubertal induction. As life expectancy of DMD adults improves, evaluation/treatment of androgen deficiency should be a priority given its potential role in well-being. SalT measurements can provide androgen status assessment of these patients at home.

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**P017**

Turner syndrome transition - audit of paediatric clinic, RHC Glasgow

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1University of Glasgow, Glasgow, UK; 2Royal Hospital for Children Glasgow, Glasgow, UK.

**Background**

Turner syndrome is a lifelong condition that requires lifelong engagement with health services. The Paediatric Endocrinologist has a role in developing a plan for transition and establishing follow-up in an adult clinic. A clinic proforma outlining expected investigations during transition has been in use in the Glasgow Turner clinic since 2015 based on the recommendations of the Turner Syndrome Study Group. More recently The Endocrine Society Transition Toolkit has provided useful guidance on essential clinical information that should be provided upon transfer to adult practice.

**Objectives**

All girls should have had the following tests in the 2-year period prior to their last appointment with paediatric services to provide comprehensive clinical information to the receiving adult physician on cardiovascular and renal health; audiometry and autoimmune disease.

Patients

A total of 17 girls were studied with a median age of 17.6 (15.6–20.6) years, at last paediatric clinic visit, and median age of diagnosis of 1.40 (0.0–16.3) years.

Criteria to be measured

- Electrocardiogram
- Echocardiogram
- Renal ultrasound
- Full blood count
- Urea and electrolytes
- Creatinine
- Thyroid function tests
- Vitamin D level
- Lipid profile
- Audiometry
- Renal and ovarian ultrasound
- Autoimmune screen
- Thyroid ultrasound
- Thyroid stimulating hormone
- Bone age

DOI: 10.1530/endobs.51.P017
Methods
Data was collected from individual case notes and electronic records, in all girls, with last Paediatric Turner clinic, 2010–2017. Girls were divided according to whether care was transferred before or after the use of a clinic proforma in 2015. The individual and overall tests are presented as percentages. A chi squared test was applied to assess if there was a difference, overall, before and after 2015 in the number of tests performed.

Results

<table>
<thead>
<tr>
<th>Number and percentage of criteria fulfilled</th>
<th>Pre 2015</th>
<th>2015 Onwards</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=9</td>
<td>n=8</td>
<td>P value</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac Echocardiogram</td>
<td>5 (56%)</td>
<td>7 (88%)</td>
</tr>
<tr>
<td>Fasting Glucose</td>
<td>4 (44%)</td>
<td>7 (88%)</td>
</tr>
<tr>
<td>Fasting Lipids</td>
<td>2 (22%)</td>
<td>5 (63%)</td>
</tr>
<tr>
<td>Renal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea + Electrolytes</td>
<td>4 (44%)</td>
<td>6 (75%)</td>
</tr>
<tr>
<td>Audiology</td>
<td>1 (11%)</td>
<td>3 (38%)</td>
</tr>
<tr>
<td>Hearing Evaluation</td>
<td>9 (100%)</td>
<td>8 (100%)</td>
</tr>
<tr>
<td>Autoimmune</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TFTs</td>
<td>8 (89%)</td>
<td>7 (88%)</td>
</tr>
<tr>
<td>LFTs</td>
<td>82%</td>
<td></td>
</tr>
</tbody>
</table>

Discussion
A coordinated approach is required to ensure successful paediatric to adult transition including the transfer of essential clinical information. The paediatric endocrinologist should endeavour to develop strategies, including use of a clinic proforma, in their clinic to aid this process.

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P019
Single centre experience of testosterone therapy for boys with delayed puberty
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Introduction
Delayed puberty is a common indication for referral to paediatric endocrine services. Although guidelines exist for management of testosterone replacement in adults, currently it is not clear what the optimum regimen for testosterone therapy is for children or how best to monitor boys throughout treatment.

Aims
To identify the characteristics of testosterone therapy in boys referred for delayed puberty.

Methods
Retrospective review of case notes of all boys treated with testosterone for pubertal delay in one tertiary paediatric endocrine unit from 1 January 2012–1 April 2017.

Results
Over the study period, 540 clinic appointments were undertaken for review of boys with possible delayed puberty, with 175 new referrals taken during this time. Of these, 46 (8.5%) were treated with testosterone (median age (range) 14 (12–18) years). The most common diagnoses were constitutional delay (n=15.33%); Duchenne Muscular Dystrophy (n=6.13%); hypogonadotropic hypogonadism (n=6.13%) and panhypopituitarism (n=4.9%). Prior to treatment 30.65% boys had a bone age X-ray; 12/26% had liver function tests (LFTs); 7/15% had an LHRH test; 7/15% had a haematoctrit and 6/13% had a DXA scan. Five boys (11%) had LFTs checked after treatment; all of whom had raised alkaline phosphatase. The median duration of treatment was 3 (range 2–12) months. Four boys (9%) were treated with oral testosterone; 1/2% with oral and IM; 1/2% with gel and IM and the rest (87%) were treated with IM testosterone alone. Of the 5 boys on oral testosterone, 1/20% was on oxandrolone; 1/20% on testosterone undecanoate 40 mg on alternate days and the rest (60%) were on testosterone undecanoate 40mg daily. Of the 41 boys on IM testosterone, 2/5% were on 1g. Nebide; the rest (95%) were on varying doses of Sustanon (median starting dose 100 (range 50–250) mg). Three (7%) were started on an increasing dose regimen; the rest (93%) on one static dose. Adverse events were recorded in 9/46(20%); 2/22% with intolerable aggression and 7/78% with lethargy.

Conclusions
Induction of puberty with exogenous testosterone is required in nearly 10% of boys referred due to pubertal concerns, with variable initiation and monitoring. Consensual guidelines may be useful to standardise management and ensure best practice.

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Miscellaneous/other

P019
Calcium/calmodulin dependent protein kinase 2 (CaMKK2) mutation – a novel genetic cause of congenital hyperinsulinism
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Background
Congenital hyperinsulinism (CHI) is a disorder of unregulated insulin secretion causing persistent hypoglycaemia. In around 50% of the patients with CHI, the underlying molecular genetic etiology is unknown. CaMKK2/calmodulin-dependent protein kinase 2 (CaMKK2) belongs to the Serine/Thrreonine protein kinase family. Alternative splicing results in multiple transcripts encoding distinct isoforms. We report, for the first time, CaMKK2 mutation as a novel genetic cause of CHI.

Patient and methods
A Caucasian child born to non-consanguineous parents at 33 weeks gestation presented with hypoglycaemic seizures at 7 months of age requiring intravenous glucose load up to 15 mg/kg per min. The investigations confirmed CHI (plasma insulin concentration of 37 pmol/l and suppressed b-hydroxy butyrate (<100 mmol/l) during hypoglycaemia). No mutation was identified in ARCC8, KCNJ11 or GCK. The 18-fluoro-DOPA PET CT scan suggested diffuse CHI and the patient responded well to diazoxide. At the age of 5 years, the patient requires 10 mg/kg per day of diazoxide and has features of developmental and speech delay.

Results
Whole exome sequencing was performed on the genomic DNA of the patient and the biological parents. A de novo heterozygous frameshift mutation (p.G539fs*4) was found at the terminal exon (exon 16) of CaMKK2 (NM_001270486.1) (isoform-7). CaMKK2 isoform-7 (WT) and the p.G539fs*4 mutant were expressed in INS-1 cells and the p.G539fs*4 mutant was noted to have significantly higher basal and Ca2+-CaM dependent kinase activity compared with WT isoform-7. Both isoform-7 and the p.G539fs*4 mutant have elevated basal activity compared with isoform-1, the major CaMKK2 isoform expressed in most tissues.

Conclusion
We describe for the first time, a mutation in CaMKK2 as a novel genetic cause of persistent CHI. Calcium has a key role in mediating glucose stimulated insulin secretion via the action of multifunctional kinases (CaM-KI and CaM-KIV), activated by CaMKK2, an upstream kinase. We hypothesise that the increase in the Ca2+-CaM dependent kinase activity as a result of the mutation, to be increasing the insulin secretion, probably via the upregulated transcription of INS-1.

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**P020**

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

Mohammed Ibrar Murtaza1, Lindsey McVey1, Alexander Fletcher1, Ellen Anderson1, Emma Leighton1, Jarod Wong1,2 & Avril Mason1,2

1University of Glasgow, Glasgow, UK; 2Royal Hospital for Sick Children, Glasgow, UK.

**Background**

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

**Aim**

To determine the frequency of HT in girls with TS in West of Scotland and to assess its association with clinical characteristics.

**Patients and methods**

Retrospective cross-sectional analysis of 126 girls with TS in the West of Scotland, with at least 2 clinic blood pressure (BP) measurements in the preceding 12 months. HT was defined by systolic or diastolic BP measurement ≥95th percentile for gender and height on 2 consecutive visits in one year. Stage 1 HT (95th – 99th centile) and stage 2 HT (>99th centile).

**Results**

Median age was 16 years (range 3, 20) and duration of follow-up was 9.25 years (4/5). Median height SDS was −2.0 (−4.92, 0.16) and Body Mass Index (BMI) SDS 1.0 (−3.15, 1.14). 71/126 had karyotype of 45X, 0. 8/126 had history of congenital anomalies.

<table>
<thead>
<tr>
<th>Normotensive (n=87)</th>
<th>Hypertensive (n=39)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>16.38 (3, 20)</td>
<td>17.15 (8, 20)</td>
</tr>
<tr>
<td>Height SDS</td>
<td>−1.06 (−4.92, 0.16)</td>
<td>−1.76 (−4.24, −0.33)</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>1.0 (−3.15, 1.14)</td>
<td>1.42 (−1.08, 1.14)</td>
</tr>
<tr>
<td>Bicuspid Aortic Valve</td>
<td>15/87 (17%)</td>
<td>4/39 (10%)</td>
</tr>
<tr>
<td>Growth Hormone*</td>
<td>57/87 (66%)</td>
<td>21/39 (54%)</td>
</tr>
<tr>
<td>Oestradiol</td>
<td>53/87 (61%)</td>
<td>29/39 (74%)</td>
</tr>
<tr>
<td>45X</td>
<td>47/87 (54%)</td>
<td>24/39 (62%)</td>
</tr>
<tr>
<td>Tanner stage (B)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Current and previous use; + Current use.

Multivariate logistic regression analysis for factors associated with HT using age (95% CI 0.96 to 1.42), BMI SDS (95% CI 1.01 to 2.21), karyotype (95% CI 0.57 to 2.86) and Tanner stage (95% CI 0.57 to 1.19) as independent factors found only BMI to be associated with HT in girls with TS.

Further dissecting the association between BMI and HT:

(24/99) with BMI SDS < +2.0 were hypertensive (11/22) with BMI SDS between +2.0 to +3.0 were hypertensive (4/5) with BMI SDS > +3.0 were hypertensive

Off the 27/126 patients with BMI SDS > +2.0, 15/27 have 2 measurements of BP > +2.0 SD in a year.

**Discussion**

Our current study demonstrated that 31% of TS girls were hypertensive based on most recent clinic measurements over a 12 month period. BMI was a strong predictor of hypertension in our study. Therefore, intensive weight control may help with prevention and management of HT in these girls. Optimal monitoring and management of BP in pubertic TS is unclear and merits future research.

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**P021**

**Novel splicing mutation in B3GAT3 associated with short stature, GH deficiency, hypoglycaemia, developmental delay and multiple congenital anomalies**

Samuel Bloor1, Dinesh Giri2,1, Mohammed Didi2 & Senthil Senniappan2,1

1University of Liverpool, Liverpool, UK; 2Alder Hey Children’s NHS Foundation Trust, Liverpool, UK.

**Introduction**

B3GAT3, encoding β-1,3-glucuronyltransferase 3, has an important role in proteoglycan biosynthesis. Homozygous B3GAT3 mutations have been associated with short stature, skeletal deformities and congenital heart defects. We describe for the first time, a novel heterozygous splice site mutation in B3GAT3 contributing to severe short stature, growth hormone (GH) deficiency, recurrent ketotic hypoglycaemia, facial dysmorphism and congenital heart defects.

**Patient and methods**

A female infant, born at 34 weeks gestation to non-consanguineous Caucasian parents with a birth weight of 1.9kg was noted to have cloacal abnormality, ventricular septal defect, pulmonary stenosis and congenital sensorineural deafness. She had multiple dysmorphic features: anteverted nares, small upturned nose, hypertelorism, slight frontal bossing, short proximal bones, hypermobile joints and down slanting palpebral fissures. She also had recurrent hypoglycaemic episodes and the results were consistent with severe ketotic hypoglycaemia. At 4 years of age, she was diagnosed with GH deficiency due to her short stature (height < 2.5SD) and commenced on GH therapy. MRI of the pituitary gland revealed small anterior pituitary. There was a history of short stature and dysmorphism in father and a stillborn previous sibling with multiple dysmorphic features, congenital heart defects and short bones.

**Conclusion**

B3GAT3 is involved in glycosaminoglycan (GAG) biosynthesis, which provides structural support within the extracellular matrix surrounding the cells. Genetic defects can thus lead to multi-system disorders. We report a novel splice site mutation in B3GAT3 associated with short stature, GH deficiency and multiple congenital anomalies.

DOI: 10.1530/endoabs.51.P021

**P023**

**Exploring the growth and nutritional status in children with Prader-Willi syndrome**

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1National Children’s Hospital, Tallaght, Dublin, Ireland; 2Trinity College, Dublin, Ireland.

**Background**

Prader-Willi syndrome (PWS) is a rare complex genetic disease. Nutritional needs vary depending on life stage, ranging from growth faltering in infancy to obesity from late childhood. Dietetic care is a main pillar of the multi-disciplinary team (MDT) approach for PWS management. National Children Hospital (NCH) is the main national centre for PWS in Ireland, with 47 children attending. We sought to explore growth and nutritional status in children with PWS.

**Methods**

All children with PWS attending NCH were invited to participate (n = 44). Growth and nutritional status was assessed using:

1. Weight and height/length
2. Blood tests (full blood count, vitamin D and ferritin levels)
3. 3-day reported food diary
4. Questionnaires assessing feeding practices. Ethical approval was obtained.

**Results**

Nineteen patients participated (n = 19), with 14 being female. Median age was 7.27 years (0.6–18.2). 13 patients were treated with growth hormone. Nutrient deficiency: Iron deficiency anaemia was present in two patients and Vitamin D insufficiency was present in two patients.

Supplementation: 11 patients (58%) reported to take vitamin/mineral/nutritional supplements, of these 3 (16%) were taking prescribed iron or vitamin D supplement.

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Feeding Issues: 13 patients (70%) required neonatal NG feeding. Average weaning age to solid food was 29.5 weeks. 9 patients (47%) reported food seeking behaviour, with mean age of onset at 4.75 years.

Food diary analysis: 15 patients (79%) were not meeting their recommended daily allowance (RDA) for iron and 9 patients (47%) were not meeting RDA for calcium (Table 1).

<table>
<thead>
<tr>
<th></th>
<th>BMI</th>
<th>0.16</th>
<th>1.6</th>
<th>0.40</th>
<th>1.27</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z scores</td>
<td>0.16</td>
<td>1.6</td>
<td>0.40</td>
<td>1.27</td>
<td></td>
</tr>
<tr>
<td>WHO, 2007</td>
<td>0.16</td>
<td>1.6</td>
<td>0.40</td>
<td>1.27</td>
<td></td>
</tr>
</tbody>
</table>

Discussion
The results depict nutritional issues in this group of children with PWS including delayed weaning, food seeking behaviours and the need for ongoing nutrition support in infancy to manage dietary overrestriction as well as prevention of obesity in later childhood. This study highlights the need for a dedicated dietician service to provide support and evidence-based nutritional advice.

Conclusion
Children with PWS have dynamic nutritional needs and require ongoing nutritional input to optimise growth and nutritional status.

DO: 10.1530/endoabs.51.P024

P024
Using CRISPR/Cas9 gene editing to study molecular mechanisms of congenital hyperinsulinism
Preetha Purushothaman¹, Ahmad Aldossary³, Stephen Hart¹ & Khalid Hussain²
¹Institute of Child Health, University College London, London, London, UK; ²Sidra Medical and Research Center, Doha, Qatar.

Background
Congenital hyperinsulinism (CHI) is a heterogeneous genetically determined condition that is characterised by unregulated secretion of insulin from pancreatic β-cells. The most common and severe cases are caused by mutations in the ABCC8 gene encoding the SUR1 subunit of the KATP channel subunit. Autosomal recessive mutations in HADH gene are a rare cause of CHI. The advances in CRISPR/Cas9 gene editing technology has enabled the induction of targeted modifications in a variety of model organisms. However, the applicability and efficiency of CRISPR/Cas9 gene editing as a tool to unravel the molecular mechanisms that lead to the unregulated insulin secretion in CHI has been little reported.

Methods
Single-guide RNAs (sgRNA) were designed using three different web tools for predicting on-target and off-target probabilities. The exons 1, 3 and 6 were targeted in the ABCC8 gene while exons 1, 3 and 4 were selected in the HADH gene in MIN6 cells line. sgRNAs were then cloned into the plasmid vector pX330 encoding the S. pyogenes Cas9 endonuclease (SpCas9) gene and transfected into the MIN6 cells. The resulting double-strand breaks were repaired by the non-homologous end joining (NHEJ) technique. Gene editing efficiency was determined by the T7 Endonuclease I mutation detection assay and Sanger sequencing.

Results
Six sgRNAs have been designed of which two have targeted the ABCC8 gene at two sites within exons 3 and 6. We demonstrated insertion and deletions (indels) within the genomic DNA of the ABCC8 gene which shows the potential generation of a knock-out mutation in the ABCC8 gene of MIN6 cells using the CRISPR/Cas9 gene editing technique.

Conclusions
The results of our study so far has demonstrated the potential of use of Cas9/gRNA system as an efficient reverse genetic tool in studying the molecular mechanisms underlying CHI. Our future aims are to: conduct further molecular interrogation to confirm the KO in ABCC8 gene; create a KO allele of HADH gene in MIN6 cell line and further, use the newly generated KO mutant cells, to analyse the function of these genes.

[Grant MR/M032365/1]

DO: 10.1530/endoabs.51.P024

P026
Albright’s Hereditary Osteodystrophy associated with resistance to insulin and thyroid hormone in three male siblings
Helen MacGlon¹, Jayanti Rangasami² & Mehul Dattani¹,²,³,⁴
¹West Midlands Hospital, Middlesex, UK; ²UCL Great Ormond Street Institute of Child Health, London, London, UK; ³Great Ormond Street Hospital for Children, London, UK; ⁴UCL Hospitals, London, UK.

Introduction
Pseudohypoparathyroidism Type 1a (PHP1a) is a rare disorder caused by mutation in GNAS, which encodes the alpha-subunit of the trimeric stimulatory G protein. Gs, and links numerous G protein-coupled receptors (GPCRs) to adenylyl cyclase. GPCRs are crucial for intracellular endocrine signalling, and since GNAS is expressed predominantly from the maternal allele in some tissues, maternally inherited loss of function GNAS mutations are associated with a highly variable Albright’s Hereditary Osteodystrophy (AHO) phenotype. We report a unique Caucasian pedigree with AHO associated with significant thyroid hormone and insulin resistance in all affected members, and with a concomitant diagnosis of inflammatory bowel disease not typically seen in the condition.

Case report
Patient 1 presented aged 2 years, with hypothyroidism, obesity, developmental delay, and lower limb subcutaneous calcifications. Patient 2 presented with neonatal hypoglycaemia (BM 1.0 mmol/l) and developed obesity by 9 months of age (weight >95th percentile, >1.54 SDS). Patient 3 was born at 33/40 (BW 1.88 kg; 31st percentile, −0.51 SDS). Postnatal issues included hypocalcaemia and congenital hypothyroidism. PHP1A due to a mutation in GNAS (c.124C>T, p.R42C) was confirmed in the proband and subsequently each sibling. Pseudohypoparathyroidism (PHP) was diagnosed in their mother and maternal aunt. Each brother developed classical AHO phenotypes: generalised obesity, short stature (height <0.4th centile), brachydactyly and learning difficulties. Features of hormone resistance (hypothyroidism and insulin resistance) were diagnosed in each child. Their significant hypothyroidism required unusually high doses of levothyroxine (400 μg, 250 μg and 400 μg per day). Severe insulin resistance with acanthosis nigricans and impaired glucose tolerance developed in each child, the latter regressing on metformin with improved glycaemic control. Notably, each child has evidence of inflammatory bowel disease of varying severity.

Conclusion
We report an unusual pedigree with PHP Type 1A in which affected siblings manifest severe thyroid hormone and insulin resistance, and developed inflammatory bowel disease. This case report illustrates the complexity of Gs signalling disorders and the need for guidelines on screening for associated conditions in managing children with this condition.

DO: 10.1530/endoabs.51.P026

P027
Is there an association between endocrine conditions, including growth hormone deficiency, and Chiari-1 Malformation? A retrospective single centre study
Saba Elbag, Jamie Shah, Ruth Krome, Melanie Kershaw, Nick Shaw, Timothy Barrett, Jeremy Kirk, Vrinda Saraff, Wolfgang Hogler, Guirish Solanki & Renuka Dua
Birmingham Children’s Hospital, Birmingham, Birmingham, UK.

Introduction
Chiari-1 malformation (C-1M) is defined as the crowding of the craniocervical junction as a result of congenital cerebellar tonsil descent past the foramen magnum. Reported association between endocrine disorders and C-1M is mostly anecdotal. Aims
To evaluate the prevalence of endocrine disorders in C-1M against the prevalence of C-1M in those with isolated Growth Hormone Deficiency (GHD) with the aim of determining if there is a significant association.
We undertook a retrospective study of all patient cases under paediatric endocrinology at our hospital with confirmed C-1M since June 2002 (N=20). This was compared to the number of patients under treatment for isolated GHD and found to have C-1M. Bar demographics and co-morbidities including endocrine abnormalities, the following data points were reviewed: age at/method of diagnosis, height/weight centiles, velocity, mid parental/final height, and endocrine function (baseline and on dynamic function testing).

21 cases were identified as suspected C-1M. N=20 had MRI confirmation and N=1 was excluded. 40% (N=8) had GHD with treatment, 15% (N=3) had GHD and short stature and a separate 20% (N=4) had idiopathic short stature (ISS). This totalled 60% (N=12) with either GHD or ISS. Other endocrine conditions found included pan-hypopituitarism, hypophosphatasia, precocious puberty, undescended testes, polycystic ovarian syndrome, osteoporosis, vitamin D deficiency and fasting hyperinsulinaemia (N=1 per condition). 20% (N=5) were obese, which was not unexpected given 25-33% of UK children are obese. N=848 patients were identified as requiring growth hormone injections since 2007. Of these, an additional N=2 patients had C-1M that were not in our original cohort.

Discussion

Less than 1.2% of patients with GHD were diagnosed with C-1M. Therefore, there would not appear to be a significant association between endocrine dysfunction and C1-M although further studies into the entire C1-M cohort need to be done.

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Early puberty in Klinefelter syndrome
Pooja Vasista, James Greening & Vaya Tziaferi
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Introduction
Klinefelter Syndrome (KS) is related to late puberty and infertility. Early puberty in KS is a rare occurrence; a case of early puberty in KS is presented.

Case report
A 10-year-old boy, diagnosed with KS (47,XXY) during investigations for learning difficulties, was referred to the endocrine clinic with a history of facial acne since the age of 8 years. His examination showed pubic hair (stage 3) with testicular size 4–5 ml on both sides. Serum Gonadotrophins were high, compatible with the diagnosis of KS, with satisfactory serum testosterone level. One year later, he was in stage 4 for pubic hair and stage 3 for axillary hair, while testicular size remained the same. His height velocity was 4.25 cm/year. By the age of 12 years, his height velocity had slowed down to 2 cm/year. Tanner staging showed stage 5 for genitalia with testicular size remaining unchanged. Bone age at this stage was 16 years, indicating precocious puberty. Subsequently, investigations were carried out to rule out neoplastic causes of precocious puberty as previously reported in KS, including tumour markers, Chest X-ray, abdominal US scan and MRI brain, which were reported to be normal. Screening for mutations in exons 8 and 9 of GNAS1 gene was negative. It was concluded that this boy had undergone central precocious puberty (Table 1).

Table 1
<table>
<thead>
<tr>
<th>Age</th>
<th>10 years</th>
<th>11 years</th>
<th>12 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pubic hair stage</td>
<td>3+</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Genitalia stage</td>
<td>–</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>Testicular volume</td>
<td>4–5 ml</td>
<td>4–5 ml</td>
<td>4–5 ml</td>
</tr>
<tr>
<td>Height velocity (cm/year)</td>
<td>–</td>
<td>4.25</td>
<td>2</td>
</tr>
<tr>
<td>LH (IU/l)</td>
<td>21</td>
<td>28</td>
<td>44</td>
</tr>
<tr>
<td>FSH (IU/l)</td>
<td>45</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>Testosterone (nmol/l)</td>
<td>6.2</td>
<td>7.3</td>
<td>6.2</td>
</tr>
<tr>
<td>hCG (IU/l)</td>
<td>–</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Alpha-foeto-protein</td>
<td>–</td>
<td>2</td>
<td>&lt;2</td>
</tr>
<tr>
<td>17OHP (nmol/l)</td>
<td>–</td>
<td>3.3</td>
<td>2.9</td>
</tr>
<tr>
<td>DHEA (nmol/l)</td>
<td>–</td>
<td>2.9</td>
<td>4.9</td>
</tr>
<tr>
<td>Androstenedione (nmol/l)</td>
<td>–</td>
<td>1.3</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Conclusion
Precocious puberty in children with KS is rare; the common causes are idiopathic central precocious puberty and extragonadal germ cell tumours. In this case the diagnosis was made in retrospect but clinicians should be aware to investigate for germ cell tumours in children with KS presenting in early puberty if there are signs of virilisation even if testicular volume is small.

When feeding becomes excessive! An unusual case of psychogenic polydipsia
Sonal Kapoor & James Greening
Leicester Royal Infirmary, Leicester, UK.

Introduction
Psychogenic polydipsia is a relatively uncommon condition characterized by overconsumption of water. It is known to be prevalent amongst psychiatric patients, but less common in the general population.

Case report
A previously well 18-month-old girl presented to the emergency department in status epilepticus. There was no history of fever, recent weight loss, infection, trauma or any systemic medications. Post event questioning established a history of bottle water feeding in excess of 3 litres a day, with a history of nocturia (heavy nappies during the night). Safeguarding concerns were excluded. Neurological examination was unremarkable post seizure and there were no other significant signs seen on systemic examination. CT scan of the head showed no significant abnormality excluding an intracerebral pathology.

Table 1
<table>
<thead>
<tr>
<th>Sodium</th>
<th>122 mEq/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium</td>
<td>4.3 mEq/l</td>
</tr>
<tr>
<td>Serum osmolality</td>
<td>276 mmol/kg</td>
</tr>
<tr>
<td>Serum Cortisol</td>
<td>286 nmol/l</td>
</tr>
<tr>
<td>TSH</td>
<td>1.9 mIU/l</td>
</tr>
<tr>
<td>CRP</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>White Cell Count</td>
<td>13.4</td>
</tr>
<tr>
<td>Urine Osmolality</td>
<td>107 mOsmol/kg</td>
</tr>
<tr>
<td>Urine sodium</td>
<td>24 mmol/l</td>
</tr>
</tbody>
</table>

Haematology and biochemistry
The seizure was controlled with routine clinical care (buccal midazolam and IV lorazepam). We treated the hyponatraemia with 20 mEq/kg NaCl bolus and 2 mEq/kg of 3% hypertonic saline. The seizure terminated following this and the hyponatraemia slowly resolved over next 6–8 h. Meanwhile, the patient was maintained on intravenous fluids and subsequently graded on to oral fluids. Overnight water deprivation revealed that the urine osmolality improved to 477 mosmol/kg with a serum osmolality of 293 mmol/kg (Table 1).

Conclusion
Diagnosis of pathological polydipsia and polyuria is difficult to recognise in a toddler in nappies. It can be often be missed and misdiagnosed as UTI. Seizure in this context is extremely rare but prompt recognition of the biochemical changes consistent with Diabetes insipidus or psychogenic polydipsia requires urgent intervention and investigation for the correct diagnosis and outcome. This case is
even more unusual in that it occurred in as far as we know a normal child without any co-morbidity. DOI: 10.1530/endoabs.51.P033

P034
Intrauterine growth restriction as a presentation of 17q12 deletion
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Chromosome 17q12 deletion is rare. It results from the deletion of a piece of chromosome 17 in each cell. The most recognised phenotype of this mutation is a combination of kidney cysts and Maturity Onset Diabetes of the Young (MODY), which is also known as Renal Cysts and Diabetes syndrome (RCAD). RCAD is caused by a mutation in the gene encoding hepatocyte-nuclear-factor-1-beta (HNF1B) which is part of chromosome 17q12.

Introduction
In 1997 while studying the genetic background of a Japanese family who had MODY, HNF1B was first affiliated with MODY. However, further studies on this gene has shown that this mutation is linked to many other phenotypes including: renal problems, neurological problems abnormal liver function, genital tract malformations, hyperuricemia and hypomagnesaemia and others. However, intrauterine growth restriction (IUGR) is not a recognised phenotype. This report will discuss IUGR as a presentation of 17q12 deletion.

Case report
A 2-year-old primigravida mother was antenatally diagnosed to have IUGR. There were no risk factors for IUGR. Delivery was induced at 37+3 weeks of gestation in view of IUGR. The baby was born in a good condition with weight, length and head circumference plotting on 2nd centiles. Neonatal check was normal. In view of symmetrical IUGR, CGH array was checked which showed 17q12 deletion. Therefore, renal ultrasound was checked in addition to glucose, uric acid and magnesium. Her investigations were normal but renal ultrasound showed duplex left kidney. This baby is under follow up by paediatric consultant to monitor growth and development and associated abnormalities.

Conclusion
It is evident that this mutation is under-recognised and linked to many phenotypes, some of which might be life detrimental if not detected early, so earlier presenting features should be further explored. A very early clinical feature is suggested in our report, which is symmetrical IUGR of unknown aetiology. It suggests that if symmetrical IUGR of unknown aetiology, by itself, does not trigger the paediatrician to do further genetic tests, it should ideally be considered to be one of the presentations secondary to 17q12 mutations.

DOI: 10.1530/endoabs.51.P034

P035
Post-prandial hyerinsulinaemic hypoglycaemia post-esophageal surgery in children
Neha Malhotra, Antonia Dastamani, Maria Güemes, Clare Gilbert, Clare Hess, Mehul Dattani & Pratik Shah
Great Ormond Street Hospital for Children, London, UK.

Introduction
Post-prandial hyerinsulinaemic hypoglycaemia (PPHH) or dumping is a recognized complication of various gastric surgeries. There are very few paediatric case reports to confirm PPHH post esophageal repair. We here report two cases who presented with dumping syndrome after a variable time period post esophageal atresia repair and response to medications.

Case 1
A 6 month old female diagnosed with Wolf-Hirschhorn syndrome, born at 38+3 weeks by elective C-section with birth weight of 2040 g. Antenatally diagnosed to have tracheo-oesophageal fistula that was corrected surgically on day 2 of life and then subsequently requiring oesophageal dilatations every month. She was reported to have hypoglycaemia in the post-operative period following oesophageal balloon dilatation. Subsequent investigations were suggestive of PPHH, initially responding to Diazoxide and continuous feeds.

Case 2
A 2 year old male born at 38/40 with an antenatal diagnosis of long segment oesophageal atresia (without fistula). On day 3 of life, a fashioned gastrostomy was done to facilitate feeding. He went on to require 6 oesophageal dilations for the strictures in the first year of life (and had normal blood glucose). At the age of 1 year he presented with a hypoglycaemic seizure. Dumping syndrome was confirmed and was initially tried on Acarbose and Diazoxide, both of which were ineffective in his case. He was finally managed with continuous feeds over 17 h and fasting up to 8 h. On his most recent visit he has been stable on bolus feeds (over 1 h) during daytime and overnight continuous feeds and is thriving well.

Conclusion
PPHH following gastric surgeries for gastro oesophageal reflux are quite common but remains to be an under recognised complication following oesophageal atresia repair in paediatric population. These cases also demonstrate that continuous feeds might be only option if unresponsive to medical therapy and PPHH can get milder over time.

Insight into clinical practise
PPHH is not well known in children undergoing surgery for oesophageal atresia repair and hence it is important to screen them regularly.

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P036
Quantification of appetite-regulating hormones in hypothalamic and simple obesity
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1University College London Great Ormond Street Institute of Child Health, London, UK; 2Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK; 3Wellcome Trust-MRC Institute of Metabolic Science, Cambridge, UK.

Introduction
Hypothalamic obesity (HyOb) is a rare form of treatment-resistant morbid obesity associated with hypothalamic damage. Its pathophysiology is incompletely understood, and is associated with hyperphagia and hyperinsulinemia. We sought to compare the physiology of various appetite-regulating hormones in HyOb and ‘simple’ obesity.

Methods
Oral glucose-stimulated serum insulin and plasma oxytocin concentrations, and fasting concentrations of serum leptin, plasma n-MSH, BDNF, ghrelin, AgRP and copetin were compared by internally validated ELISA in obese (BMI ≥ +2SDS) and lean children with hypothalamic damage (HyOb and HyLean) to ‘simple’ obesity (Ob) and lean controls. Hyperphagia was quantified using the Dykens’ Hyperphagia Questionnaire Score (DHQS).

Results
Patients (49 HyOb, 29 HyLean, 24 Ob, 19 Lean) were of mean age 11.3±3.9 years with a BMI SDS of 2.8±0.6 and 0.4±1.4 in the obese and lean groups respectively. HyOb patients were more hyperphagic compared to lean controls (median DHQS 24 (17–34) vs 17 (12–21), P=0.04), but not Ob patients (DHQS 24 (18–31), P=1.0), with a strong positive correlation between BMI SDS and DHQS (r=0.4, P<0.001) regardless of aetiology. Insulin (R=0.4, P<0.001) and leptin (R=0.8, P<0.001) were positively correlated whilst ghrelin (R=−0.3, P=0.045) and AgRP (R=−0.2, P=0.03) were negatively correlated with BMI SDS. A lower leptin was independently associated with more rapid increases in BMI SDS (β=−0.7 (95% CI 1.3–0.0, P=0.04) at one year. There were no significant differences in hormone concentrations between HyOb and Ob subcohorts. HyLean patients exhibited intermediate insulin and leptin concentrations between HyOb and Lean controls despite normal BMIs, with 3/15 becoming obese within one year.

Conclusion
There are no differences in appetite-regulating hormone concentrations or hyperphagia in HyOb and simple obesity, with anorexigen being increased and orexigen being suppressed. HyLean patients exhibit early hormone dysregulation and remain at risk of HyOb. These data suggest a relationship between baseline leptin concentrations and weight gain requiring further investigation.

DOI: 10.1530/endoabs.51.P036

Endocrine Abstracts (2017) Vol 51
P037
Congenital hypopituitarism and hyperinsulinemia hypoglycaemia: a challenging association
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Great Ormond Street Hospital, London, UK.

Introduction
To date, few cases with both congenital hypopituitarism (CH) and hyperinsulinemia hypoglycaemia (HH) have been reported in the literature. We now report a cohort of 12 cases with CHI associated with HH.

Clinical Phenotype
An association between congenital hypopituitarism (CH) and hyperinsulinemia hypoglycaemia (HH) was present in 12 patients (M:F 9:3). Mean age at diagnosis of HH was 0.9 months, whereas mean age at diagnosis of CH was 2.0 years (data based on n=10). Seven out of 12 patients have developmental delay, one has epilepsy, and four children have normal development. Nine patients had a small anterior pituitary identified on MRI, two had a normal pituitary gland, and no comment was made on the pituitary gland in one patient. Three patients with a small anterior pituitary also had an ectopic posterior pituitary gland. Ten out of 12 patients were diazoxide-responsive, although 50% of patients came off treatment in the first year of life. Molecular analysis led to the identification of genetic changes in a number of patients (dominant maternal ABCC8 mutation (n=1), denovo ABCC8 mutation (n=1), paternal intronic change in ABCC8 (n=1), KDM1 hypomethylation (n=1), EIF2S3 mutation (n=3, three males from a single pedigree)). Although EIF2S3 mutations have been previously associated with microcephaly and intellectual disability, this is the first description of disordered pancreatic function and hypoglycaemia associated with EIF2S3 mutations.

Conclusion
This study reports a significant cohort of children in whom HH is associated with CH. A transient form of HH was identified in the majority of cases, and this was diazoxide-responsive in majority of cases too. Molecular analysis identified mutations in 7 of 12 children; although apart from the pedigree with the EIF2S3 mutation, the cause of hypoglycaemia remains yet to be elucidated.

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P038
Growth hormone neurosecretory dysfunction as part of the spectrum of growth hormone deficiency disorders which benefit from growth hormone treatment
Silvania Caiulo1, Hoong-Wei Gan2, Claire R. Hughes3, Rakesh Amin1, Helen Spoudeas2, Catherine Peters1, Peter Hindmarsh1, Pratik Shah1 & Meuhl Dattani1
1Great Ormond Street Hospital, London, UK; 2Institute of Child Health, London, UK; 3Royal London Hospital, London, UK.

Objectives
Current provocative tests for GH deficiency (GHD) are neither 100% sensitive nor specific. GH neurosecretory dysfunction (NSD) refers to the presence of growth failure, normal stimulated GH responses, but impaired spontaneous GH secretion. We describe our experience in managing GHNSD over 7 years.

Methods
We retrospectively reviewed a cohort of 106 children admitted for 12-hour overnights GH profiles (with 20-min sampling) between 2010 and 2016. Auxological, biochemical and neuroradiological data were collected at the time of profiling, at 1-year and 3-year follow-up. GHNSD was defined when the overnight profile showed <3 spontaneous peaks of GH >2 μg/l.

Results
Seventy-nine boys and 27 girls presenting at a mean age of 7.6 ± 3.8 years, with a mean height SDS of −3.3 ± 1.5 and a mean height velocity (HV) SDS of −2.1 ± 1.7 SDS were included. 103 patients had GHFS, with auxological outcomes available for 53 at 1 year and 30 at 3 years (39 and 25 treated with GH respectively). Height SDS was not significantly different between the treated and untreated groups (1-year: −3.4 ± 2.8 vs −3.3 ±1.4, P = 0.952; 3-year: −2.3 ± 1.0 vs −3.4 ± 1.9, P = 0.068) but HV SDS was significantly increased in the GH-treated group (1-year: +1.9 ± 2.3 vs −1.8 ± 1.6, P = 0.001; 3-year: +1.4 ± 1.7 vs −1.4 ± 1.5, P = 0.002). Height SDS also significantly increased at 3 years with treatment (+1.2 ± 1.0 vs +0.1 ± 0.6, P = 0.03). Exclusion of patients with syndromes affecting growth or gaining puberty during follow-up did not reveal any difference in findings. Anterior pituitary hypoplasia was present in 71% of GHNSD patients and 54.5% of patients with a normal GH profile (P = 0.306), whilst other endocrine deficits were present only in patients with GHNSD (12.9%).

Conclusions
Children with abnormal auxology and a normal GH peak to provocative testing may warrant an overnight GH profile to identify GHNSD. Children with GH deficiency secondary to NSD display similar responses to GH replacement as in frank GHD, and therefore should be considered part of the spectrum of GHD disorders. Longer-term outcomes including adult height data are still required to establish the long-term efficacy of treating GHNSD.

DOI: 10.1530/endoabs.51.P038

P039
Can the TSH index be used as a predictor of central hypothyroidism in children?
Elena Monti1, Kevin Stroock2, Grazia Morandi3, Nicola Improda4, Elena Rapti5, Maria Celeste Mattone6 & Meuhl Dattani1,7,8
1Great Ormond Street Hospital Paediatric Endocrinology, London, UK; 2Academic Medical Center, Amsterdam, Netherlands; 3Azienda Ospedaliera Universitaria Integrata di Verona, Dipartimento di Pediatria, Verona, Italy; 4Federico II University, Department of Medical Translational Sciences, Naples, Italy; 5AHEPA Hospital, Department of Internal Medicine, Division of Endocrinology and Metabolism, Thessaloniki, Greece; 6Hospital de Pediatría Garrahan, Buenos Aires, Argentina; 7UCL Great Ormond Street Institute of Child Health, Section of Genetics and Epigenetics in Health and Disease, London, UK; 8UCL Hospitals, Adolescent Endocrinology, London, UK.

Introduction
Central hypothyroidism (CH) is diagnosed when low thyrotropin (TSH) is associated with a free thyroxine (fT4) below the normal range. Jostel proposed a ’fT4-adjusted TSH’ (TSH index: TSHI = log TSH + 0.1345 - fT4), to estimate the degree of pituitary dysfunction (Jostel et al Clin End 2009).

Methods
Retrospective analysis of patients investigated for pituitary hormone deficiencies (n = 276; M:F 166:110) in our centre.

• Group A: 120 patients with multiple pituitary hormone deficiencies (MPHD); A1 (27) remained euthyroid, A2 (93) had CH and of these 73 started levothyroxine together or before growth hormone (A3Early) and 14 after growth hormone (A3Late).
• Group B: 156 patients with different conditions with increased hypothalamic pituitary dysfunction risk; B1 (52) had isolated growth hormone deficiency (IGHD).

Results

<table>
<thead>
<tr>
<th>Group</th>
<th>A1 (n=27)</th>
<th>A2 (n=93)</th>
<th>A3Early (n=73)</th>
<th>A3Late (n=14)</th>
<th>B1 (n=52)</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>2.09 ±0.08</td>
<td>2.43 ±0.04</td>
<td>4.06 ±0.67</td>
<td>5.27 ±0.96</td>
<td>2.84 ±0.55</td>
<td>1.76 ±0.09</td>
<td>3.14 ±1.56</td>
<td>12.08 ±2.27</td>
</tr>
<tr>
<td>fT4 (μg/l)</td>
<td>2.00 ±0.07</td>
<td>2.38 ±0.03</td>
<td>3.65 ±1.17</td>
<td>12.6 ±0.12</td>
<td>2.80 ±0.27</td>
<td>1.70 ±0.08</td>
<td>3.09 ±1.80</td>
<td>11.26 ±0.13</td>
</tr>
<tr>
<td>TSHI</td>
<td>4.87 ±0.21</td>
<td>2.07 ±0.27</td>
<td>4.93 ±1.36</td>
<td>11.2 ±1.11</td>
<td>3.89 ±0.38</td>
<td>1.91 ±0.20</td>
<td>3.20 ±1.17</td>
<td>11.26 ±1.95</td>
</tr>
<tr>
<td>TSH (mIU/ml)</td>
<td>1.35</td>
<td>1.25</td>
<td>1.90</td>
<td>2.08</td>
<td>2.08</td>
<td>1.90</td>
<td>1.90</td>
<td>2.08</td>
</tr>
<tr>
<td>T3 (pmol/l)</td>
<td>2.58 (0.98)</td>
<td>2.63 (1.37)</td>
<td>2.67 (1.61)</td>
<td>14.11 (2.45)</td>
<td>2.68 (1.82)</td>
<td>2.68 (1.82)</td>
<td>2.68 (1.82)</td>
<td>2.68 (1.82)</td>
</tr>
<tr>
<td>T4 (μg/dl)</td>
<td>4.68 (1.83)</td>
<td>2.87 (1.87)</td>
<td>2.86 (1.82)</td>
<td>2.86 (1.82)</td>
<td>2.86 (1.82)</td>
<td>2.86 (1.82)</td>
<td>2.86 (1.82)</td>
<td>2.86 (1.82)</td>
</tr>
<tr>
<td>fT4 (μg/l)</td>
<td>2.42 (1.06)</td>
<td>2.65 (1.28)</td>
<td>2.88 (1.79)</td>
<td>2.75 (1.79)</td>
<td>2.88 (1.79)</td>
<td>2.75 (1.79)</td>
<td>2.88 (1.79)</td>
<td>2.75 (1.79)</td>
</tr>
</tbody>
</table>

At diagnosis group A patients had lower TSH than group B (P <0.01). TSH, fT4 and TSHI were not significantly different between group A1 and B1. At diagnosis no significant difference was found in TSH, fT4 and TSHI between A3Early and A3Late (P = 0.608, 0.254, 0.299 respectively). Interestingly TSH and TSHI remained significantly different throughout the followup, between A1 and A2 (P = 0.001). T4 was significantly lower in A3Early compared to A1 (P = 0.005) at diagnosis and, following GH, it decreased in A3Late. GH secretion impacts on thyroid function; however following GH treatment TSH and TSHI did not change significantly within each subgroups (B1, P=0.820 and 0.26; A3Early and A3Late P = 0.54 and 0.37 respectively).

Conclusion
Our data suggest that TSHI can be a predictor of CH, enabling earlier diagnosis of CH in “at-risk” patients.

DOI: 10.1530/endoabs.51.P039

Endocrine Abstracts (2017) Vol 51
UK Consensus Statements for the diagnosis of growth hormone deficiency (GHD)
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Growth hormone deficiency (GHD) is a licensed and NICE approved indication for growth hormone (GH) treatment but there are no nationally agreed standards for investigation of suspected GHD. Variable practice across the UK could have governance issues and impact on patient experience and equality of access to specialist GH investigation and treatment. Some GH provocation tests carry significant risk and it is therefore essential that these specialist investigations are carried out in centres with appropriate expertise and infrastructure.

Aim
BSPED clinical committee initiated process to identify consensus for UK standards for investigation of suspected GHD.

Method
DELPHI consensus process in two rounds (R1 and R2). R1: 10 statements with four fixed responses and free text comments regarding standard practice for investigation of GHD were developed by the clinical committee and a group of experts. These were sent to the 21 BSPED UK specialist endocrine centres. Each had identified colleagues to complete the online survey including tertiary endocrine consultants, general paediatricians with an endocrine interest, and paediatric endocrine clinical nurse specialists. Conflicts of interest were recorded. Consensus was considered to be achieved when 70% of respondents agreed with the statement.

Results
R1: 141 surveys were sent out: 21 were blocked by NHS firewalls. R1 response rate of remaining 120 was 57% (n=68). Consensus was achieved for seven statements, with useful free text comments. Common themes include the recognition that investigation should be carried out by experienced personnel to improve safety and that sex steroid priming should be included in the standards. R2 will address the outstanding statements modified using the free text comments.

Conclusion
Seven consensus statements for standards to investigate GHD have been identified using Delphi methodology, a further three are under consideration. Implementing standards will allow an evolving process amenable to audit to ensure best clinical practice and patient experience, and optimise the use of resources.

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ACTH deficiency and potential for reversibility in children and young people (CYP) with craniopharyngioma
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Introduction
ACTH deficiency is life-threatening, but difficult to differentiate from ACTH suppression especially in children and young people (CYP) receiving perioperative corticosteroids for pituitary tumour surgery. In our experience, ACTH is the most, and GH the least robust anterior pituitary hormone, with LH/FSH and TSH intermediate in hierarchical loss.

Aim
To assess potential misdiagnosis of ACTH suppression versus deficiency and time to adrenal recovery in a longitudinal cohort of CYP with craniopharyngioma treated at our centre over 26 years. To assess whether pre-dose 8am plasma ACTH detectability might predict ACTH recovery.

Methods
Fifty-three patients (29 male) with craniopharyngioma were identified from local neuroendocrine databases and their clinical records reviewed.

Results
At diagnosis, patients were aged 6.87 (1.12–17.18) years and followed for 6.66 (1.35–26.73) years. Of the 53 patients, 9 (16.98%) diagnosed at 6.28 (1.12–17.18) years, continued showing undetectable ACTH although all were GH deficient, only 5/6 (83.3%) had deficiency in LH/FSH, 4/6 (66.7%) in TSH and 5/6 (55.6%) in ADH deficient at a 6.53 (1.35–17.53) year follow-up when BMI and height SDS were +1.03 (+0.20 to +2.93) and +0.05 (+1.11 to +1.42) respectively. All had detectable ACTH 36.2 ng/l (13.9–52.9) at recovery and although all were GH deficient, only 5/6 (83.3%) had deficiency in LIFFSH, 4/6 (66.7%) in TSH and 2/6 (33.3%) in ADH. The remaining 38/53 (71.7%) patients, diagnosed at 6.28 (1.12–17.18) years, continued showing undetectable ACTH levels. <5 ng/l and require cortisol, GH and thyroxine replacement 5.94 (1.43–26.73) years later whereas all but one of the remaining 32 who were post-pubertal (31/32 (96.9%)) were LIFHSF deficient and 31/38 (81.6%) ADH deficient. There was a significant difference in TSH (P<0.01) deficiency between CYP with and without cortisol requirement.

Conclusions
Overdiagnosing ACTH deficiency after pituitary tumours may delay adrenal recovery, aggravate hypothalamic obesity and be erroneously attributed to surgery or radiation. The 13.6% adrenal recovery demonstrated suggests ACTH suppression, which may increase with time. We suggest a detectable pre-dose early morning ACTH > 10 ng/l in CYP on physiological replacement and the absence of concomitant TSH and post-pubertal LIFHSF deficiency should alert physicians to readdress the ongoing need for hydrocortisone in a population prone to obesity and its complications.

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Height as a clinical biomarker of disease burden in adult mitochondrial disease
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Introduction
Patients with mitochondrial disease have abnormal cellular adenosine triphosphate (ATP) generation that results in a broad phenotype with a diverse clinical presentation. Abnormal growth and short stature have been observed in children and adults with mitochondrial disease and we hypothesized that stature in affected individuals would reflect disease severity.

Method
We extracted height, weight and molecular genetic data from the UK Mitochondrial Disease Patient Cohort. Height and body mass index (BMI) were compared to the UK reference data. The overall disease severity of individual patients was evaluated using the Newcastle Mitochondrial Disease Scale for Adults (NMDSAS), a validated clinical scale to study multi-system involvement and disease progression. We determined the relationship between final height and NMDSAS scores in all adult patients by comparing mean height to for NMDSAS bands using a one-way ANOVA; further analysis was conducted in a particular genotype, m.3243A>G mutation, a maternally inherited mutation which is the most common cause of mitochondrial disease.

Results
Adults with mitochondrial disease (n = 539) were short with a mean final height of 1.47 ± 0.07 (CI 95%: 1.07–1.88). In 72.2% (n = 172) of adults, onset of mitochondrial disease was after the age of 18 years. There was a negative association between height SD and NMDSAS score (F = 3.535, P = 0.006) also observed in the m.3243A>G sub-group (F = 3.218, P = 0.01). Mean BMI s.d. was 0.53 (CI 95%; 0.51–0.55) with no overall association between BMI and NMDSAS score (F = 3.441, P = 0.072) but a negative association in the m.3243A>G sub-group (F = 3.197, P = 0.05). Mean BMI s.d. was 0.53 (CI 95%; 0.52–0.55) with no overall association between BMI and NMDSAS score (F = 3.441, P = 0.072) but a negative association in the m.3243A>G sub-group (F = 3.197, P = 0.05).

Conclusions
Short stature in mitochondrial disease is a biomarker of future disease severity as final height is often attained before the onset of overt clinical symptoms. Whilst the etiologies of the short stature are likely multi-factorial, we speculate that abnormal growth plate chondrocyte function secondary to dysfunctional ATP synthesis may be an underlying factor. Further mechanistic studies are warranted.

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P043
SOX3 gene duplication (OMIM 313430) associated with midline CNS malformations, hypopituitarism and neurodevelopmental abnormalities: 3 unrelated cases
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Introduction
Duplications of the SOX3 gene at Xq27.1 are known to be associated with a spectrum of forebrain midline defects, isolated or multiple pituitary hormone deficiencies, spina bifida and sometimes learning difficulties. We report three cases of SOX3 duplication with hypopituitarism and differing presentations.

Case reports
1) A male infant presented in neonatal period with poor feeding, prolonged jaundice, central hypothyroidism and inadequate cortisol response to Synacthen. Hormone replacement with hydrocortisone, thyroxine and subsequently growth hormone was commenced. MRI showed pituitary hypoplasia and ectopic poster pituitary with normal septum pellucidum and corpus callosum. Karyotype in infancy was normal. Array CGH (aged 2 years) revealed duplication of the SOX3 gene (maternal copy derived). He has a maternal adult male cousin with hypopituitarism. By age 4 years he had severe expressive language delay which improved with therapy. Aged 9.9 years he is of normal stature. 2) A 15-year-old boy was referred with short stature and pubertal delay. He had brachycephaly, learning difficulties, dyspraxia and hyposmia. Initial endocrine assessment was consistent with constitutional delay and he received a course of testosterone treatment. He subsequently failed to progress spontaneously in puberty (G3, P3, TVs 5.6–6.1 m aged 16 years). IGF-1 was low, peak GH 6.1 mg/l (post glucagon) with normal cortisol. MRI showed partial agenesis of corpus callosum and absent septum pellucidum. Array CGH showed maternally derived duplication of SOX3. Aged 20 years he is on full testosterone replacement. 3) A male infant was noted on antenatal scan to have lumbar meningomyelocele (repaired with VP shunt). Post-natal imaging showed hydrocephalus and agenesis of corpus callosum. He had microprosencephaly, small testes; normal thyroid function and cortisol response to Synacthen in week 1 of life. Array CGH revealed de novo duplication of SOX3 and part of chromosome 6. Age 2 years peak GH 4.4 ug/l and cortisol 452 nmol/l (post-glucagon). IGF1 4.8 nmol/l (RR-3.5). He has severe visual impairment (bilateral optic atrophy) and left temporal lobe epilepsy with severe developmental delay.

Conclusion
These cases expand our knowledge of the clinical phenotype associated with SOX3 duplication in boys. Array CGH can readily identify this genetic basis and permit appropriate counselling.

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P044
Changing patterns of growth in children with prader-willie syndrome (PWS) over 12 years
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Introduction
Children with Prader-Willi syndrome (PWS) show alterations in infantile, childhood and pubertal growth. Growth Hormone (GH) therapy is recommended due to reported improvements in height velocity (HV) and body composition. We aimed to identify changes in growth patterns when comparing growth parameters between 2000–2002 and 2013–2017. In 21 children who received GH (median age at GH start 4.92 years (2.7,7.8), consecutive measurements were available at –1, 0, +1 and +2 years from GH start.

Results
Overall, 60 children (31F/29M) were included. Three phases of growth after the age of 1 year were identified: 1–5 years, with acceleration in both HSDS (P0.305, P=0.001) and BMISDS (r=0.595, P<0.0001); 6–12 years, with stabilisation in both HSDS (r=0.063, P=0.417) and BMISDS (r=0.154, P=0.087); and 13–18 years, with deceleration in HSDS (r=0.389, P<0.0001) and unchanged BMISDS (r=0.051, P=0.647). At age 5, children in 2013–2017 (n=12) had higher HSDS (median 0.508 (1.74,1.54) vs 1.04 (4.6,0.53)) than those in 2000–2002 (n=18) (P=0.03). At age 12, children in 2013–2017 (n=5) had higher HSDS [median, 1.13 (0.62,1.59) vs 1.35 (4.27,0.23)] (P=0.027) and lower BMISDS [median 1.05 (0.13,1.12) vs 2.44 (0.13,4.33)] (P=0.032) than those in 2000–2002 (n=11). After 2 years on GH, median HSDS improved from –1.43 (–4.59,0.95) to 0.11 (–3.53,1.57) (P<0.0001) and median HVSDS from 0.62 (–5.9,4.17) to 2.8 (–2.2,5.2) (P=0.027). BMISDS was unchanged.

Conclusion
We were able to delineate 3 distinct phases of growth in PWS. Changes in our clinical practice have led to improvements in both height and BMI. GH therapy was associated with an increase in height and stabilisation of BMI.

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P045
Growth hormone secreting adenomas and the challenges of treatment in children
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Introduction
In children, tumours occupying the pituitary fossa are mainly craniopharyngioma (80–90%) and pituitary adenomas (2–3%). We present two cases of pituitary adenoma and the challenging management when complete surgical resection is not possible. Case 1: A 13.5 year old girl presented with tall stature. Pituitary hormone profile revealed high IGF1 123 nmol/l (24.5–56) and prolactin 722 mU/l (102–496). Growth hormone (GH) was not completely suppressed on the oral glucose tolerance test (nadir 4.5 mg/l). She was in established puberty although no menarche. MRI showed pituitary enlargement with no definite microadenoma. She underwent transphenoidal pituitary exploration. An adenoma was removed and immunohistochemistry showed GH and prolactin expression in the tumour cells. Post-operatively, GH suppressed to 0.3 µg/l on OGTT. During the following year, IGF1 rose to 85.4 nmol/l. Repeat MRI revealed bulky pituitary, suggestive of residual tumour. She underwent second transphenoidal surgery with evidence of TSH, ACTH and gonadotrophin deficiency on follow up with a suppressed GH level of 0.1 µg/l on OGTT and low IGF1 9.8 nmol/l (34.8–64.2). Case 2: An 11.4 year old boy presented with a 6-month history of worsening headaches and an intracranial mass on CT scan. Clinical examination revealed features of gigantism. Hormonal assessment showed grossly elevated random GH – 722 µg/l and IGF1 at 77.6 nmol/l (11.1–32.3). Rest of anterior pituitary function appeared normal and he was in early puberty. MRI brain showed a large macroadenoma with suprasellar extension. Ophthalmology assessment confirmed somatomatotroph adenoma. Post-operatively IGF1 remained elevated and Lanreotide autogel 60mg was commenced with minimal effect on IGF1 levels after 3 months. He underwent further surgery (transcranial) and complete resection proved impossible. Medical treatment intensified with increased dose of Lanreotide without achieving biochemical control. He progresses through puberty with a height velocity of 1.4 cm/yr. Recent MRI showed increased intracranial mass on CT scan.

Conclusion
These cases demonstrate the challenges of managing pituitary adenomas in children particularly when complete surgical resection is not possible and evidence for optimal management in this age group limited.

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**P046**

**Association between congenital hypopituitarism and agenesis of the internal carotid artery**

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Introduction

Abnormalities of the Internal Carotid Artery (ICA) are rare and agenesis has an estimated incidence of 0.01% in the general population. We here report a probable association with congenital hypopituitarism.

Case report

A baby girl presented with respiratory distress after the birth and 1 month later, because of prolonged jaundice, was found to have low FT3, FT4, and TSH (FT3 was <2.3 pmol/l FT4 was <3.5 pmol/l TSH which was <0.1 microIU/l). She also had an undetectable Cortisol (<0.9 mmol/l) and IGFI (<3.3 mmol/l). MRI imaging demonstrated an ectopic posterior pituitary gland and the anterior pituitary gland appeared very small/hypoplastic. It also showed absence of the right ICA with an anastomotic vessel arising from the cavernous segment of the left ICA, crossing the midline, reconstituting the terminal right ICA and forming the right Middle Carotid Artery further on. Genetic testing of the patient using a targeted gene approach revealed likely pathogenic variants in HESX1 and OTX1 genes which encode proteins with structural relevance to the intracranial abnormalities described. The clinical significance of these variants and their potentially additive effect contributing to disease phenotype will be discussed.

Conclusions

The case report described is about a 5 months old patient with congenital hypopituitarism secondary to a hypoplasia of the pituitary gland, an ectopic posterior pituitary gland and the agenesis of the ICA. So far this is the 14th case with the association between congenital hypopituitarism and abnormalities of the ICA and the 4th one before the first year of age. Considering that a reduction of the blood supply is very unlikely to be the cause of the hypopituitarism (n = 1), the hypothesis of a new, unknown, genetic mutation that could have caused both the pituitary hypoplasia and the agenesis of the ICA seems to be more likely.

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**P047**

**Frequency of cranial MRI abnormalities in isolated growth hormone deficiency over a 20-year period**

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Background

Patients with isolated growth hormone deficiency (GHD) will routinely have an MRI scan of the pituitary and brain to assess pituitary size and presence of any intracranial lesions. The result may change the threshold for monitoring for further hormone deficiencies. However the test may also detect unexpected or unrelated abnormalities.

Aim

To review the incidence of normal and abnormal MRI scans in children with a diagnosis of isolated GHD.

Methods

The biochemistry and MRI reports of children with isolated GHD (peak growth hormone (GH) <7 ug/l) born in a tertiary centre between 1997 from 2017 were reviewed. All children with multiple pituitary hormone deficiencies, septo-optic dysplasia spectrum, and those children with known malignancies were excluded. Extracranial abnormalities such as sinustitis and mucosal thickening were excluded.

Results

81 children were diagnosed with isolated GHD. 71 children had MRI results available (4 pending). Of these, 38 (54%) were reported as normal and 33 (46%) abnormal. The median age of diagnosis was 5.99 years (range: 0.62 to 18.69), with a median height SDS of −3.45 (−0.33 to −8.41) at diagnosis. The median GH level was 3.25 ug/l. The rate of MRI abnormalities was similar in the group above and below the median GH level. Of those with MRI abnormalities: 12 showed a small or hypoplastic pituitary gland, 2 had a microadenoma and 1 a cyst. 9 had an abnormal infundibulum and in 6 the posterior pituitary gland was not visible. A total of 15 MRI scans showed additional cranial anomalies (Chiari malformation (CM) n=4, arachnoid cysts (n=3), enlarged ventricles (n=1), small optic nerves (n=1), other (n=6)). 3 of the children with pituitary hypoplasia had a CM.

Conclusions

Nearly half the children with isolated GHD had an abnormal MRI scan. The most frequent abnormality is pituitary hypoplasia, followed by infundibulum and then posterior pituitary abnormalities. One fifth had additional cranial anomalies; with 4 (5.6%) having a CM. CM in GHD is an uncommon but recognised association, and patients with this condition may need additional monitoring if given growth hormone treatment.

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**P048**

**Growth hormone use in Prader-willi syndrome – Experience of a dedicated paediatric clinic**

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Introduction

In Prader-Willi Syndrome (PWS), multidisciplinary evaluation is recommended both prior to GH initiation and at regular intervals during treatment.

Methods


Results

An increasing number of children are attending the clinic each year (r = 0.993, P<0.0001). Overall, 44 children (76%) received GH therapy. In 2013–2017, 3948 children (81%) received GH, while 1021 (48%), 1026 (38%) and 1742 (40%) received GH in 2000–2004, 2005-2008 and 2009–2013 respectively (P<0.0001). Median age at starting GH during 2013–2017 was 2.13 years (1.0, 10.4) and was lower than those of commenced GH during 2000–2004 [4.9 years (4.4, 7.9)], 2005–2008 [3.7 years (3.6, 5.6)] and 2009–2012 [3.03 years (2.5, 7.0)] (P = 0.025). Before commencing GH, 72% of children had a sleep study performed and this was significantly higher in 2013–2017 (96%) compared to 2000–2012 (42%) (P<0.001). Overall, 53% of children had a spine x-ray, and this was significantly higher in 2013–2017 (67%) compared to 2000-2012 (25%) (0.018), IGFI/GH provocation test was performed in 86%, stimulated cortisol in 58%, thyroid function in 69%, fasting insulin/glucose in 67% and bone age in 11%. During annual monitoring, sleep studies (50% vs 9%, P<0.0001), spine x-rays (64% vs 9%, P<0.0001), thyroid function tests (44% vs 25%, P=0.032), IGFI (65% vs 42%, P = 0.01) and Hba1c (33% vs none, P<0.0001) were performed more frequently in 2013–2017 compared to 2000–2012, while bone age (5% vs 42%, P<0.0001) was performed less frequently.

Discussion

Our PWS clinic has witnessed an increased number of children attending the service and an increase in number of those children on GH and at younger ages. Multidisciplinary assessments have improved but as yet have not been universally adopted.

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**P049**

**Comparison of insulin tolerance test to arginine test for the diagnosis of growth hormone deficiency in children**

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Introduction

Growth hormone (GH) stimulation testing is necessary for the diagnosis of growth hormone deficiency (GHD). Insulin tolerance test (ITT) has been considered the gold standard for evaluating GHD in adults. However, it carries a risk of rare but severe adverse effects secondary to hypoglycaemia and is therefore avoided in many centres. There is no consensus for the first test in children.

Aim

Audit to compare ITT to Arginine test as a first line test for GH deficiency evaluation in children presenting with short stature.

Methods

All patients with possible GHD seen in the Endocrine Department of Birmingham Children’s Hospital between February 2015 and February 2017 were tested for GH secretion assessment. During 2015 all patients had ITT as a first test with 0.1 Units/kg of insulin, unless otherwise indicated, and if that was positive for GHD, a second test followed (usually Arginine/Glucagon). During 2016 Arginine...
provocation was used as a first line test, along with short synacthen test, and was followed by an ITT or Glucagon test. Patients with brain tumours or other conditions, not requiring a second test, and those undergoing end of growth test for adult GHD were excluded. Patients with a peak GH result <6.7 μg/L underwent a second test. Children >10 years with no signs of puberty were primed with stilboestrol (1 mg BD for 2 days).

Results
14/30 children with ITT first needed second test (47%), while 12/40 children with Arginine test first needed second test (30%) (P = 0.15). 64.3% of the children who had an ITT first had a false positive result for GHD, while only 8.3% of those who had Arginine test first had a false positive result (P = 0.0053). There was no correlation between lack of priming and false positive results.

Discussion
Even though ITT is considered the gold standard for the diagnosis of GHD, there is a high incidence of false positive results. Therefore, Arginine should be considered as a first line test, as it is a relatively safe test, easily applicable in most centres and could reduce the number of repeat stimulation tests. Larger studies are needed to confirm these results.

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**P050**

**Siblings with 3-M Syndrome show good response to Growth Hormone (GH) therapy over a 4 year follow-up growth data**

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Introduction
3M syndrome is a rare autosomal recessive condition that causes short stature, unusual facial features and skeletal abnormalities with normal intelligence. Mutations in CUL7, OBSL1 and CCDC8 genes have been identified as pathogenic. GH treatment outcomes for 3M syndrome appear controversial. Use of human recombinant GH for the treatment of short stature has been trialled in previous studies with some suggesting dysregulation in GH/IGF1 axis while others report no effect of GH treatment in 3M syndrome.

Aim
We report on 4 years of serial growth data in two siblings with a genetic diagnosis of 3M syndrome, which show a good response to GH therapy. Case 1: Term male infant with birth weight 2.3 kg and length of 39 cm (~ 5 SDS). At age 5, a genetic diagnosis of CUL7 gene mutation was made with characteristic phenotypic features such as triangular face, square-off chin, down-sloping palpebral fissures, hypertelorism, long eyelashes, a small fleshy nose with anteverted nares and a long philtrum. He had short 5th fingers with a single flexion crease. He had short 5th toes with clinodactyly and prominent heels. There was flattening of the thoracic spine. He commenced GH therapy at age 7.3 year at height SDS ~3.8; he is currently age 11.3 year with a height velocity of 6.7 cm/yr with a height SDS ~2.6. Case 2: Term male infant with birth weight 2.5 kg and length of 41 cm (~ 4 SDS) with similar facial features to his sibling. GH therapy was commenced at age 6yr with an initial height SDS ~3.8. He is currently age 10.3 year with a height velocity of 6.5 cm/yr and a height SDS ~2.8. Both siblings tested negative for GHD. Both remain clinically prepubertal. The DNA samples from parents confirm that they are both carriers of 3M syndrome. Both siblings are compound heterozygotes for the two pathogenic CUL7 gene mutations.

Conclusion
In contrast to published evidence of doubtful efficacy of GH, this case series illustrates successful height SDS increase over a 4 year follow-up. Clinicians should be aware of significant individual variation in relation to GH response in 3M syndrome.

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**P051**

**Nurses’ viewpoints on growth hormone delivery devices**

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Background
There are a variety of growth hormone delivery devices (GHDD) available to children requiring growth hormone (GH) therapy. Many paediatric endocrine nurses can offer patients and their families a choice of the products that are available, which can sometimes be overwhelming. However, factors such as a licenced clinical indications have to be considered, as well as cost. This study explored nurses viewpoints on GHDD.

Aim
The purpose of this project was to explore whether other factors should be considered when exploring choice of GHDD.

Methods
Participating nurses (N = 10) attended an interactive training session on all of the GHDD. Subsequently, each nurse was given a box of marketing materials for each GHDD, including training materials, patient information literature and DVDs. The nurses were given five case study scenarios on different conditions, and were advised to work in pairs. In their groups, the nurses were asked to feed back on their choice of GHDD, detailing why they had chosen that specific device, utilising a problem based learning approach. Themes were extrapolated using thematic analysis.

Results
Nurses had a variety of devices to choose from (N = 11): three groups had chosen different devices (N = 3) apart from two groups had chosen the same device. Influencing themes that emerged included: knowledge of patients learning difficulties, social and housing implications, child’s body composition, child friendly device design, and ease of use. Cost was also discussed, but was not the deciding factor for a final decision.

Conclusions
Themes that emerged from the study demonstrate that the nurses’ clinical judgement and prior knowledge of the patient’s needs is an intrinsic factor to consider when implementing patient choice in GHDD.

Clinical Implications
Further research needs to be conducted on a larger scale to examine nurses’ thoughts and opinions on the different GHDDs available, and the need to remain conscious of underlying issues which may not be obvious or apparent to the child and family. From this, a reduced number of choice of devices can therefore be demonstrated to children and their families, thereby giving the nurse more time to focus on the most appropriate devices.

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**P052**

**IGF-1 titration of GH in Turner syndrome**

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Introduction
The pathogenesis of short stature and growth failure in Turner syndrome (TS) is multifactorial, and includes low birthweight, ovarian failure and skeletal dysplasia. Although abnormalities of the GH/IGF1 axis are implicated, patients are not GH-deficient (GHD) and consequently non-GHD doses of GH are utilised ie. 45–50 μg/kg per day or 9.8 mg/m2 per week. Although initially used in GHD patients, IGF1 titration is increasingly being used in all GH-treated patients, with little evidence base.

Methods
Girls with TS attending a tertiary growth centre have been retrospectively reviewed. Girls were included if they had been IGF-1 titrated, received GH for at least a year and were more than a year from stopping GH.

Results
A total of 20 girls were identified, median age 12.8 years (range 7.1–16.2). Ten had a 45X karyotype; 7 were TS mosaic and the remainder TS variants. The mean(s.d.) GH dose was 25(6.7) mg/kg per day or 5.9(1.8) mg/m2 per week; none were receiving the currently recommended dose of GH. Twelve girls were also receiving oxandrolone, 10 oestrogen, including 8 who were receiving both. The mean(s.d.) height velocity was 5.2(1.4) cm/years or 2.1(0.9)SDS. IGF1 levels performed at the same time were within the normal range in 11 (but high normal in 2), and raised in 9. Four girls (2 with 45X karyotype) have achieved final height: all have a height > 150 cm (range 150.4–156.3) with a final height SDS for TS ranging from +1.6 to +2.7.

Conclusions
IGF1 titration in girls with TS results in much lower GH doses than those recommended within the GH license. Whilst growth is maintained and limited data indicates an acceptable final height, further work is required to assess whether this is equivalent to that achieved with standard doses of GH, and also whether IGF1 levels are raised at the onset of GH therapy, indicating IGF1 resistance.

DOI: 10.1530/endoabs.51.P052
**P053 Growth hormone treatment in a regional centre: licensed and unlicensed indications**

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Introduction
In the UK, GH therapy is licensed for use in GH deficiency, Turner Syndrome, Small for Gestational Age (SGA), Prader Willi Syndrome (PWS), SHOX deletion and Chronic Renal Failure (CRF). Worldwide there are a number of additional indications. The aim was to review the use of GH prescriptions in relation to indications and to evaluate if there were similarities or differences between the licensed and unlicensed groups.

Methods
All children started on GH over a 4 year period from 2013 to 2017 in a large tertiary hospital were reviewed. The primary indication was recorded and the pre-treatment height, weight and BMI SDS were calculated.

Results
167 children had GH (94 male, 73 females). 47% were for GHD. The median age for starting GH was 7.2 years. The median height SDS was −3.2 SDS, with the unlicensed group having the lowest median heights of all groups (−3.5 SDS). 32 (19%) of the children (22 male) did not have a licensed indication. Some uses included children with syndromic short stature (7), Russell Silver Syndrome (RSS)(3), Juvenile Idiopathic Arthritis (1), 3M (1), Cohrns (1). No cause was apparent in the majority of this group.

<table>
<thead>
<tr>
<th>Indication</th>
<th>GHD</th>
<th>SGA</th>
<th>Turner</th>
<th>CRF</th>
<th>PWS</th>
<th>Unlicensed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (% of total)</td>
<td>79 (47%)</td>
<td>35 (21%)</td>
<td>19 (11%)</td>
<td>8 (5%)</td>
<td>3 (2%)</td>
<td>20 (12%)</td>
<td>167 (100%)</td>
</tr>
<tr>
<td>Age Median (10th, 90th)</td>
<td>6.8 (5.3, 9.3)</td>
<td>5.9 (4.2, 7.1)</td>
<td>7.9 (5.2, 9.6)</td>
<td>5.6 (4.2, 6.2)</td>
<td>7.2 (4.6, 10.4)</td>
<td>12.1 (8.1, 18.2)</td>
<td></td>
</tr>
<tr>
<td>Height SDS</td>
<td>−3.1 (−4.6, −2.3)</td>
<td>−3.5 (−4.1, −2.8)</td>
<td>−2.9 (−3.6, −2.0)</td>
<td>−3.0 (−3.5, −2.6)</td>
<td>−3.2 (−3.6, −1.9)</td>
<td>−3.1 (−4.4, −1.5)</td>
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</tr>
<tr>
<td>Median (10th, 90th)</td>
<td>6.6</td>
<td>2.2</td>
<td>1.2</td>
<td>2.4</td>
<td>1.2</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Weight SDS</td>
<td>−1.8 (−3.6, −1.0)</td>
<td>−3.2 (−4.0, −1.7)</td>
<td>−2.6</td>
<td>−2.9 (−4.0, −2.1)</td>
<td>−4.5 (−6.2, 0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (10th, 90th)</td>
<td>0.9</td>
<td>0.2</td>
<td>0.1</td>
<td>0.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI SDS Median</td>
<td>0.8 (−1.1, 2.0)</td>
<td>2.0 (−0.9, 4.8)</td>
<td>0.4 (−1.1, 1.9)</td>
<td>0.8</td>
<td>0.0 (−1.2, 0.5)</td>
<td>0.6 (−1.7, 3.4)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions
The vast majority of GH use is for licensed indications. Thorough evaluations can potentially move children from licensed to unlicensed indications. The unlicensed group had the shortest heights. This indicates that there is judicious use for treatment depending on the individual circumstances in a centre serving a large population with complex pathologies.

DOI: 10.1530/endoabs.51.P053

**P055 Long-term unidentified complication of IGF-I treatment: Pulmonary hypertension**

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In this report, we described pulmonary hypertension (PH) in two patients with growth hormone insensitivity (GHI) who are taking IGF-I (somatropin) for long time.

Case 1
6-year-old male patient who has been followed for 4 years with the diagnosis of GHI. He was admitted to the hospital with complaints of hypoglycemia and severe short stature (height SDS: −7.4). His physical examination, laboratory findings (GHD<40 μg/dl, IGF-I<10ng/ml, and genetic analysis (GHR c.875G>A homozygous mutation on exon 8) confirmed that he had GHI syndrome. He has been taking increc doses within the range of 120–160 μg/kg per day. At the beginning of the therapy his ECO examination was normal. Drug dosage was implemented in accordance with growth velocity. Within the 4th year of his therapy, he has developed exercise induced cyanosis. We detected PH on his ECO examination.

Case 2
12 year-old girl who was admitted to the hospital at the age of 5 for the first time with the severe growth retardation had height SDS −7.8. Her physical examination, laboratory findings (gh>40 ng/ml, IGF-I<2 ng/ml) and genetic analysis (GHR c.875G>A homozygous mutation on exon 8) confirmed her diagnosis of GHI. At the beginning of the therapy her ECO examination showed only minimal mitral insufficiency. She was responding adequately to the treatment and the last height SDS was regressed to −3.5. Within the 4th year of her therapy she has developed adenoid vegetation and for this reason she was operated. For the last one year she has developed exercise induced cyanosis and PH was detected on her ECO examination. Those both patients with the same mutation and PH develops, we raise the question of whether this complication is a long-term IGF-I treatment or a late presented genotype-phenotype relationship.

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**P056 Embedding electronic growth charts into clinical practice at a children’s hospital**

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Background
Accurate evaluation of growth is a key assessment of child health, in the UK use of a paper growth chart is currently standard practice. Our trust had a drive to become paper light thus there needed to be a way to store growth data electronically. Growth data is often incompletely documented. A previous review of children’s outpatient attendances at our hospital found that across medical, surgical and tertiary specialties only 33% of children had growth data documented. We describe our experience and findings of implementing electronic growth charts (EGCs) in both inpatient and outpatient settings in a children’s hospital.

Methods
EGCs were developed maintaining the same visual identity and using the same optimal growth data as the UK-WHO growth charts. These were initially rolled out to surgical and tertiary specialties only 33% of children had growth data documented. We describe our experience and findings of implementing electronic growth charts (EGCs) in both inpatient and outpatient settings in a children’s hospital.

**Endocrine Abstracts (2017) Vol 51**

[DOI: 10.1530/endoabs.51.P055]
P057
Analysis of UK patients in PATRO children: a non-interventional study of the long-term safety and efficacy of Omnitrope in children
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Introduction
PATRO children is an international, non-interventional, longitudinal study of the long-term safety of a biosimilar recombinant human growth hormone (Omnitrope, Sandoz). In particular, the study assesses the diabetogenic potential of Omnitrope and the risk of malignancies. The long-term efficacy is a secondary objective of the study. Here we present safety and efficacy data of UK patients recruited since 2008, following an interim analysis in May 2017.

Methods
The study population includes infants, children and adolescents receiving Omnitrope therapy according to local prescribing information. All adverse events (AEs) are monitored and recorded for evaluation of Omnitrope safety. Laboratory values (including glucose metabolism) are requested at least once a year. Height standard deviation score (SDS), height velocity and height velocity SDS are calculated using height measurements and UK-specific reference tables to evaluate Omnitrope efficacy.

Results
As of May 2017, 217 patients from 14 sites had been enrolled in the UK. The mean (range) duration of treatment was 32.3 (0.0–106.9) months, with 114 (52.5%) patients completing three years of treatment. To date, 490 AEs have been reported in 119 (54.8%) patients, which were of mild or moderate intensity in 460/490 cases. 119 (54.8%) patients were suspected to be treatment-related, none of which were considered serious. Twelve treatment-related AEs (TRAEs) were mild in intensity, 13 (6.0%) patients were suspected to be treatment-related, none of which were considered serious. Twelve treatment-related AEs (TRAEs) were mild in intensity, four moderate and two unrecorded. Headache was the most common TRAE (n = 5 patients). Eight TRAEs had resolved and the remaining events were ongoing or unrecorded. There were no reports of diabetes mellitus or malignancies that were suspected to be related to Omnitrope treatment. After three years of treatment, Omnitrope resulted in improvements in most growth parameters across paediatric indications, irrespective of gender and pre-treatment status.

Conclusions
This interim analysis of patients from the UK demonstrates that Omnitrope is safe, well tolerated, and effective across paediatric indications. This analysis provides no evidence of an increased risk of developing diabetes mellitus or malignancies during Omnitrope treatment.

DOI: 10.1530/endoabs.51.P057

P058
Growth hormone treatment in children: an audit of compliance with NICE Guidance
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Background
In the UK, Growth Hormone (GH) is indicated for treatment of children with short stature secondary to growth hormone deficiency (GHD), Prader Willi syndrome (PWS), Turner syndrome (TS), SHOX gene mutation, chronic renal insufficiency and born small for gestational age (SGA).

Objectives
The aim was to assess the compliance of our local practice with the NICE guidance for GH therapy in children in addition to local guidance that TSHs and IGF-1 concentration should be checked annually in children with GHD whilst on treatment.

Methodology
All patients commenced on GH therapy by the Paediatric Endocrine Team at Addenbrooke’s Hospital between November 2014 and February 2017 were identified. Patients seen in outreach clinics were excluded as we did not have access to their records. Data were collected from clinical records.

Results
91 patients were identified. However only 47 met the inclusion criteria. 36 (47.7%) of patients were treated for GHD (18/36(50%) idiopathic and 18/36(50%) acquired), 5/47(10%) TS, 2/47(4%) PWS and 4/47(9%) SGA. All patients fulfilled local standards for commencement of GH for the documented indication. An appropriate GH dose for the indication was offered and documented in all patients. All patients were followed up within a specialist clinic with the appropriate MDT and all were offered their choice of GH device following discussion with our nurse specialists. 86% of patients with GHAD had (TFT’s) documented at diagnosis and annually. 11% patients with idiopathic GHD were treated for hypothyroidism in comparison to 55% patients with acquired GHD. 89% of patients with GH deficiency had IGF-1 evaluated at diagnosis and 86% annually. In patients with idiopathic GHD IGF-1 concentration prior to therapy was 17.6±12.9 mmol/l and 45.3±17.8 mmol/l a year after starting therapy (P<0.0001). In patients with acquired GHD IGF-1 concentration prior to therapy was 42.0±11.6 mmol/l and 47.4±13.3 mmol/l 12 months after starting treatment (P<0.0005). Differences between baseline and on GH were compared using a paired t-test.

Conclusions
There was good compliance with NICE guidance at diagnosis and implementation of GH treatment. Compliance with local guidance for annual surveillance of TFT’s and IGF-4 did not meet our target. We have raised awareness within the team and planned a re-audit for 2019.

DOI: 10.1530/endoabs.51.P058

P059
Improvement in motor function after growth hormone replacement in children with growth hormone deficiency and developmental delay
Reeba Joy, Verghese Mathew, Sanjay Gupta & Sandhya Jose
Hull Royal Infirmary, Hull, UK.

Introduction
GH has been proven to improve lean body mass and muscle strength. We report three cases where growth hormone replacement had a significant effect on gross motor function.

Case series
A 15 month old boy was born at 33 weeks of gestation. During infancy, he was noted to have developmental delay in his gross motor skills. He was commenced on replacement at a small dose in January 2015. At his next neurology review ten months later, he was able to walk unaided for short distance with an associated significant improvement in his muscle tone and general alertness. He was able to walk unaided for short distances. A 10 year old boy with developmental delay and was not able to walk. On investigation for short stature, he was noted to have isolated growth hormone deficiency and was commenced on replacement. 3 months later, he was noted to have made significant improvement in his muscle tone and general alertness. He was able to walk unaided for short distances. A 10 year old boy with global developmental delay and was not able to walk. On investigation for short stature, he was noted to have isolated growth hormone deficiency and was commenced on replacement. 3 months later, he was noted to have made significant improvement in his muscle tone and general alertness. He was able to walk unaided for short distances.
A novel IGSF1 mutation in a large Irish kindred highlights the need for family screening in the IGSF1 deficiency syndrome
Edna Roche1, Ann McGowran2, Olymnia Koulouri3, Marc-Olivier Tarjean3, Adeline K Nicholas4, Emmeline Heffernan4, Ranna El-Khouri2, Greta Lyons2, Luca Persani5, Mehul T Dattani6, Mark Gurnell2, Daniel J Bernard7 & Nadia Schoenmakers8
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Introduction
Loss-of-function mutations in IGSF1 result in X-linked congenital central hypothyroidism (CeCH), occurring in isolation or in association with additional primary hormone deficits. Intrafamilial penetrance is highly variable and a minority of heterozygous females are also affected. We identified and characterized a novel IGSF1 mutation and investigated its associated phenotypes in a large Irish kindred.

Methods/Design
A novel, hemizygous IGSF1 mutation was identified by direct sequencing in two brothers with CeCH and its functional consequences were characterized in vitro. Genotype-phenotype correlations were investigated in the wider kindred.

Results
The mutant IGSF1 protein (c.2318T>C, p.L773P) exhibited decreased plasma membrane expression in vitro due to impaired trafficking from the endoplasmic reticulum. Ten hemizygous males and 11 heterozygous females exhibited characteristic endocrine deficits. Ireland operates a TSH-based CH screening programme, which does not detect CeCH; therefore genetic ascertainment preceded biochemical diagnosis of moderate CH in five of seven boys, and their 75 year-old grandfather. Tissue manifestations of hypothyroidism were variable; normal free T3 (FT3) levels and low/low normal reverse T3 (rT3) measurements suggested that preferential deiodination of FT4 to FT3 may help maintain tissue euthyroidism in some individuals. However, jaundice, impaired growth, speech delay and obesity were associated with delayed diagnosis of endocrinopathy in seven cases in whom diagnosis was delayed.

Conclusion
As observed with other loss-of-function IGSF1 mutations, L773P results in variable penetrance IGSF1 deficiency syndrome. Our observations emphasise the need for multi-generation genetic ascertainment in affected families, especially where TSH-based CH screening programmes may fail to detect CeCH at birth.

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Diabetes
P061
Serum leptin levels in children with diabetes type 1 and its relation with diabetic nephropathy and retinopathy
Agnieszka Brandt1, Ewa Malinowska1, Katarzyna Zorena1 & Małgorzata Miśiwiec1
1Clinic of Pediatrics, Diabetology and Endocrinology, Gdansk, Poland; 2Medical University of Gdansk, Gdansk, Poland.

Introduction
Type 1 diabetes mellitus is one of the most common chronic diseases in children. Precise knowledge of the pathogenesis of diabetes mellitus type 1 and its chronic complications is the enormous challenge in modern diabetology. In recent years, the role of leptin in the pathogenesis of microvascular diabetic complications has been highlighted.

Aim
The aim of the study was to investigate serum leptin level and correlations between leptin levels and clinical and biochemical parameters in patients with diabetes mellitus.

Materials and methods
The study included 110 patients with diabetes type 1, lasting 6.05±3.25 years, aged 14.37±3.13 years from Clinic of Pediatrics, Diabetology and Endocrinology, Medical University of Gdansk, Poland and 50 matched controls. Patients with type 1 diabetes mellitus were divided in two subgroups with and without late diabetic complications (albuminuria and ophthalmological changes). In all included to the study children: HbA1c, C-reactive protein, lipid profile, albuminuria and serum leptin level with enzyme immunoassay were performed. Results
Statistically significant differences in serum leptin level, among patients with long-term type 1 diabetes mellitus (7.63±8.41 ng/ml) and group of healthy children (9.58±6.61 ng/ml) were shown with the highest level in control group (P=0.04). In patients with symptoms of late diabetic complications were reported significantly higher levels of leptin (9.88±8.74 ng/ml) compared with patients with DM1 who have no signs of diabetic nephropathy or retinopathy (7.15±7.91 ng/ml) (P=0.03). In addition, in patients with long-term type 1 diabetes mellitus significant positive correlations between leptin level and C-reactive protein level (R=0.21; P=0.02) was shown.

Conclusion
Increasing serum leptin level in children with long-standing DM1 and its positive correlation with C-reactive protein suggests a growing body inflammatory reaction in these patients and may predispose them to the development of diabetic microangiopathy.

DOI: 10.1530/endoabs.51.P061

P062
How effective is stabilisation at reducing HbA1c levels in children with T1DM on the high HbA1c pathway in Nottingham?
William Moreton, Vreni Verhoeven, Louise Denvir, Tabitha Randell & Pooja Sachdev
Nottingham Children’s Hospital, Nottingham, UK.

Background
Recent NPDA 15/16 data shows that nationally 17.9% of children and young people (CYP) with type 1 diabetes mellitus (T1DM) have a HbA1c level >80 mmol/mol (7.9% at Nottingham Children’s Hospital (NCH)), putting them at increased risk of diabetic ketoacidosis and long-term sequelae. To support patients on the high HbA1c pathway (>80 mmol/mol) at NCH, a 5-day inpatient stay for stabilisation is offered. The process involves daily re-education from paediatric diabetes specialist nurses and dietitians. Stabilisation quizzes are offered to identify gaps in knowledge and psychological or social care involvement is offered if necessary. Stabilisation is designed to educate and support patients and carers to improve the self-management of the young person’s condition.

Method
This single-centre study utilised retrospective data from medical records on all patients admitted to NCH for stabilisation between April 2014 and June 2017. Information on the age at admission, diabetes duration, pre-admission and post-admission HbA1c, psychological and social care involvement was recorded. The pre- and post-stabilisation HbA1c levels were then compared using Excel.

Results
In total 27 patients (51.8% female) were admitted, mean age at the time of stabilisation was 13.5-years (s.d. ±2.87). Two patients were admitted twice for stabilisation 72% of patients saw a reduction in their HbA1c value, measured at the next clinic appointment after stabilisation, compared with their pre-stabilisation value. The cohort’s mean pre-stabilisation HbA1c was 98.95 mmol/mol (s.d. ±15.89). 80% of patients saw a reduction in their HbA1c values 6 months post-stabilisation compared to their pre-admission HbA1c, with the mean HbA1c value 6 months’ post-stabilisation being 78.6 mmol/mol (s.d. ±20.67). 68% of patients saw a reduction in their HbA1c values 12 months’ post-stabilisation compared to their pre-admission HbA1c, with the mean HbA1c value 12 months’ post-stabilisation being 83.2 mmol/mol (s.d. ±20.56).

Conclusion
There is no clear evidence about how to best manage CYP with poorly controlled T1DM however, this study shows that stabilisation is effective at reducing HbA1c values, with the greatest decrease occurring six months after the inpatient stay.

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Endocrine Abstracts (2017) Vol 51
**P063**

**Glycaemic targets are achievable in children presenting in diabetic ketoacidosis: 6 month outcomes**

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1Clinic of Pediatrics, Diabetology and Endocrinology, Medical University of Gdans, Gdans, Poland; 2Alder Hey Children’s Hospital, Liverpool, UK.

Introduction and objective

Early glycaemic control is predictive of long-term control. Children who present with diabetic ketoacidosis (DKA) at the time of type 1 diabetes diagnosis are at risk for poorer long-term glycaemic control. Intensive education and support with multidisciplinary team (MDT) input is vital to overcoming these outcomes. In this retrospective analysis, we compared 6-month HbA1C outcomes in children with and without DKA at diagnosis.

Methods

All newly diagnosed children presenting to a large university teaching hospital over a 2-year period (Dec 2014 to Nov 2016) were included in the study (n = 57). All children received intensive MDT support geared towards rapidly achieving glycaemic goals within 3 to 6 months of diagnosis. Basal-Bolus therapy with multiple daily injections (MDI) with insulin adjustment according to carbohydrate counting was commenced in all patients, prior to discharge. Children were supported to achieve glycaemic goals through a tailorred approach including, as appropriate, rapid conversion to insulin pump therapy and glucose sensing using Continuous Glucose Monitoring (CGM) with alarms or Flash glucose monitoring, in addition to clinic, home and school visits and psychological support. HbA1C outcomes at 6 months after diagnosis were compared among children who presented in DKA vs. children who were not in DKA.

Results

There was a marked uptake of FGS/CGM use from 15% to 53% from 2015 to 2016, following paediatric approval.

<table>
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<th>DKA</th>
<th>No DKA</th>
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</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>16 (28%)</td>
<td>41 (72%)</td>
<td>57</td>
</tr>
<tr>
<td>&lt; 5 years</td>
<td>4 (23%)</td>
<td>7 (37%)</td>
<td>11 (19%)</td>
</tr>
<tr>
<td>Median HbA1c (diagnosis)/mmol per mol</td>
<td>118</td>
<td>115</td>
<td>115</td>
</tr>
<tr>
<td>Median HbA1c (6mo)/mmol per mol</td>
<td>51.5</td>
<td>49.0</td>
<td>50</td>
</tr>
<tr>
<td>Pump use by 6mo</td>
<td>11 (66%)</td>
<td>29 (70%)</td>
<td>70%</td>
</tr>
<tr>
<td>Pump use by 6mo by 6mo</td>
<td>3 (19%)</td>
<td>13 (32%)</td>
<td>26 (28%)</td>
</tr>
<tr>
<td>CGM with alarms</td>
<td>16%</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Flash Glucose Monitoring</td>
<td>7 (44%)</td>
<td>9 (22%)</td>
<td>9 (22%)</td>
</tr>
</tbody>
</table>

Conclusion

A large proportion of patients continue to present in DKA, however DKA at presentation is not a barrier to achieving early good glycaemic control. Multimodal intensive therapy tailored to the children and families’ needs is an effective strategy for achieving control in both groups.

DOI: 10.1530/endoaabs.51.P063

**P064**

**Hyperinsulinism Hyperammonemia (HI/HA) syndrome due to GLUD1 mutation: Phenotypic Variations Ranging from Late Presentation to Spontaneous Resolution**

Himal Gurung1, Myat Win2 & Nandu Thalange3

1Norfolk and Norwich University NHS Hospital, Norwich, UK; 2Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK.

Introduction

The hyperinsulinism/hyperammonemia (HI/HA) syndrome is the second most common cause of hyperinsulinemic hypoglycaemia (HH), caused by activating mutations in GLUD1 [which encodes the mitochondrial enzyme glutamate dehydrogenase (GDH)].

Methods

We describe phenotypic variations in three patients from 3 non-related families with HI/HA syndrome due to GLUD1 mutation.

Results

Patient 1, a 10-year-old Caucasian female born to non-consanguineous parents, presented with persistent hypoglycaemia and seizures at 7 months of age. Subsequent investigations during hypoglycaemia showed an inappropriately raised plasma insulin concentration (80 pmol/l) with supressed ketones and fatty acids confirming the diagnosis of HH. She had persistently high serum ammonia concentration [90–100 nmol/l (normal <70 nmol/l)]. A protein load test demonstrated protein-sensitive HH. Diazoxide was commenced (5 mg/kg per day) with good response and anticonvulsants were weaned and discontinued. At 8 years of age, diazoxide was gradually weaned and stopped as some high blood glucose values were noted. A 20-hour controlled fast [off diazoxide] and an oral protein load test did not show any hypoglycaemia. She continues to remain free from seizures and hypoglycaemia. Patient 2, a 4-year-old Caucasian boy born to non-consanguineous parents, presented with seizures at 8 months of age requiring anticonvulsant medications. Initial investigations at local hospital did not suggest HH but further investigations during seizures at 4 years of age confirmed HH. Diazoxide (6 mg/kg per day) was commenced with a good response and he continues on anticonvulsants. Patient 3, an 11-year-old Caucasian girl born to Polish non-consanguineous parents with a history of transient neonatal hypoglycaemia, presented with absence seizures at 12 months of age. Further investigations confirmed HI/HA with hyperammoninaemia and good response to diazoxide (10 mg/kg per day) was noted and she did not require anticonvulsants. The genetic analysis in all three patients confirmed GLUD1 mutation.

Conclusions

The cases highlight the highly variable presentation of HI/HA syndrome leading to diagnostic challenges. Mild persistent hyperammonemia and hypoglycaemia in patients presenting with seizures should suggest HI/HA syndrome. Diazoxide may help weaning anticonvulsants in some patients. We noted complete spontaneous resolution of HH/HA in one patient at the age of 8 years, which has not been previously reported in the literature.

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**P065**

**Quality of life outcomes and glycaemic control in a paediatric diabetes population since the introduction of the Best Practice Tariff**

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Introduction

The recent increase in type 1 diabetes at a large university teaching hospital (2015 to 2016, following paediatric approval) was associated with an improvement in the self-reported QoL of young people with diabetes. Method

In 2011, n = 55 children and young people with diabetes completed the Generic Pediatric Diabetes Best Practice Tariff, which includes increased contact with the multi-disciplinary team and uptake of psychology support, has impacted positively on the quality of life (QoL) and glycaemic control of young people with diabetes.

Results

The 2015 cohort included n = 74 with type 1 (T1DM) and n = 4 with type 2 diabetes (T2DM) at median (range): age of diabetes diagnosis 8.0 (1.2–17.5) years, age of psychology assessment 15.1 (7.7–19.3) years and HbA1C 74 (38–130) mmol/mol. QoL scores relating to diabetes management and treatment adherence were significantly higher in the 2015 cohort compared with the 2011 cohort at mean(SD): treatment Barriers score 77.4(18.4) vs 68.9(19.0), P = 0.012; Treatment Adherence score 83.1(14.3) vs 77.6(15.5), P = 0.036. Further analyses performed on the 2015 cohort, revealed that older children (r = -0.24, P = 0.036), girls (mean(SD): girls 73.7(13.6) vs boys 81.7(11.2), P = 0.007) and patients with T2DM (57.3(5.3) vs 78.8(12.4), P = 0.003) had lower Generic PedQL scores. HbA1C was significantly associated with age (r = 0.26, P = 0.025) and with lower QoL, relating to diabetes symptoms (r = -0.24, P = 0.034). Regression analysis showed that age was the strongest predictor of poor glycaemic control correcting for age, diabetes and gender treatment.

Conclusion

Increased provision of support following the introduction of the Best Practice Tariff in 2012, was associated with an improvement in the self-reported QoL of children and young people in relation to the management of their condition. However, patients who were female, older and with T2DM were at greater risk of poor QoL. The finding that poorer glycaemic control was related to specific areas of QoL should be explored further.

DOI: 10.1530/endoaabs.51.P065
Clinical implications of changes to fluid therapy in 2015 BSPED DKA guideline – a comparative audit, pre and post guideline implementation. Selena Snow1, Nicola Bridges2, Kingi Aminu1, Kyriaki Alatzoglou1 & Saji Alexander1
1Monash University, Melbourne, Australia; 2Chelsea and Westminster Hospital NHS Foundation Trust, London, UK.

Introduction
In August 2015, the British Society for Paediatric Endocrinology and Diabetes (BSPED) released new guidelines for the management of DKA. These new guidelines recommended a much more conservative approach for fluid management in order to reduce the risk of cerebral oedema.

Aim
Based on local anecdotal evidence, we hypothesised that with the new guidelines, we had to increase maintenance fluid infusion rates more often and that the children required a longer duration of IV therapy.

Method
We collected data from all paediatric patients who presented with DKA to a large inner city hospital from January 2015 to May 2017. The results are analysed in two groups – ‘pre-2015’ and ‘2015’ implementation. The two groups were compared for any change in fluid therapy within 8 h, duration of IV therapy, and duration taken to normalise pH (pH > 7.3).

Results
A total of 25 children (pre2015- n = 10; 2015- n = 15) were studied. The groups were comparable for age, sex and frequency of new diagnosis. The mean presenting pH (7.108 vs. 7.119) and bicarbonate was lower in the pre-2015 group. Plasma fluids was administered far less frequently (33.3% vs 69%) since the 2015 guideline. Only one child needed a change in rate of IV fluid therapy, pre 2015. In contrast, 33.3% (5/15) children in the 2015 group needed a change in therapy (two- increase in rate, two- additional fluid bolus and 1 needing both). The new guideline recommended a fluid infusion rate lower by up to 39-99ml/h on average (range 20–92.5 ml/h). Interestingly, the mean duration of IV therapy was longer in the pre2015 group (13.5 vs 10.53 hrs). There were no complications in either groups.

Discussion
This audit showed that a higher proportion of children needed a change in their fluid therapy when treated according to the current 2015 paediatric DKA guidelines, compared with the previous guideline. Clinicians should be vigilant to the considerable reduction in infusion rates, especially in those with a higher weight. However, acidosis in this group recovered quicker. Further studies should look at whether the new fluid guidelines have changed time spent in hospital or reduced adverse events.

DOI: 10.1530/endoabs.51.P066

Siblings with monogenic ABCC8 diabetes – phenotypic variability and implications
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Introduction
ABCC8 gene mutations cause transient and permanent forms of neonatal diabetes with variable modes of inheritance. Almost all patients present with diabetes under 6 months old with rare cases upto 12 months. We report 2 siblings with diabetes and identical homozygous mutations of the ABCC8 gene, one of whom presented classically under 6 months old and the other unusually at 3 years of age.

Cases
The index case, a British Pakistani female, was diagnosed with diabetes aged 3 years following investigation for recurrent napkin dermatitis. She presented with elevated blood glucose (20.3 mmol/l), glycosuria (4 +) and HbA1C of 102 mmol/l, but was not in diabetic ketoacidosis (DKA). Her parents are first cousins and there was no family history of diabetes. She was born at term, weighing 3.3 kg, with no other significant past medical history. Her physical examination was normal and she was not obese. A presumptive diagnosis of Type 1 diabetes was made and basal bolus insulin regime was initiated. Subsequent results of islet cell and glutamic acid decarboxylase antibodies were negative. Three months later, her brother was born at term, weighing 2 kg. At 10 weeks age he presented with loose stools, weight loss, and DKA (pH 7.27, base excess —11, glucose 60 mmol/l). He was treated according to the DKA protocol and then transferred to day for intermediate-acting subcutaneous insulin. Genetic analysis (Exeter Genetics Service) of both siblings subsequently demonstrated identical homozygous missense mutation (c.320T>G) at exon 26 for the ABCC8 gene encoding SUR subunit of KATP channels on pancreatic beta cells. Both siblings were then switched from subcutaneous insulin to oral glibenclamide with continuation of target glycaemic control (HbA1c < 38 mmol/mol).

Conclusions
Mutation analysis for neonatal diabetes is currently offered to all infants diagnosed with diabetes under 9 months old. Without the classic presentation of the younger sibling, genetic analysis for ABCC8 would not have been undertaken so promptly. The criteria for genetic screening in children with diabetes from consanguinuous family needs consideration. The different presentations between the 2 siblings with the same mutation emphasises the difficulties with genotypic–phenotypic correlations that can occur in monogenic diabetes.

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Review of diabetes antibody profile in children and young people with diabetes
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Aim
Previous studies have shown that diabetes associated antibodies are present in 85–90% of patients with Type 1 diabetes. NICE guidelines do not suggest routine use of antibodies screening at initial presentation. The aim of our study was to identify the incidence of antibody positivity in our centre and also review the clinical profile of children diagnosed with diabetes who were antibodies negative.

Method
Retrospective case notes review of 243 newly diagnosed diabetic children (<18 years) between January 2010 and December 2016. The children were tested for Islet cell antibody, Anti-GAD antibody and IA2 antibodies.

Results
Diabetes autoantibodies testing was done in 224/243 patients (92.2%). 187/224 (83.48%) tested positive for diabetes autoantibody. 53 patients had three autoantibodies present; 69 had two autoantibodies present and 65 had one autoantibody present, confirming the diagnosis of Type 1 diabetes. Remaining 37 (16.5%) tested negative for antibodies. 24/37 children were presumed type 1 diabetes; 8 children had Type 2 diabetes, all of them obese with median BMI 34 kg/m², 1 child had Maturity onset diabetes of the Young, 2 had drug induced diabetes. 1 had permanent neonatal diabetes and 1 had diabetes secondary to pancreatitis. Eight out of 24 patients treated as Type 1 diabetes presented in DKA (32%) at diagnosis. Rest 16 patients were noted to have median insulin requirement of 0.8 units/kg/day during follow-up after 1 year. We compared autoantibody positive and negative groups in children with type 1 diabetes; no difference was noted in the mean age at diagnosis (8.8 vs 8.9 years). DKA at presentation (31.5% vs 32%) and mean HbA1C levels at presentation (99 vs 97 mmol/mol).

Conclusion
187 out of 211 (88.7%) children and young people with type 1 diabetes have at least 1 positive diabetes antibodies in line with incidence reported in the literature. There was no significant difference between antibody positive and negative type 1 diabetes children. Children diagnosed as Type 1 diabetes that are antibody negative will need further evaluation if there is no natural history of type 1 diabetes.

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A review of patients not carbohydrate counting in a Paediatric Diabetes Clinic
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Nottingham Children’s Hospital, Nottingham, UK.

Background
NICE recommendation is to use multiple daily insulin injections and to offer level 3 carbohydrate-counting education at diagnosis of Type 1 diabetes (TIDM), and at least at annual intervals thereafter. Best Practice Tariff states that every person with diabetes should be offered at least one additional appointment per year with a paediatric dietitian with training in diabetes. Our aim was to identify details of all the patients in the current cohort who were not carbohydrate counting, explore the reasons for this and provide additional support to struggling families.
P070

Does maximising the use of bolus calculator glucose meters improves glycaemic control in children and adolescents with type 1 diabetes?

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St George’s University Hospital NHS Foundation Trust, London, UK.

Introduction
Bolus calculator glucose meters (BCGM) facilitate self-management of patients with type 1 diabetes (T1DM). However, their effectiveness is dependent on the accuracy of the data entered, use of their smart functions and adherence to the insulin dosages advised. This study investigates whether optimising the use of BCGM is associated with better glycaemic control in children and adolescents with T1DM, and obstacles to preventing their effective use.

Methods
Subjects were BCGM (AccuChek Expert meter) users with T1DM on a daily multiple injection (MDI) regimen under a single paediatric diabetes centre in London. Patient demographics (current age, gender, age and time since diagnosis, deprivation scores) and most recent HbA1c were collected from the clinic database. Capillary blood glucose (CBG) and carbohydrate (CHO) recordings over 1 month within the corresponding 3-month period of HbA1c collected were recorded. Data were entered, long term non-compliant, taught but struggling with implementation, developing their ability, stable on fixed rate. Results: patients (%) were not carbohydrate counting; 57% were boys, 28% > 16 years, 28% <10 years. Average HbA1c 64 (SD 1.689) significantly higher than the clinical overall at 60.9 (SD 16.2). 62% had been seen by a dietician in the last year. All patients were on MDI (multiple daily injections). Three patients were newly diagnosed. 4 patients long term non-compliant. 5 patients had been taught carbohydrate counting but struggling with implementation. 1 patient was developing their abilities. 3 patients stable on fixed rate insulin and the other 4 patients were a combination of these reasons.

Conclusions
Even though only a small percentage of our T1DM patients do not carbohydrate count, the reasons for this need to be identified clearly and additional support offered to patients and carers especially in the context of undiagnosed learning disability. While an insulin carbohydrate ratio is documented regularly for each patient who does carbohydrate count, the level of carbohydrate counting (level 1/2/3) or if the ratio is being used effectively, is not routinely documented which needs to improve.

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P071

Patient centred multidisciplinary approach to diabetes education, using puppet making and film skills to facilitate learning

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Introduction
For the last 2 years we have been giving regular diabetes education sessions in conjunction with our hospital school, based around maths skills. These went well, but we wanted to develop these further, making them more patient centred. We gained a grant from the Diabetes Research and Wellness Foundation and designed a 4 day programme with ‘The Puppet Project’ and ‘WAC arts’. This was done very much in collaboration with our hospital school who are very accomplished educators.

Method/design
10 young people attended and split into two groups over four separate sessions. On arrival they wrote each other name tags and we did an ice breaker. Every young person made a puppet, and during this time we had regular break out ‘circle time’ to discuss what diabetes meant to them and also for them to ask questions ‘How do i get diabetes?’ ‘Why did this person say..., about my diabetes?’ It isn’t true is it that sugar gave me diabetes?’ ‘What is a virus’ etc. The young people were told that they were going to design a diabetes script for their puppets and the theme was up to them as a group. Then they were to film them show themselves with their new skills.

Results
We believe the project was a resounding success as all the young people were desperate to ensure they could make all sessions, becoming increasingly vocal and confident. We obtained eight questionnaires from the ten participants and asked them to score each question out of five (average scores in brackets): useful talking to other children with diabetes (4.3), more confident discussing the myths about diabetes (3.5), making puppets was a good way to meet other children with diabetes (4.8), would rather describe their experiences on video rather than face-to-face (4.3), more likely to watch a video rather than listen to a doctor (4.4)

Conclusion
This project took diabetes education to a new level. All young people with diabetes should have the opportunity to learn in an exciting environment. We plan to role this out further across our trust with our sister hospitals.

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P072

Tackling the challenge of training and keeping paediatric doctors up-to-date in Type 1 diabetes following recent service improvements

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Introduction
The current estimate of prevalence of type I diabetes in children under 15 years in England and Wales is 187.7 per 100,000, with an estimated 31,500 children with diabetes under 19 years. It is a condition that is becoming increasingly common with 28.2 per 100,000 new diagnoses each year. Increasingly, management of these children is led by children and young people diabetes(CYPD) multi-disciplinary teams(MDT). As a result, despite better outcomes in diabetes care, it is proposed that paediatric doctors feel increasingly less confident in the management of paediatric diabetes. Even though trainees have time earmarked for attending clinic they rarely complete their diabetes curriculum and risk becoming under skilled to adequately manage such scenarios. This project aimed to coach paediatric doctors through a diabetes masterclass, with the view to enhance knowledge and confidence in management of paediatric diabetes care as well as to fulfil the RCPCH Diabetes curriculum.

Method
Paediatric doctors at our trust did a questionnaire covering: new diagnosis, discussions to families, diabetic ketoacidosis, hypoglycaemia, carbohydrate counting, insulin; prescribing with dose adjustment and ongoing management in outpatients. This was followed by a two hour diabetes masterclass delivered by the CYPD MDT and then a post session questionnaire. Paediatric consultants also participated.

Results
19 doctors took the pre masterclass questionnaire which was standard set and had a total score of 48. The mean score was 29.2 (61%) with breakdown as follows; Level 1 trainees 29.6 (61.7%), Level 2-3 trainees 33.6 (70%) and GP/foundation
trainees 26.5 (55%). After the masterclass 13 doctors took the same questionnaire again. The mean score had improved significantly to 37.6/48 (78.3%), an increase of 17.3% with higher means at every trainee level.

Conclusion
The results demonstrated the masterclass to be an extremely successful and valuable educational session. In addition, all paediatric doctors reported they felt more equipped with improved knowledge and confidence in dealing with the practical aspects of paediatric diabetes. In view of these positive outcomes, the CYPD MDT aim to deliver the masterclasses biannually to ensure competence in diabetes prevails amongst all paediatric doctors.

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P073
Safeguarding intervention and resolution of type 2 diabetes mellitus
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Introduction
Research has shown that Type 2 diabetes can be reversed in early stages if diet control is exercised. We present herewith a case of a 13-year old girl with Type 2 diabetes with a background of brain tumour, epilepsy and learning difficulties. Due to wider psychosocial issues the patient was placed in foster care. Adherence to healthy lifestyle principles led to weight loss and subsequent resolution of the Diabetes.

Case report
A 5-year-old Asian girl presented with seizures and hemiparesis. She was diagnosed with hypothyroidism, chronic low-grade glaucoma and was successfully treated with surgery and chemotherapy. The patient was regularly followed up at the late effect clinic. She was diagnosed with central precocious puberty at 7 years and treated with GnRH analogue. She was noted to be morbidly obese (BMI of 38.5 kg/m²) with acanthosis nigricans and irregular periods at 13 years. There was a family history of type 2 diabetes and hence she was closely monitored. She eventually developed type 2 diabetes with Hba1c levels of 53 mmol/mmol and an abnormal OGTT and was started on Metformin. Her fasting insulin levels were 107 miu/l with HOMA IR of 38. Meanwhile due to persistent social concerns, after much deliberation the child was removed from the family environment to foster care. Healthy diet along with regular exercise not only led to improvement in the weight profile but also enhanced her glycemic control. The Hba1c came down to 29 mmol/mmol and she was weaned off metformin. Her insulin levels came down to 23.7 miu/l with HOMA IR of 4.4. BMI dropped to 23 kg/m² and her periods became regular.

Conclusion
Though there is evidence to suggest that diet control and weight loss can lead to reversal of Type 2 diabetes, our case is unique with regards to her age, social profile and different management approach. It highlights the fact that a more holistic approach, which may seem extreme (as in this case) can yield desired results and hence should be considered.

<table>
<thead>
<tr>
<th></th>
<th>Pre intervention</th>
<th>Post intervention</th>
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<tr>
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<td>54.3</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>38.5</td>
<td>23.3</td>
</tr>
<tr>
<td>Fasting Glucose (mmol/l)</td>
<td>4.4</td>
<td>4.2</td>
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<tr>
<td>Fasting Insulin (miu/l)</td>
<td>194</td>
<td>23.7</td>
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<tr>
<td>HOMA</td>
<td>38</td>
<td>4.4</td>
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<tr>
<td>Hba1c (mmol/mmol)</td>
<td>53 (7.0%)</td>
<td>29 (4.8%)</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
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<td>1.2</td>
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</tbody>
</table>

P074
Carbohydrate counting in children and young people with type 1 diabetes – perceptions of healthcare professionals
Rachel Wray 1 & Lisa Robinson 1
1County Durham and Darlington NHS Foundation Trust, Darlington, UK; 2Newcastle University, Newcastle, UK.

Introduction
A systematic review and meta-analysis undertaken by Bell et al, 2013 found limited evidence to recommend carbohydrate counting as the standard dietary therapy in Type 1 Diabetes (T1DM). There seems to be a gap in current knowledge about comparing carbohydrate counting with other meal planning approaches for children and young people (CYP) with diabetes and the effects on clinical outcomes (Gillespie et al. 1998). Current literature also suggests that there are limitations in the approaches to insulin dosing primarily based on carbohydrate counting (Bell et al. 2015).

Aim
To explore the barriers and facilitators to carbohydrate counting from the perspective of nurses and dietitians working with CYP with T1DM.

Method
A qualitative study based on 8 semi-structured interviews with nurses and dietitians. The three dimensions (Process, Content and Context) of Pettigrew and Whipp’s theoretical framework were used to undertake structured data analysis.

Results
Participants perceived mathematical calculation and the school environment as barriers to carbohydrate counting. Nurses and dietitians found the concept of fat and protein counting to be complex but felt that it may facilitate diabetes management if educational resources and technology were developed to support it.

Conclusion
The outcome of the study suggests that carbohydrate counting has been embedded in clinical practice in the acute setting for patients diagnosed after the introduction of the Best Practice Tariff, but new models of working need to be looked at for teenage patients and in the school environment. Future research into the role of fat and protein counting in the provision of a stronger evidence base for clinical decision making also needs to be considered.

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P075
Deliberations and considerations before reaching a diagnosis of sulphonylurea overdose in children
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Sulphonylurea is an oral hypoglycaemic agent which stimulates the release of insulin from the pancreas and may induce raised plasma insulin and c-peptide levels. Sulphonylurea overdose is associated with profound refractory hypoglycaemia and can cause neurological deficit and acute renal failure. We report the case of a 15 year old non-diabetic girl who presented to our emergency department with sudden onset generalised tonic clonic (GTC) seizures secondary to hypoglycaemia of indeterminate cause. She was resuscitated with intravenous dextrose and discharged home the same day. She reattended the same evening with another GTC seizure and unrecordable blood glucose. On this occasion she was given besides the dextrose bolus, IV hydrocortisone and subcutaneous glucagon before she improved. She was commenced on 10% dextrose infusion, which was weaned over 24 hours followed by dextrose saline infusion, which was weaned after 48 hours when she achieved normoglycaemic status. History and examination revealed a girl with a history of self-harm, with ongoing psychosocial difficulties. Blood tests revealed stage 3 renal failure. Further investigations showed non-ketotic hypoglycaemia, with inappropriately raised plasma insulin and c-peptide suggestive of an endogenous insulin production and prompted further investigations to look for a cause of this endogenous production which was inconclusive. No other organic causes of hypoglycaemia could be found. The evolving biochemical and clinical picture of persistent hypoglycaemia and renal failure prompted urine toxicology screen for oral hypoglycaemic drugs which tested positive for gliclazide. There was no family history of diabetes forthcoming during repeated consultations until this result, when the family informed us of the patient’s late maternal grandfather being on gliclazide for Type 2 diabetes. The patient eventually confirmed she had ingested the tablets due to ongoing mental health difficulties. This confirmed the diagnosis of deliberate overdose with Sulphonylurea as a cause of refractory hypoglycaemia and acute renal injury. Our patient’s case highlights the importance of considering sulphonylurea overdose in paediatric cases of acute unexplained hypoglycaemia especially along with features of renal injury inspite of raised insulin and c-peptide levels. It argues the importance of screening for oral hypoglycaemic agents in extended toxicology screen for such patient in conjunction with careful history and examination.

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P076
Longitudinal audit of diabetes control with insulin pump therapy over seven years of treatment at Brighton – interim results
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Introduction
Continuous Subcutaneous Insulin Infusion (CSII) therapy is an established treatment of Type 1 Diabetes Mellitus (T1DM). NICE recommends a target HbA1c of £6.5% to minimise long-term complication risks1. CSII can be considered in patients £12 years and in those with high HbA1c (£8.5%) on multiple daily insulin injections, despite a high level of care2. The aim of this audit is to review diabetes control over time in T1DM patients managed with CSII at our hospital.

Methods
Retrospective review of diabetes control of T1DM patients managed with CSII at our hospital (Mar 2009–Jan 2017). All CSII patients with complete data, namely a locally recorded pre-CSII HbA1c and managed with CSII for at least one full year, were included. Pre-CSII HbA1c indicates mean of up to three HbA1c values prior to initiating CSII therapy; annual CSII HbA1c indicates mean of all HbA1c values recorded for a whole year on CSII.

Results
A total of 57 patients were managed with CSII at our hospital over the last 7 years; seven patients did not meet the inclusion criteria. There was a slight male preponderance (1.08:1) with a mean (s.d.) age at diagnosis/transfer of 7.6 (4.5) years and switching to CSII at 10.2 (4.8) years. The mean (s.d.) pre-CSII HbA1c was 8.4% (1.1) and first year HbA1c on CSII was 7.7% (0.7); thereafter it was 7.7% (0.8), 7.7% (0.9), 7.6% (0.8), 7.7 (0.8), 8.0% (1.3) and 7.6% (0.4) at 2, 3, 4, 5, 6 and 7 years respectively. Sub-group analysis showed that patients with better control pre-CSII generally maintained better control on CSII.

Conclusion
Mean annual HbA1c of CSII patients at our hospital have remained relatively stable over the seven-year study period; other studies however have demonstrated gradual worsening of diabetes control over time3. Patients with better control pre-CSII continued with good control on CSII suggesting additional protective factors within the patient/family context, other than CSII therapy. Due to the small number of patients, especially in the latter years, a larger longitudinal study would be helpful to confirm these findings.

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P077
Care of children with type 1 diabetes (T1D) whilst in school
Theodora Papanikolaou, Jan Ikdowiak, Roshini Tharmaratnam & Juliana Chizou Agwai
Sandwell and West Birmingham NHS Trust, Birmingham, UK.

Introduction
Previous UK study (2009) showed that parents rather than school staff were responsible for supporting the majority of children with insulin administration (IA) whilst at school. Since then, the law has changed and the Children and Families Act 2014 (UK) places a legal duty on schools to provide the right care and support.

Objective
To establish what support & facilities are available to Children & Young people (CYP) with T1D whilst in school.

Methodology
CYP with T1D attending Sandwell and West Birmingham Diabetes services completed a questionnaire (June 2016 to date). Questions related to if school staff were available to supervise IA or to offer assistance with carbohydrate counting (CC), presence or not of a designated room at school for blood glucose monitoring (BGM) and IA.

Results
In total, 71 children (5–16 years) attending 48 different schools completed the questionnaire; 25 in Primary School (PS), 46 in Secondary School (SS). Help with IA was required by 27/71 CYP. In 22/27, lunchtime IA was undertaken by school staff and in 5 by parents only. 64/71 CYP confirmed their school had a designated room for BGM and IA. In 57/1, there was no DR and two had to use the disabled toilet. In 8 cases, the DR did not have hand washing facilities. Only 54/71 CYP used the designated rooms, the rest preferring to use other locations. 21.7% of children in SS reported that they did not have access to sharps box. Regarding CC, 41/71 had packed lunches which were already carbohydrate counted from home. Of those that ate school dinners and required help with CC, help was given by school staff in 5/10.

Conclusion
Compared to 2009 study, there has been significant improvement in support for IA in schools. Further work needs to be done to ensure all CYP have access to the necessary facilities for IA, BGM and support with CC.

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P078
Email? Nah! Just send me a letter Doc. Or may be a text message
Poppy Bennett, Santwana Dwivedi, Gaurav Popli & Muhammad Javed Walsall Manor Hospital, Walsall, UK.

Aims and objectives
Poor attendance in clinics remains a concern shared by diabetes services nationally and internationally. We surveyed our children’s diabetes service users to identify local reasons for non-attendance. We used the opportunity to seek feedback from service users about service design.

Study population group
The group included parents/carers of children and young people who use children’s diabetes service delivered by Walsall Healthcare NHS Trust. The survey was also offered to children and young people over 12 years age.

Method
Survey questions followed multiple choice format with opportunity to add free text comments. The survey was offered online as well as in paper form. It was advertised on social media, clinics and via post. The results of both the online and paper version were collated and analysed.

Results
Total 51 returns were received. There was similar representation from all age groups. Girls/women constituted 49% of respondents. Commonest quoted reason for clinic non-attendance was not receiving letter or text reminder (29%) and receiving more than one letter with different dates (18%). For structured education, 32% would like annual and 25% would like twice yearly workshops. The preferred venue for workshops was hospital (34%) and health centre (25%). Most (62%) would prefer letter, text message, phone as mode of contact. Only 13% favoured email and 10% favoured social media. There were several comments to improve psychology provision. The service users expressed positive free-text comments about the service provided.

Conclusion
Issues with appointment letters or text message reminders were quoted as most common reason for non-attendance. This issue is shared with other departments in the hospital and is being looked at using trust-wide Listening into Action approach. Our current clinic structure and frequency, time and venue of educational sessions suits most of the respondents. Patients find seeing the whole team in one clinic and HbA1c measurement helpful. Contrary to our expectations, in information technology and social media age, respondents did not express much appetite to be contacted via email or social media. Majority preferred to receive letter or a text message reminder about clinic appointment.

DOI: 10.1530/endoabs.51.P078

P079
Understanding young people with diabetes: using experience based co-design to provide a patient-centred Diabetes Transition Service
Arpana Soni & Esther Freeman
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Aim
To use experience based co-design to improve the Diabetes Transition Service.

Design
Young people with diabetes (type 1 and 2) managed by a district general Paediatric Diabetes Team, were invited to attend a focus group. The focus group, held in a local café, after school, was facilitated by two members of the Paediatric Diabetes team and the Diabetes Psychologist. A graphic designer attended to support the young people to visually explore and communicate their experiences and ideas.

Results
Five young people attended the group, ages 15–17 years. Each attendee was invited to tell their diabetes story, followed by facilitated individual and group discussions about the transition service and health and social wellbeing of young people in relation to diabetes. Recurrent themes that emerged included: promotion of independence, consistency of care, access to information and support via email and the internet, and the desire for peer-support opportunities.

DOI: 10.1530/endoabs.51.P079
Acute treatment induced diabetic neuropathy in a 15 year old boy
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1Child Health Department, Ipswich Hospital, Ipswich, UK; 2Diabetes Centre, Ipswich Hospital, Ipswich, UK.

Acute Treatment-Induced Diabetic Neuropathy (ATDN) is a reversible small nerve fibre neuropathy involving pain and autonomic nerves precipitated by a rapid improvement in glycaemia. It is well described in adults with type 1 and 2 diabetes, but not in children. A 15 year old boy developed ATDN shortly after starting treatment for type 1 diabetes. He presented with polyuria and polydipsia and a blood glucose of 51.4 mmol/L. He was started on a basal bolus regime. Eight weeks later he developed severe burning pain in both feet, worse at night and pain on light touch (alldynia) for which his GP referred him for an orthopaedic opinion. A week later when seen in the paediatric service his pain was so intense and worse on ambulation that he was restricted to hobbling short distances preventing him from attending school. Clinical examination revealed normal lower limb reflexes, vibration, and 10gm monofilament sensation. There was hyperalgesia and alldynia in the feet. He had a resting tachycardia, suggestive of vagal denervation, but no postural hypotension or symptoms of autonomic neuropathy. His HbA1c had dropped from 168 mmol/mol (17.8%) at diagnosis to 48 mmol/mol (6.5%). He was diagnosed with ADTN. His pain responded well to simple analgesia and 6 weeks after onset had fully resolved; as had the tachycardia. Good diabetes control was maintained throughout. ATDN is a completely reversible neuropathy associated with disabling pain, distress and social disruption during its course. It is rare in childhood and this case is also unusual in its occurrence soon after diagnosis and resolution within weeks rather than the expected 12–24 months. The absence of large fibre abnormalities is typical and can lead to a delay in diagnosis. With increased treatment intensification from diagnosis, such cases may become more common so it is important that paediatric diabetes teams are aware of the condition.

DOI: 10.1530/endoabs.51.P082

Data analysis of the paediatric diabetes out of hours advice service – an 8 year review
Ruth Francks
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Project Aim
To review the data from the Out of hours service across the 8 years it has been running to identify common themes in calls, review service usage, identify gaps in patient/parental knowledge and review if admissions have reduced during this time.

Objectives
• To understand the frequency of calls to the out of hours service
• To highlight patterns and trends in the numbers and frequency of calls
• To identify the common themes in calls to highlight areas of improvement in education to C&YP and their families
• To determine if hospital admissions for diabetes related illness have reduced since the introduction of the Paediatric Diabetes Out of Hours Service

Method
(i) Analysis of data collected from all out of hours calls over an 8 year period
(ii) Review of hospital admission data
(iii) Patient feedback as to the usefulness of the service

Summary of Results
• A total of 1224 calls have been received since the service started in 2009 - Receive an average of 13.6 calls per month.
• May - August are the quietest periods for the service
• The service receives on average 2 calls overnight per month (22:00–08:00) and 3 calls per month on Saturday/Sunday
• High blood glucose/Low blood glucose & Sick day advice are the most common reason to call
• 78% of calls were from mums
• 87% of calls were resolved over the phone
• 6% of calls were referred to PAU (Paediatric Assessment Unit) for further assessment
• 88% of calls to the service were considered appropriate
• Admissions to hospital with diabetes related illness has fallen slightly since the service began

Conclusions
The out of hours service is an invaluable resource to our patients and families and one that is used widely. It deals with a wide range of calls and provides reassurance to families that one of their own diabetes nurses is available 24 hrs a day for urgent advice and support. It has highlighted that more emphasis and education is required for sick day management and management of high and low glucose levels to enable greater independence and confidence of our patients.

DOI: 10.1530/endoabs.51.P081
**P083**

Introduction of school-based diabetes clinics: Q1 project to engage frequent non-attenders and improve young people’s self-management

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Great North Children’s Hospital, Newcastle-upon-Tyne, UK.

Background
Optimizing attendance rates in outpatient’s clinics is important to ensure good clinical care and to avoid waste of scarce medical resources. In 2016, we identified a cohort of 17 teenagers that frequently Do Not Attend (DNA) the Paediatric Diabetes Multidisciplinary Clinics, compromising patient care and reducing compliance with NICE and BPT standards. As this cohort was found to be enrolled in a cluster of 5 schools we explored the benefit of taking diabetes clinics into school.

Objectives
Design and deliver additional school-based clinics to increase patient contact. Measure the effect of the intervention on HbA1c and other patient related outcomes, hospital resources, attendance and adherence to standards.

Patients and methods
Between January and June 2017, quarterly school-based clinics were offered to all teenagers with T1DM in these 5 schools. A semi-structured interview was administered to identify their concerns about diabetes. Patients were invited to provide feedback about hospital clinics, HbA1c was checked and glucose meters downloaded. Outcome data was compared with previous 9 months. Families were informed by letter, allowing them to opt-out. 34 teenagers were targeted (17 initially identified as frequent non-attenders and 17 controls at same schools). 50% had pre-intervention HbA1c > 75 mmol/mol.

Results
The hospital DNA rate was reduced in the intervention group by 50%. School-based clinics improved clinical contacts, providing opportunities to empower teenagers and to re-engage with patients that were difficult to reach pre-intervention. Gaps in patient’s knowledge and psychosocial/lifestyle concerns not previously appreciated by the diabetes team were identified in 50% of the patients. These issues were addressed on an individual basis, involving parents, relevant diabetes healthcare professionals and school’s nurses/carers. Negative feedback included anxiety about results, waiting times and parental or healthcare professional’s judgemental attitudes. HbA1c levels remained unchanged over the study period. Five patients in the control group who were at imminent risk of reaching HbA1c levels > 75 mmol/mol, managed to stabilise their glycaemic control during the intervention.

Conclusions
(i) This pilot shows promise in improving contact in this difficult to reach group
(ii) School clinics are an effective way to engage young people in self-management, actively preparing them for transition.
(iii) A well powered trial may allow HbA1c improvement to be shown.

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**P084**

Effectiveness of education programmes in type 1 diabetes for children and parents, comparing multiple daily injection and insulin pump groups

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Background
Structured education is offered by healthcare professionals for patients with type 1 diabetes and their families. The aims of education are to ensure competency in self-management and improve self-efficacy and glycaemic control. Therefore, this results in a reduced risk of adverse events related to diabetes and upholds quality of life.

Aims
To evaluate the effectiveness of education programmes offered by healthcare professionals in Southampton Children’s Hospital, comparing between insulin pump and multiple daily injection (MDI) groups, by assessing the competency of children and parents at managing problem-based scenarios related to type 1 diabetes.

Methods
Problem-based questionnaires were distributed to children and parents in two separate groups depending on the child’s method of insulin administration; MDI (n = 12) and insulin pump (n = 18). Participants were aged 11 to 18, having been diagnosed with type 1 diabetes for at least two years, or a parent of a child with diabetes. Questionnaires were marked using a flexible framework and scores were recorded as percentages.

Results
The average score of the cohort (n = 30) was 51.34%. The adult group (n = 15) averaged 52.43% (S.D. = 11.89), whereas the child group (n = 15) total mean was 50.25% (S.D. = 12.12). Using an unpaired T test, the results between the two groups were non-significant (P = 0.623). When comparing scores of participants by method of insulin administration, the mean of pump (n = 18) and MDI (n = 12) groups were 53.49% (S.D. = 13.70) and 48.11% (S.D. = 7.81) respectively. An unpaired T test was performed again, confirming no significant relationship between scores and method of insulin therapy (P = 0.229).

Conclusions
No association was identified between questionnaire scores and method of insulin therapy. Also, there was no relationship between scores and whether the participant was a child or parent. However, the average score in each group was lower than expected and therefore, problem-based diabetes education needs to be improved to ensure optimal competency of patients and families, resulting in a better quality of life.

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**P086**

Short-term use of the flash glucose monitoring system increases insulin bolusing and self-confidence in paediatric Type 1 diabetes

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Introduction
The Flash glucose monitoring system (FGS) has recently received a licence for children and young people aged 4-17 years with Type 1 diabetes (TID) in the United Kingdom. Although many families attending a single UK diabetes centre reporting utilising FGS even prior to its licence we aimed to assess the patient experience.

**P085**

Differences in HbA1c among different ethnicities

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Introduction
Several studies have described ethnic differences in HbA1c. Non-Caucasian patients have been found to have a higher HbA1c than the Caucasian ones. These differences have often been attributed to disparities in access to medical care or quality of the care. However differences in HbA1c in ethnic minorities could also relate to biological factors so we looked at mean levels of glycaemia. The aim of our study was to observe if there is a similar correlation between HbA1c and mean glucose among different ethnicities and if, at the same level of mean glucose, the HbA1c of Non-Caucasian patients was higher than the Caucasian ones.

Methods
We enrolled 179 patients with type 1 and type 2 diabetes (35.19% blacks and 64.81% whites) from 3 different hospitals of London who had checked the glycaemia at least twice a day. From each patient’s history we chose a HbA1c value and, starting from the date of that value, we collected, via Diasend®, the correspondent mean glucose of the previous 3 months.

Results
Mean HbA1c of non-caucasian patients was 8.88 ± 1.69 while caucasian patients’ mean HbA1c was 8.17 ± 1.17 (P < 0.001). Differences between mean glycaemia of caucasian and non caucasian patients was not statistically significant: 11.06 mmol/l ± 2.3 for blacks vs 10.9 ± 2.27 for whites (P = 0.83). The correlation between linear regression showed that at a same level of mean glycaemia black patients have higher HbA1c than white patients (P < 0.001) and that this difference doesn’t change if the disease duration changes. (P < 0.01)

Conclusions
In the group of black patients with diabetes the HbA1c was higher than other groups for a similar level of mean glucose. This could indicate that there are other factors that may influence the final value of HbA1c in this ethnic group (interindividual variation in red cells turnover, genetic variation in haemoglobin glycation).

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P087
An audit of our adherence to BSPED/ISPAD guidelines in the management of DM in a Secondary Level Irish Hospital
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Aims
We sought to audit our practice with the primary aim of improving diabetes self-management and improved insulin delivery. Further studies are needed to determine whether sustained use of UGS improves insulin adherence and glycaemic control.

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P088
A case of learning difficulties, dysmorphic features, Type 2 diabetes, ulcerative colitis and suspected Albright osteodystrophy
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A 17 year old young lady with known learning difficulties, dysmorphic features and ulcerative colitis presented with hyperglycaemia aged 15 years and 8 months. To diagnose her learning difficulties and dysmorphisms: Karyotype and buccal swabs were normal with no evidence of mosaic Downs, normal FISH for Smith Magenis syndrome (17p deletion), DNA testing for Prader Willi syndrome showed biparental inheritance (therefore ruling out diagnosis except in very rare cases), Fragile X molecular testing normal. EHMT1 no mutations (sequencing and MLPA). Most recent tests through the Deciphering Developmental Disorders study results show GNAS1 variation associated with Albright Hereditary Osteodystrophy. The GNAS1 variant is classed as a VUS (variant of uncertain significance) and also has a second variant in NALCN gene, which does not really fit with her phenotype. Her bone profile was checked and it came back acceptable with a borderline high PTH. To date she has not shown any bony abnormalities. She was diagnosed with Type 2 diabetes in March 2015. Her anti GAD antibodies were negative and her anti Islet antibodies were weekly positive and she was obese so she was diagnosed with Type 2 diabetes. She has been maintained with good control on Glarginie, metformin for her diabetes management. In October 2015, She was diagnosed with Ulcerative colitis via colonoscopy, To our knowledge, there are no reported cases of type 2 diabetes or ulcerative colitis associated with this disorder.

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P089
A toolbox of interventions to optimise age appropriate diabetes self-management: Inclusion of both face to face and digital solutions?
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Background
Currently only 26% of children and young people with diabetes achieve national targets. Developmentally appropriate interventions including age specific learning outcomes and goals, delivered by trained educators, which are auditable and can be integrated into routine practice are recommended to optimise the management of children and young people (CYP) with diabetes and promote lifelong self-management.

Method
Health care professionals in the CYP Diabetes Network were trained in ‘Goals of Diabetes Education’, a new initiative congruent with national recommendations. Participants were asked to complete a questionnaire which sought to understand variation in current provision, any gaps and challenges faced, as well as providing an opportunity to share innovative practice. Questionnaire design was peer reviewed to ensure it was aligned with research aims and was refined accordingly. A coding sheet was simultaneously developed to support data handling and analysis.

Results
Participants totalled 14 (dietitians, nurses, doctors) and represented 10 out of 22 CYP diabetes centres in Y&H. Preliminary data suggest inconsistency with regards current provision of age appropriate structured education criteria which was associated with absence of age specific written learning outcomes. Websites, mobile Apps and short videos were repeatedly mentioned by HCP’s as either forming part of their intervention to support education and self-management or recognising the potential.

Discussion
Embedding ‘Goals of Diabetes Education’ into routine care has the potential to reduce variation within and between centres. This is essential as this is thought to be the key difference in high performing teams. Learning outcomes which are age specific, written down and shared at the right time and in the right depth have the potential to involve children in clinic consultations more and ensure a more proactive and collaborative approach with the whole family. Meaningful involvement of CYP in the development and validation of both face-to-face and digital solutions will be imperative in optimising self-management.

DOI: 10.1530/endoabs.51.P089
Efficacy of Degludec in control of HbA1c in children with type 1 diabetes
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Introduction
Use of degludec [residual] in children and adolescents with type 1 diabetes was approved by EC 2015 and FDA in December 2016. Degludec is a new ultra-long acting basal insulin with terminal half-life of approximately 25 hours and duration of action of more than 42 hours. Constant release of insulin throughout the day leads to better control of blood glucose for more than 24 hours with significant reduction in HbA1c.

Aim
To compare and assess HbA1C control before and after starting degludec.

Methods
We did retrospective case note review of 24 children over a period of 4 months from October 2016 to January 2017. We have assessed the quality of glycaemic control before and after starting degludec in our unit. We also looked at the hospital admission with hypoglycaemia or DKA and changes in the insulin dose, basal insulin requirement after starting degludec.

Results
Sex distribution in our study was 54% boys and 46% girls. Majority age group was 11 to 18 years. 58% were using Glargine and 42% using insulin pump. Transition to adult care at Darent Valley Hospital (DVH). Our hypothesis is that is transitional care for diabetes at DVH meeting NICE guidelines or not? Also is there a need for specific pathway to suit local needs?

Methods
Case control study between November 2016 – February 2017, by surveying patients who had transitioned to young adults’ diabetes clinic at DVH about
quality of care, aged 16–21. Retrospective cohort study performed on the HbA1c values of patients who had transitioned since 2005 at DVH.

Results
40–70% of patients reported no education on topics especially pertaining to transitional diabetic care (Crowley et al., 2017). 40% of patients dependent on others to arrange their own appointments. 30% of patients felt a change in diabetes control. N = 23, HbA1c values of 95% of patients increased over the first two years post-transition, averaged +1.14 over the first year, 95% CI (−0.1, 2.4, P < 0.05). N = 89.

Discussion
There is no effective transitional care process for Diabetes at DVH, and it is not meeting patients’ needs or clinical guidelines (NICE, 2016). We propose a new pathway to meet patient needs, clinical guidelines, and by meeting DoH best practice tariff criteria (Randell, 2015), it is financially sustainable. This can be extrapolated to other chronic long term diseases, and to improve clinical outcomes, reduce hospital admissions, and reduce long-term care costs (NICE, 2016).

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P094
Use of Insulin Degludec in adolescent paediatric patients with Type 1 Diabetes Mellitus
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This case series compared the efficacy of long acting basal Insulin, Insulin Degludec compared to Insulin Glargine in adolescent patients. There were seven patients in total aged 14 to 18 years. Changes in HbA1c, BMI and reduction in nocturnal hypoglycaemic episodes were compared in all seven patients. Insulin Degludec showed a decrease in HbA1c levels, particularly in patients who had HbA1C higher than 48 mmol/mol on Insulin Glargine. There was a 2.4% decrease in HbA1c. Insulin Degludec showed good effect in maintaining BMI compared to Insulin Glargine in patients above the 50th centile for BMI while showing a small but significant increase in BMI in patients who were below the 50th centile. Insulin Degludec’s effects on nocturnal hypoglycaemic episodes varied depending on prior glycaemic control on Insulin Glargine. Patients with poor control on Insulin Glargine showed a significant reduction in nocturnal hypoglycaemic episodes. This case series demonstrates non-inferiority of Insulin Degludec compared to Insulin Glargine in improving glycaemic control, but could be considered in patients who have issues with compliance and poor control on insulin Glargine which may lead to nocturnal hypoglycaemias and also adolescents who have issues with BMI, especially those with BMI above the 50th centile.

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P095
The transition of care from paediatric to adult services in diabetes
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Background
The transition from paediatric to adult care can be challenging for patients with Type 1 diabetes. Poor continuity of care provided by the diabetes team may worsen an already difficult time for these patients. Good transition of care is vital to minimise the risk of worsening patient outcomes. In 2016, two patients failed to transition from paediatric to adult diabetes care and subsequently received no adult appointment. This breakdown of continuity of care was a result of several failures in the patients’ transition of care, including the use of the Transfer of Care (TOC) document.

Objectives
We aimed to assess if recent changes to our transition pathway improves outcomes by comparing two cohorts of transitioned patients. We also aimed to review the use of the TOC document. We used our TOC flowchart, introduced following the aforementioned cases, as the standard pathway of transition care.

Methodology
This retrospective audit compared two cohorts of Type 1 diabetic patients who transitioned between 2010 and 2013 (Cohort 1) and 2014–2017 (Cohort 2). We assessed: glycemic control; risk factors (retinopathy and nephropathy); attendance to diabetic appointments and admissions to hospital for diabetic pathology e.g. DKA. We compared the results preceding and following the transition date. In the most recent cohort, we also evaluated how successfully the new TOC flowchart is being documented and completed.

Results
In both cohorts, overall glycaemic control (mean HbA1c) worsened following transition to adult care. Cohort 1 saw a large reduction in attendance to diabetic appointments following transition. Cohort 1 demonstrated a large increase in admissions to hospital for DKA following transition, whereas Cohort 2 saw a decrease in admissions. The majority of catalogued TOC documents were in a format used previously; however, of those in the new format, only a minority were fully completed and clearly recorded as a TOC document.

Conclusion
Our service aims to improve outcomes through the use of an increasingly structured and documented transition process with better coordination of care with the adult diabetes team. Our data provides a baseline prior to the implementation of these processes, and is an early indication of improvement.

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Obesity
P096
An audit of pediatric obesity in secondary care
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Introduction
Despite public health interventions, paediatric obesity in the UK is increasing, with almost one third overweight or obese. The direct cost of obesity to the NHS is estimated at 4.2 billion a year. The North-East has some of the highest rates of obesity in the country. A recent clinical practice guideline (March 2017) from European and US Endocrine societies aims to inform assessment, treatment and prevention of paediatric obesity.

Aim
To evaluate current practice and improve care of obese and overweight children.

Method
Retrospective audit of obese patients attending a paediatric secondary care multidisciplinary team obesity clinic from January 2016 to May 2017.

Results
One hundred and forty patients were referred to the clinic in this period, of which 103 were seen. Patients had a median age of 8.6 years. 54% (n = 56) were male. Median BMI at presentation was 32.5 kg/m², with 34% (n = 35) classed as extremely obese (BMI > 35 kg/m²). The average BMI z-score at presentation was 3.72 (± 7.02) s.d. above the mean. Of those measured, reductions in BMI z-scores were seen in 66% (n = 38), 63% (n = 33) and 70% (n = 14) at 3, 6 and 12 months, respectively. The average BMI z-score reduction was −0.25 s.d. and −0.41 s.d. at 6 and 12 months, respectively. There were high rates of disengagement with 51% missing at least one appointment. A third had mental health diagnoses, of which 46% had ASD/ADHD. 23% (n = 32) had safeguarding involvement. Blood investigations were variable, 55% (n = 63) had a HbA1c, 7% had pre-diabetes and 1% diabetes. 77% had thyroid function tests, one showing a raised TSH. 37% (n = 51) had lipids checked; 16% had dyslipidaemia. 67% (n = 93) had an ALT; 29% were abnormal. One patient took metformin for type 2 diabetes and another captopril for hypertension. All patients had involvement from a paediatric consultant, paediatric dietitian and clinical psychologist.

Conclusions
When children stay engaged in obesity services there are considerable BMI z-score reductions. The high prevalence of mental health problems emphasises importance of psychology input. There is wide variation in regional service provision. Investigations were variable and co-morbidities possibly missed. Guidelines should be implemented standardising care of obese children.

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