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Abstract Unavailable.

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Abstract Unavailable.

CME Day: Session Two

CME2.1

Abstract Unavailable.

CME2.2

Management of growth and body composition in children with Prader-Willi Syndrome

Shankar Kanumakala
Brighton and Sussex University Hospitals NHS Trust, Brighton, UK.

Prader-Willi Syndrome (PWS) is a rare genetic disorder with a multitude of problems, often attributed to hypothalamic dysfunction. A child with PWS has a genetic predisposition to develop obesity due to appetite dysregulation, hyperphagia and excess calorie intake on the one hand; hypotonia, decreased muscle mass and decreased ability to spend the calories on the other hand. Although, there is no cure for PWS, lives of children with PWS can be significantly improved with specialist multi-disciplinary care and obesity should not be considered or viewed as an inevitable end point. Optimal management of growth and body composition are discussed, including growth hormone therapy; active calorie restriction and dietary monitoring; improving physical activities; supporting families to overcome challenging behaviours and overall helping PWS children lead healthy and fulfilling lives.

DOI: 10.1530/endoabs.58.CME2.2

CME Day: Session Three

CME3.1

Approach to a child with recurrent fractures

Paul Arundel
Sheffield Children's NHS Foundation Trust, Sheffield, UK.

Long bone fractures are common in childhood. However, recurrent fractures and certain types of fractures may indicate an underlying problem such as bone fragility. It is important to be able to identify those children who require closer evaluation and to consider how best to investigate such children. This should be done with an understanding of the likelihood and range of disease that may present with fractures, as well as the role of various modes of assessment. For those with underlying bone disease, treatment choices will vary depending on the diagnosis and likely prognosis. A current understanding of the threshold for the use of drugs such as bisphosphonates and how to manage associated risk is essential for the physician seeking to treat children with bone fragility.

DOI: 10.1530/endoabs.58.CME3.1

CME3.2

Abstract Unavailable.

CME Day: Session Four

CME4.1

Structured pathway for management of High HbA1c

Tabitha Randell
Nottingham Children's Hospital, Nottingham, UK.

Maintaining good diabetes control is essential to avoid long-term complications. NPDA data show that the percentage of children and young people achieving good control has increased year on year since 2011 and the percentage with very poor control (HbA1c >80 mmol/mol) has nearly halved in that time (28.7% in 2010-11, 16.4% in 2016-17). In Nottingham, we have managed to reduce the percentage of children and young people with very poor control from nearly 40% when we first submitted data to the NPDA to 4.6% in 2016-17. In addition, the adjusted percentage of children and young people with and HbA1C <58 mmol/mol was 56.5% for the same year. I will discuss our pathway for managing young people with poor control but hope to convince you that the answer to this problem is to prevent poor control in the first place.

DOI: 10.1530/endoabs.58.CME4.1

CME4.2

Abstract Unavailable.

Main Symposia

Endocrine Track 1: Symposium 1

S1.1

Abstract Unavailable.

S1.2

Abstract Unavailable.

S1.3

Abstract Unavailable.

Endocrine Track 1: Symposium 2

S2.1

Vitamin D – beyond bone

Martin Hewison
University of Birmingham, Birmingham, UK.

The role of vitamin D in human health continues to attract much attention, both from academic research and the public media. This is due, in part, to continued concern about the prevalence of vitamin D-deficiency in countries such as the UK and the impact this may have on skeletal health, notably in children. However, in recent years vitamin D has also been linked to a wide range of extra-skeletal functions, suggesting that vitamin D-deficiency has a much broader impact on human health. Although much of this new perspective on vitamin D stems from disease association studies, it is also important to recognise the novel basic vitamin D biology research that supports a wider role for vitamin D in human physiology. The review presentation will highlight key developments in extra-skeletal vitamin function, notably immune regulation and placental and fetal development that have attracted recent attention. The overall aim of the talk will be to highlight key areas of vitamin D function that are likely to provide meaningful targets for future research and vitamin D supplementation studies.

DOI: 10.1530/endoabs.58.S2.1

S2.2

Abstract Unavailable.

Endocrine Track One: Keynote Speaker

KNS1

Palaeopathology: diseases and excavations

Tony Waldron
University College London, London, UK.

Palaeopathology is the study of disease in human remains, most often, skeletal remains. The discipline serves a number of functions, from noting the first appearance of a particular disease, to studying trends in the prevalence of disease over time and space. Joint disease and dental disease are by far the most common disorders found in the skeleton, but examples of infectious disease, malignant disease, and cardio-vascular disease may also be found, and so are many examples of trauma, both accidental and deliberate. Although children always form a large proportion of a skeletal assemblage, it is seldom that any lesions are found in their skeletons.

DOI: 10.1530/endoabs.58.KNS1

Diabetes Track 1: Symposium 3

S3.1

Abstract Unavailable.

S3.2

Abstract Unavailable.

Diabetes Track 1: Symposium 4

S4.1

Abstract Unavailable.

S4.2

Abstract Unavailable.

S4.3

Abstract Unavailable.

Nurses Day for Endocrine Professionals

S5.1

Abstract Unavailable.

S5.2

Abstract Unavailable.

PENS Presentation

PENS1.1

Case study – polycystic kidney disease and hyperinsulinaemic hypoglycaemia

Kate Morgan & Pratik Shah
Great Ormond Street NHS Foundation Trust, London, UK.

This case study presentation formed the summative assessment aspect of "The principles of care for the child and young person in Endocrinology" module at London Southbank University. Hyperinsulinaemic Hypoglycaemia (HH), is characterised by the inappropriate secretion of insulin from the pancreatic β-cells in relation to the blood glucose concentration, and is the most common cause of severe and persistent hypoglycaemia in infancy and childhood. Approximately one-third of patients with HH develop some form of developmental delay. Insulin inhibits fatty acid release and ketone body synthesis, the main alternative fuels which protect the brain during hypoglycaemia. Therefore, early recognition and successful management is critical to prevent hypoglycaemic brain injury. The incidence of HH is estimated 1 in 35,000-40,000 and up to 1 in 2500 in areas with higher rates of consanguinity. Mutations in at least 12 different genes involved in β-cell insulin release have been identified so far, including the recent reported co-existence of HH and congenital polycystic kidney disease (PCKD) caused by a promoter mutation in the phosphomannomutase 2 gene (PMM2). This case study demonstrates the effectiveness of Nifedipine therapy in a child with PMM2 mutation. A review of the literature was undertaken to identify effectiveness of L-type calcium channel blockers such as Nifedipine in the treatment of different forms of HH, when used either on its own or in combination with other medications and dietary management. The clinical presentation, diagnosis and medical management of a child with PCKD and HH was reviewed. The role of clinical nurse specialist (CNS), with particular emphasis on the holistic approach to the child and family in relation to the medical and nursing intervention was discussed. To conclude, it was important to reflect on current clinical practices, new therapies in HH and demonstrating openness to new ways of working, that will help to improve our patients and families experience.

DOI: 10.1530/endoabs.58.PENS1.1

PENS1.2

Abstract Unavailable.

Diabetes Professionals Sessions

Diabetes Professionals Day: Session 1

DP1.1

Empowering type 1 diabetes patients to self-manage by embracing the digital landscape of Diasend

John Pemberton, Ruth Krone & Renuka Dias
Birmingham Women's and Children's Hospital, Birmingham, UK.

Successful management of diabetes requires an empowered patient/family that is well-educated about their condition and feels confident to self-manage with the support of their medical team. The linchpin to assessment and effective change is the quality of available information. Most patients/families have no way of pulling all their diabetes information together efficiently, and consequently often feel helpless and do not take charge of making their therapy adjustments. Diasend allows upload of all devices, creates easy to read reports and allows a productive dialogue between healthcare professionals and patient/family. We put a team together to onboard 50% of our type 1 diabetes cohort to Diasend in 2017. The audit produced some surprising results for 2016 (no diasend) vs. 2017 (home diasend):

- For all patients ($n = 103$), HbA1c did not change: 64.5 mmol/mol vs. 64.9 mmol/l.
- For the Pro-Diasend Group, those who uploaded at home twice or more every three months ($n = 52$), HbA1c dropped: 67.2 mmol/mol vs. 61.9 mmol/mol.
- For the No-Diasend, those who uploaded one time or less every three months ($n = 51$), HbA1c increased: 61.7 mmol/mol vs. 68.1 mmol/mol.

Qualitative inquiry suggested that the No-Diasend group stopped reviewing diabetes results because it was easier to upload once before clinic and 'Let the diabetes team do it!' – Disempowerment. Whereas the Pro-Diasend group increased the frequency of review of diabetes results because it was 'quicker than keeping a diary and easier to see patterns.' Following this audit, we have created a new policy. Patients wanting to use Diasend must upload before every clinic and in-between clinics. Also, they must take proactive steps to review diabetes results, identify patterns and consider changes. If not, we ask them to keep a written diary. Our next step is to review this policy.

DOI: 10.1530/endoabs.58.DP1.1

DP1.2

Abstract Unavailable.

DP1.3

Optimising transition in young adults with diabetes

Rebecca Skelding & Sophia Salahuddin
Queen Elizabeth Hospital Birmingham, Birmingham, UK.

An MDT approach to facilitating a workable transition between paediatric and adult services for young people with T1 and T2 diabetes. Management of young people with T2 diabetes is an emerging field that provides new challenges to the healthcare team in enabling young people to live with a lifelong condition that may also be affecting the wider family. Our service is delivered across two sites looking after young people with diabetes aged between 14–19 years in paediatric services and 16–24 years in adult services. It is often difficult to bridge the gap between services, especially when the 'wrap around services' provided in paediatric care are not readily available within adult services. We aim to Engage individuals in their own healthcare to encourage an environment of open-ness and acceptance. In order to achieve this we have a team that is interested in the speciality management of young people with diabetes.

DOI: 10.1530/endoabs.58.DP1.3

Diabetes Professionals Day: Session 2

DP2.1

Abstract Unavailable.

DP2.2

Abstract Unavailable.

Diabetes Professionals Day: Session 3

DP3.1

Abstract Unavailable.

DP3.2

Abstract Unavailable.

DP3.3

Abstract Unavailable.

Diabetes Professionals Day: Session 4

DP4.1

Abstract Unavailable.

DP4.2

Abstract Unavailable.

Endocrine Nurse Session

Nurses Day for Endocrine Professionals: Session One

EN1.1

Abstract Unavailable.

EN1.2

Abstract Unavailable.

Nurses Day for Endocrine Professionals: Session Two

EN2.1

Growing up with Silver Russell Syndrome

Jenny Child, Nick Child & Georgia Child

The additional issues associated with parenting a child, teenager and then adult with Silver Russell Syndrome are wide and diverse. They can start early in the pregnancy when it can be noted that the foetus is not growing as it should. There is then an expectation that when the baby is born it will be small but will rapidly catch up, but hope erodes as the baby shows little interest in feeding, vomits the small quantity of milk ingested and fails to thrive. There can be a feeling of helplessness as in its unhealthy state, the baby easily succumbs to illnesses, and the search for understanding the cause of the problems continues, with many different possible causes and syndromes being considered. But often, finding the appropriate Healthcare Professionals can be extremely challenging. The age at which children are diagnosed with SRS is getting younger and younger, and now can even be in-utero. Our daughter Georgia was clinically diagnosed at the age of 14 months and received a clinical diagnosis of SRS MUPD7 at the age of 8 years. In September Georgia celebrated her 21st birthday. We will speak from a very personal experience of the difficulties, experiences and high points of bringing up our wonderful daughter. Medical issues have included gastrostomy feeding, growth hormone, hypoglycaemia, hypermobility and many other problems. Education has been a mix of special needs nursery, main stream school and then special needs college. Currently Georgia is not quite ready to commence employment but we expect she soon will be; she is a valuable member of the community. Current issues include her mental health and wellbeing, anxiety and a recent diagnosis of Autism.

DOI: 10.1530/endoabs.58.EN2.1

EN2.2

Abstract Unavailable.

Oral Communications

Oral Communications 1

OC1.1

Differentiating between SIADH and NSIAD in an infant presenting with hyponatraemia

Xanthippi Tseretopoulou, Hitesh Prajapati & Talat Mushtaq
Leeds Teaching Hospitals NHS Trust, Leeds, UK.

Introduction
An 18 day old term male baby presented with faltering growth and hyponatraemia. Extensive investigations suggested the cause of hyponatraemia was water excess which may result from either overproduction of Antidiuretic hormone (SIADH) or the nephrogenic syndrome of inappropriate antidiuresis (NSIAD). Genetic testing demonstrated a hemizygous mutation in the AVPR2 gene.
Case report
The infant presented with 8% weight loss and hyponatraemia (lowest Na: 114 mmol/l), serum osmolality was 233 mosm/kg with an inappropriately elevated urine osmolality of 629 mosm/kg. Endocrine investigations included a normal 17OHP (3.7 nmol/l), Synacthen test (peak cortisol 1013 nmol/l) and urine steroid profile. The plasma aldosterone was 1032 pmol/l with a suppressed plasma renin of <0.2 nmol/l per hr. Metabolic tests were normal apart from a heavy aminoaciduria. There was no evidence of proximal tubular dysfunction. The renal ultrasound scan and magnetic resonance imaging of the brain were normal. The results indicated excess free water secondary to SIADH or NSIAD. The Copeptin (marker of vasopressin levels) was in the low normal range at 2.9 pmol/l.
Treatment
Sodium supplements had minimal effect on the serum sodium. Fluid restriction increased the sodium to 126 mmol/l, however this resulted in inadequate calorie intake and poor weight gain. Addition of a vasopressin receptor antagonist (Tolvaptan) allowed some relaxation of the fluid restriction with unchanged sodium levels. The poor growth however persisted. Genetic tests confirmed a rare gain of function mutation in the AVPR2 gene leading to excessive water retention. Diuresis was achieved by providing an increased osmotic load by increasing dietary protein intake to 6 g/kg per day and subsequently giving oral urea. These measures normalized the serum sodium levels and the child is now thriving. The urinary aminoaciduria is improving.
Conclusions
Both SIADH and NSIAD respond to fluid restriction, but this is at the expense of nutritional intake. SIADH but not NSIAD respond to Tolvaptan. Measurement of copeptin levels and genetic testing can help differentiate between the two conditions. Osmotic diuresis with the introduction of a high protein diet and oral urea can normalize hyponatraemia in NSIAD.

DOI: 10.1530/endoabs.58.OC1.1

OC1.2

The complications of a goitre secondary to iodine deficiency

Elspeth Ferguson & Paul Dimitri
Department of Paediatric Endocrinology and Diabetes, Sheffield Children's NHS Foundation Trust, Sheffield, UK.

Introduction
Iodine deficiency in Western countries is considered a historic disease. In 1924 up to 30% of school aged children in the UK had a goitre. The UK however remains one of the most iodine deplete countries in the world. Those following restricted diets are also at particular risk of iodine deficiency.
Case Report
A nine year old female on a significantly restricted diet due to multiple food allergies presented with a goitre. Ultrasound scan confirmed a diffusely enlarged heterogenous thyroid gland. The patient was clinically and biochemically euthyroid, TSH 2.16 mIU/l (0.5–3.6), FT4 14.2 pmol/l (10–16.9). Urinary iodine levels confirmed a goitre secondary to iodine deficiency (urinary iodine 0.09 micromol/l) (0.39–1.97)). Treatment of the iodine deficiency proved challenging, with difficulties finding an appropriate preparation and ensuring compliance with the regime. Preparatory sea kelp, containing 150 micrograms iodine was used. Support from dieticians and the allergy team was also required. One year later, she presented with tremor, heat intolerance and poor concentration. Clinical assessment was in keeping with a hyperthyroid state, confirmed on biochemical testing: TSH <0.01 mIU/l (0.5–3.6), FT4 42.8 pmol/l (10–16.9), T3 $>$ 30.7 pmol/l (4.4–6.8). TSH receptor antibodies, thyroid peroxidase antibodies and anti-thyroglobulin antibodies were negative. The Jod-Basedow Effect was diagnosed secondary to repletion of iodine stores. She was initially managed with carbimazole and propranolol. As her thyroid function normalises, her medications are now being weaned and stopped.
Conclusions
This case highlights the importance of a dietary history and consideration of iodine deficiency in any patient presenting with a goitre. The Jod-Basedow Effect may be seen as a rare complication of treatment with iodine, and should be considered if iodine-deficient patients on treatment present with thyrotoxicosis. Prognosis is excellent with complete resolution in antibody-negative patients

DOI: 10.1530/endoabs.58.OC1.2

Oral Communications 2

OC2.1

An audit of hypoglycemia screens in paediatric and neonatal patients in two district general hospitals

Harry Dougherty, Georgina Cameron, Sriparna Kar & Aileen Alston
Epsom and St Helier University Hospitals, London, UK.

Introduction
The thorough investigation and prompt management of hypoglycaemia is crucial in determining the diagnosis and preventing associated morbidity and mortality. Delay in obtaining blood samples during the 'Golden Hour' of hypoglycaemia, and sampling incorrectly or insufficiently may result in missed diagnosis and necessitates readmission for a fasting glucose profile. This audit was undertaken to evaluate the successful implementation of hypoglycaemia screens in children and neonates in secondary care setup, against current trust guidelines on the management of Paediatric Hypoglycaemia.
Methods
Retrospective audit of case notes of Children (0–16 years) attending the emergency department, and newborn babies (0–3 days) in SCBU with documented hypoglycaemia (blood glucose <2.6 mmol on glucometer or blood gas measurement) who had blood and urine samples obtained in accordance to recommended hypoglycaemia screening. The aim was to critically evaluate the time lapse from initial recorded hypoglycaemia to samples obtained and the completeness of the investigations carried out. Time scale = four months.
Results
Overall four children and seven newborns had blood and urine samples obtained during hypoglycaemia (n total $=11$). 67% of the children and 40% of the neonates had samples collected appropriately and sufficiently for analysis. 50% of children, versus 57% of newborns, had samples obtained within the first hour of hypoglycaemia. 100% children, versus only 14% of newborns ($n=1$) had ketones (point of care, urine or laboratory Beta-hydroxybutyrate) measured during a hypoglycaemic event.
Conclusions
To improve the quality of hypoglycaemia screens in secondary care we have incorporated several measures to benefit clinical practice. Firstly, to educate healthcare professionals on ketotic versus non-ketotic hypoglycaemia, to guide which samples are of the utmost importance to obtain during hypoglycaemia; focusing on diagnosis. Secondly, ensuring availability of point of care Ketone testing and hypoglycaemia blood sampling packs in clinical areas, creating an online hypoglycaemia order set, to assist in the correct ordering and labelling of investigations. Finally, we updated our local paediatric hypoglycaemia guidelines.

DOI: 10.1530/endoabs.58.OC2.1

OC2.2

The relationship of baseline, incremental and peak cortisol following a Short Synacthen Test – single-centre analysis of three years' data

Apoorva Aji[1], Sharon Colyer[2], Sarah Burn[2], Paul Dimitri[2], Neil Wright[2], Nils Krone[1,2] & Charlotte Elder[1,2]
[1]The Univeristy of Sheffield, Sheffield, UK; [2]Sheffield Children's NHS Foundation Trust, Sheffield, UK.

Introduction
There is evidence that an early morning plasma cortisol (EMC) below <160 nmol/l is predictive of failing the SST and the corollary is seen with an EMC above >340 nmol/l. Using an EMC to screen patients for AI has been advocated, although there is a paucity of paediatric studies. Modern sensitive and specific cortisol assays make deriving local diagnostic thresholds important. We analysed our SST data since the introduction of a new cortisol assay to derive screening thresholds for SST and examined the relationship between the basal, incremental and peak plasma cortisol.

Methods
All SST performed between September 2014 and 2017 were retrospectively analysed. Cortisol quantification was performed on the Abbott Architect i1000 chemiluminescent immunoassay (CVs $<5\%$). A 'pass' for the SST is currently 430 nmol/l. Basal cortisol was used as a surrogate for EMC and correlation coefficients with increment and peak examined. Subgroup analysis was performed using sex and an age-approximate for pubertal status (0–9 and 10–16 years of age). Positive and negative predictive values using a basal plasma cortisol of <160 nmol/l and >340 nmol/l respectively were calculated. Predictive values were calculated using different cuts offs.
Results
Overall 393 SSTs were included (209M, 184F, 175 'prepubertal', 218 'post-pubertal'). The correlation coefficient for basal and peak cortisol was 0.63, (0.63 female, 0.62 male; 0.65 0–9 years, 0.66 10–16 years). There was no relationship in any of the groups between basal and incremental cortisol (overall data correlation coefficient -0.061). Of the cohort 28% had basal cortisols <160 nmol/l of whom 58% 'failed' the SST, PPV $=0.58$. Correspondingly 13% had basal cortisols >339 nmol/l, none of whom 'failed' the SST, NPV $=1$. Moving the basal cut off to >320 nmol/l would have resulted in missing three patients who subsequently failed their SST.
Conclusions
There is a reasonably strong relationship between basal and peak cortisol on the SST. No relationship exists between basal and incremental cortisol. Subgroup analysis did not strengthen the correlations. On the Abbott Architect plasma cortisol assay an EMC of >339 nmol/l appears to safely predict passing the SST and <160 nmol/l yields a high PPV for failing the SST.

DOI: 10.1530/endoabs.58.OC2.2

Oral Communications 3

OC3.1

Serial overnight growth hormone profiling in diagnosing growth hormone excess in McCune Albright Syndrome

Nadia Amin[1] & Talat Mushtaq[2]
[1]University of Leeds, Leeds, UK; [2]Leeds Children's Hospital, Leeds, UK.

Introduction
McCune Albright syndrome (MAS) is characterised by at least 2 of 3 features: polyostotic fibrous dysplasia (FD), café-au-lait skin pigmentation and autonomous endocrine hyperfunction. Growth hormone excess if present (GH) can worsen symptoms of FD.
Case report
A 3 year old girl presented with vaginal bleeding. A single café-au-lait patch was present (3 cm). A diagnosis of MAS was made, with a c.601 $>$ T mutation found in the GNAS gene. Gonadotrophin independent precocious puberty was treated with an aromatase inhibitor. On imaging she had cranial FD encircling the left optic nerve. There were concerns that GH excess associated with FD could compromise her vision. The IGF-I levels were in the upper normal ranges. A GH suppression test reduced the GH from 6.9 to 0.8 ug/l. Due to incomplete GH suppression she had overnight profiling (GH taken at 20min intervals from 8pm to 8am). The GH showed good variability (mean 3.9 μg/l, range 0.7–9.8 μg/l). In conjunction with a normal growth rate it was deemed to be an acceptable profile. Her height SDS ranged from $+0.4$ to $+1.0$ SDS. Two further overnight GH profiles followed by GH suppression tests were repeated at annual intervals. By the third profile the GH did not fall below 1 μg/l either on the overnight profile (mean 4.4 μg/l, range 1.1–11.8 μg/l) or suppress below 0.5 μg/l on the OGTT. Due to concerns about the impact of excess GH on FD she was commenced on a somatostatin analogue (Lanreotide LA injections), resulting in a reduction of IGF-I to within the mid-normal range for her age.
Conclusion
GH excess in MAS and is associated with a worsening of the fibrous dysplasia. Overnight GH profiling can aid in the diagnosis of GH hypersecretion, particularly when an OGTT is equivocal. This is crucial in patients with craniofacial fibrous dysplasia as early diagnosis and treatment of GH excess may prevent GH excess associated morbidity, specifically vision loss.

DOI: 10.1530/endoabs.58.OC3.1

OC3.2

Haemolytic Uraemic Syndrome (HUS) – a rare cause of diabetes

Alghanay Abubaker Alghanay, Paul Leach, Shikha Jain, Nirupa D'Souza & Alissa Vereschinsky
Princess of Wales Hospital, Bridgend, UK.

HUS is a condition well known to have multi-systemic effects. Whilst the predominant organ to be affected is the kidneys, it is also well recognised that the pancreas can be affected during the acute phase of the illness, causing a transient diabetes mellitus. Less well documented, however, is that HUS has been linked to long-term diabetes, with patients developing insulin deficiency, years after contracting HUS. We report on the case of a twelve-year-old girl who developed insulin dependent diabetes by the age of ten, with a past medical history of haemolytic uraemic syndrome at the age of two. She displayed transient hyperglycaemia requiring insulin during recovery from HUS. Autoimmune antibody testing was negative in this patient when she presented with diabetes, as described in similar cases. The literature suggests up to one third of survivors may develop permanent diabetes as late as eleven years after the acute illness. The pathophysiology is very different to immune-mediated type one diabetes mellitus, with testing for autoantibodies being negative in case reports of these patients. The full extent of the mechanism by which insulin deficiency occurs is unknown, however, it is recognised that the pathological processes occurring in the body during the acute illness can lead to physical destruction of the pancreas. Fibrosis, pancreatic arteriolar thrombosis and microangiopathy of the pancreatic microvasculature leading to beta cell death have all been described. Whilst absolute numbers of patients developing diabetes secondary to HUS remain small, the literature supports the theory that diabetes may be a lasting consequence in patients who have had HUS and that these patients may benefit from routine follow up screening or increased awareness of this possible long-term complication.

Keywords: Haemolytic uraemic syndrome; *E. coli* O157:H7; diabetes mellitus; long-term complications.

DOI: 10.1530/endoabs.58.OC3.2

Oral Communications 4

OC4.1

Hydrocortisone granules in capsules for opening: phase 3 trial in children with adrenal insufficiency and long-term safety data

Alexander Lewis[2], Uta Neumann[1], Susanna Wiegand[1], Heiko Krude[1], Dina Digweed[2], Bernard Voet[2], Richard Ross[3], Madhu Davies[2] & Oliver Blankenstein[1]
[1]Institute for Experimental Paediatric Endocrinology, Charite Universitatsmedizin Berlin Campus Virchow-Klinikum, Berlin, Germany; [2]Diurnal Ltd., Cardiff, UK; [3]Department of Endocrinology, The University of Sheffield, The Medical School, Sheffield, UK.

Introduction
Children with adrenal insufficiency requiring hydrocortisone rely on compounded adult medication. This study aimed to evaluate the absorption, palatability and safety of Alkindi® (hydrocortisone granules in capsules for opening).
Methods
The phase 3 study was an open-label, single-dose study in a total of 24 children (aged 0–6 years) with adrenal insufficiency. Fasted children were given a single dose of Alkindi® as dry granules administered directly from capsule or spoon followed by a drink. The primary endpoint was serum cortisol concentration 60 min after administration. Secondary endpoints were palatability and adverse events.
Results
All children showed an increase in cortisol above baseline after administration of Alkindi® ($P<0.0001$), with geometric mean $\pm$S.D. cortisol concentration at 60 min of 575.8 ± 299.5 nmol/l. There were no difficulties with administration and 95.5% of parents/carers reported they preferred Alkindi® over their child's current medication. Six children completed an age-appropriate palatability questionnaire: 80% responses were very good, good, or neutral and 20% were bad or very bad. No serious or severe treatment-emergent adverse events were reported. Subjects were invited to continue to receive Alkindi in an ongoing extension study, in which Alkindi was administered at home, according to usual clinical practice (three times per day). The primary endpoint was safety. Interim analysis up to 12 months reported 80 Treatment Emergent Adverse Events, all typical illnesses in young children, and none suspected to be related to Alkindi. One SAE of moderate erysipelas was reported and successfully managed with stress dosing of Alkindi. No cases of choking or adrenal crises have been reported to date. Cortisol levels remained above baseline at most visits. All Tanner

developmental stage assessments remained at grade 1. Z scores for height and weight showed no trends for accelerated or reduced growth.
Conclusions
Alkindi is well tolerated, easy to administer, and produces cortisol levels similar to those reported in healthy children. In an extension study, no adverse events were suspected to be related to Alkindi, and no adrenal crises have been reported.
DOI: 10.1530/endoabs.58.OC4.1

OC4.2

Gene expression signatures in children with growth hormone deficiency (GHD) and Turner syndrome (TS) predict response to growth hormone
Peter Clayton, Adam Stevens, Philip Murray & Terence Garner
University of Manchester, Manchester, UK.

Background
Recombinant human growth hormone (r-hGH) is the primary therapeutic agent for disorders of growth including growth hormone deficiency (GHD) and Turner syndrome (TS). There is a high cost associated with treatment and existing methods to predict response (and hence alter management) can only account for 40–60% of the variance.
Methods
GHD ($n=71$) and TS patients ($n=43$) were recruited as part of a study (PREDICT) on the long term response to r-hGH over five years of therapy[1]. Change in height over the entire study and height velocity at each year of the study were used as endpoints to measure the effect of r-hGH. Pharmacogenomic analysis was performed using 1219 genetic (DNA) markers along with whole genome transcriptome (mRNA) from blood. Transcriptomic data were initially analysed using partial least square discriminant analysis (PLS-DA) to determine potential predictive value. Similarity in response to r-hGH between GHD and TS was assessed using gene interaction networks. Random forest, a machine learning technique, was used to define predictive value of gene expression data associated with growth response at each year of the study.
Results
No genetic marker passed the stringency criteria required for predictive value. Using PLS-DA and random forest we demonstrated that the transcriptomic data can be used to predict growth response to r-hGH at each of the five years and over the entire duration of the study in GHD and TS. Network models identified an identical core set of genes present in both GHD and TS at each year of therapy whose expression can be used to classify therapeutic response to r-hGH.
Conclusions
DNA markers are useful in growth prediction. However the transcriptome can be used to predict both short and long term therapeutic response to r-hGH. For the first time, core sets of genes ***identical*** in both TS and GHD patients can be used to predict response to r-hGH at each of the five years of the study.
Reference
1. Clayton P, Chatelain P, Tato L, *et al*. *Eur J Endocrinol* 2013; **169**(3): 277-89.
Acknowledgement: PREDICT investigator group.
DOI: 10.1530/endoabs.58.OC4.2

OC4.3

Recommendations for management of paediatric phaeochromocytoma/paraganglioma (PCC/PGL): On behalf of the UK Paediatric PCC/PGL Guideline Development Group
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Background
Phaeochromocytoma/paraganglioma (PCC/PGL) are rare in children and young people (CYP) under 19 years of age. National registry data reveal an annual incidence between 0.2 and 0.3 per million in 5–9 and 10–14 year age groups respectively. Almost all result from a genetic predisposition and can present a significant management challenge.
Aims
We aimed to provide the first interdisciplinary management guidelines using the AGREEII framework for CYP with confirmed or suspected PCC/PGL, and endorsed by the Royal College of Paediatrics and Child Health, UK Children's Cancer & Leukaemia Group and the British Society for Paediatric Endocrinology & Diabetes.
Methods
A specialist Guideline Development Group (GDG) formulated 113 PICO clinical questions, and systematic literature searches were conducted via Ovid MEDLINE and Cochrane Library Databases, identifying 526 articles. 397 publications were reviewed using GRADE. A two-stage Delphi consensus process was conducted where evidence was lacking or conflicting in order to make recommendations.
Results
Thirty-nine recommendations spanning clinical assessment, investigations, medical/surgical management and long-term follow up of survivors are made. Importantly, the GDG recommend CYP with PCC/PGL are managed in a specialist endocrine centre, linked to tertiary paediatric oncology, by a designated, age-appropriate multi-disciplinary team and experienced lead clinician. Clinical assessment and a 3-generation family history should be targeted to identify genetically determined PCC/PGL, and genetic testing offered for all CYP with PCC/PGL after appropriate counselling. For CYP who undergo bilateral/completion adrenalectomy or cortical sparing surgery, peri-operative steroid replacement should be led by a nominated endocrinologist, and continued until adrenocortical reserve is tested post-operatively. All CYP diagnosed with PCC/PGL should have life-long follow up because of the propensity for new events.
Conclusions
These national guidelines provide the first evidence- and consensus-based recommendations for the management of PCC/PGL in CYP, and highlight a need for further audit and research in this rare, but potentially serious, condition. Their implementation should improve the quality of care and long-term health related survival of CYP with PCC/PGL.
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OC4.4

Identification and characterisation of a small-molecule ACTH receptor/Melanocortin-2-receptor antagonist
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The overproduction of ACTH, in conditions such as Congenital Adrenal Hyperplasia (CAH) leads to significant morbidity. Current treatment with glucocorticoids does not adequately suppress plasma ACTH, resulting in excess adrenal androgen production. At present, there is no effective medical treatment that would directly block ACTH action. Such a therapy, especially one that can be orally administered, would be of great clinical value allowing a 'block and replace' treatment strategy. ACTH acts on a highly selective receptor, the ACTH-receptor, also known as the melanocortin-2-receptor (MC2R). ACTH is the only known naturally occurring agonist for this receptor. This lack of redundancy and high degree of ligand specificity suggests that antagonism of this receptor could provide a useful therapeutic strategy in the treatment of CAH. Here we describe the identification of a specific small-molecule MC2R antagonist. We screened ~200,000 low molecular weight drug-like compounds from the Medical Research Council Technology library for MC2R antagonist activity using a high throughput cAMP homogeneous time-resolved fluorescence assay in CHO cells stably co-expressing human MC2R and its accessory protein MRAP. ~700 unique hits with MC2R antagonist properties were counter-screened against the β2-adrenergic receptor, another Gs-coupled GPCR. 208 compounds capable of inhibiting activation of MC2R by 50% or more, with little effect on β2 activity, were profiled further. Hit confirmation and dose-response analysis on these MC2R compounds revealed four novel lead compounds. 10 μM of these compounds caused a log shift in the half maximal effective concentration (EC_{50}) of ACTH. Schild plot analyses and determination of antagonist affinity (pA2), suggest a competitive nature of antagonism (pA2 5.872-5.737). Using mouse Y-1 adrenocortical cells, endogenously expressing murine MC2R and MRAP, we demonstrated that one of the four lead molecules, Compound 4, could significantly inhibit cell signalling and steroidogenesis (lowering progesterone release from 400 pg/ml to 150 pg/ml). No antagonistic activity of Compound 4 was seen with the other four melanocortin receptor family members when stimulated with α-MSH or ACTH, highlighting the specificity of Compound 4 for the MC2R. Studies are now underway to study the effectiveness of Compound 4 *in-vivo*.
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OC4.5

Delayed or Absent? – use of next generation sequencing diagnostic tools in a UK puberty cohort

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Objectives
Several different pathogenic mechanisms may converge on a final common pathway to produce the phenotype of delayed pubertal timing. 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 pathophysiology and genetic regulation remain unclear.
Methods
We have been actively recruiting a UK cohort of patients with severely delayed pubertal onset, or arrested puberty, since 2013. To date, 32 probands and 18 family members DNA have been collected. We have performed next generation sequencing (NGS) - either whole exome sequencing (WES) or whole genome sequencing (WGS) in 20 probands and 4 relatives from this UK self-limited DP patient cohort. The data returned was filtered for genes with rare, predicted deleterious variants that segregated with trait within families with potential biological relevance for delayed puberty.
Results
To date, NGS has been carried out in 48% of the collected cohort ($n=24$, probands $=20$, family members $=4$). A definitive pathogenic mutation has been identified in 18% of those sequenced. Notable mutations include a known homozygous mutation in the GnRH receptor *GNRHR*, a known homozygous mutation in the gene encoding Neurokinin B, *TAC3*, a novel heterozygous mutation in *FGFR1* and several other potentially pathogenic variants in relevant genes and pathways, including *SEMA3E* and *CCDC141*.
Conclusions
The clinical diagnostic distinction between hypogonadotropic hypogonadism and self-limited DP in adolescence is often a difficult one to make. In some cases, identification of definitive genetic mutations can be very informative for management and future planning. These genetic diagnoses also inform our understanding of biology of absent and delayed puberty. There remains uncertainty about the clinical significance of many of the potentially pathogenic variants identified by NGS. This is likely to improve with better knowledge of NGS interpretation, but despite this a definitive genetic diagnosis may not be possible in all patients.

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OC4.6

Implementation of a novel non-invasive test for monitoring control in individuals with congenital adrenal hyperplasia

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Introduction
Monitoring of hormonal control represents a key part in the management of congenital adrenal hyperplasia (CAH). It remains suboptimal and relies on frequent blood tests, which are traumatising in children and young persons (CYP). Recent evidence suggests a crucial role of adrenal-derived 11-oxygenatedC19 androgens in the pathogenesis of CAH. Therefore, we aimed to establish a non-invasive test for monitoring of adrenal-specific androgens in CAH.
Objective
To establish the correlation between plasma and salivary androgens in CYP with CAH.
Patients and methods
Patients ($n=78$, 43 girls, 35 boys, 8–18 years (12.87 ± 3.04 years) and matched controls ($n=62$) were recruited in a multicentre prospective study of CYP with CAH across the United Kingdom. Using liquid chromatography tandem mass spectrometry, we measured plasma and salivary concentrations for five steroid hormones: 17-hydroxyprogesterone, androstenedione, testosterone, 11-hydroxyandrostenedione and 11-ketotestosterone and established the correlation (Spearman) between plasma and salivary steroids to assess their usefulness in clinical practice.
Results
Plasma and salivary steroid concentrations show a good correlation, with androstenedione and 11-ketotestosterone providing the best information when used as non-invasive measurement from saliva: androstenedione ($r_s=0.928$, $P<0.001$), testosterone ($r_s=0.864$, $P<0.001$), 17-hydroxyprogesterone ($r_s=0.871$, $P<0.001$), 11-hydroxyandrostenedione ($r_s=0.877$, $P<0.001$), 11-ketotestosterone ($r_s=0.944$, $P<0.001$). In addition, a high correlation was found in CYP with CAH when analysing subgroups based on gender and age. Clear differences were found for all plasma and salivary steroids between patients and controls. Analysing patients according to CAH control by 17-hydroxyprogesterone concentrations (<15 nmol/l; 15–30 nmol/l; >30 nmol/l), established clear correlations with plasma and salivary 11-ketotestosterone.
Conclusions
We have established close correlation between plasma and salivary concentrations of steroid hormones assessed for therapy control in CAH patients. Importantly, the best correlations were found for the adrenal-derived 11oxygenatedC19 androgen 11-ketotestosterone as well as 17-hydroxyprogesterone and androstenedione, which are widely used for CAH monitoring. Thus, we believe that this novel and improved combination of salivary steroid hormones can serve as a non-invasive monitoring tool in CAH providing a significant amount of additional information, and will ultimately improve patient acceptability, management and outcomes in CAH.

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OC4.7

Clinical outcomes of focal congenital hyperinsulinism – a UK perspective

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Background
The focal type of Congenital Hyperinsulinism (CHI) is characterized by a cluster of abnormal insulin over-secreting β-cells within a restricted area of the pancreas. Early identification and intervention of the focal lesion is critical in CHI management, preventing both acute and chronic complications.
Objective
The purpose of this study is to review outcomes of treatment response in focal CHI.
Design
Retrospective review of patients diagnosed with focal type of CHI from 2003–2018 at 2 regional specialist centres.
Results
Data from 52 individuals with focal CHI were analysed; 37 were male and 15 female. Paternally-inherited heterozygous mutations in K-ATP channel genes

(*ABCC8*, *KCNJ11*) were identified in 48 patients (42 *ABCC8*; 6 *KCNJ11*). Three patients had negative CHI genetic testing, while one of them showed somatic loss of heterozygosity in the resected pancreatic tissue. The Fluorine-18 L-3,4-dihydroxyphenylalanine positron emission tomography computerized tomography (18F-DOPA-PET/CT scan) confirmed a focal lesion in 48 patients, with the pancreatic head being the most prevalent lesion location. In the remaining 4 patients, imaging was inconclusive; in these patients the diagnosis was established by frozen section histopathology at surgery. Prior to surgery the majority of the patients ($n=49$) were unresponsive to Diazoxide treatment, with 19 responding to Octreotide, 3 partially responsive to Sirolimus and 1 to Lanreotide. Ten patients were treated conservatively without surgery; at last review 2 patients had stopped medications, while 8 were still on medications but able to tolerate age-appropriate fasting. Forty-five patients underwent pancreatic surgery; 35 had lesionectomy, 7 had sub-total pancreatectomy and 3 had biopsies. Post-surgery, CHI resolved in 36 patients, while 6 required medication (Diazoxide or Octreotide) and four stopped mediations 2–10 years post-surgery. Among those whose underwent sub-total pancreatectomy, 2 patients developed pancreatic insufficiency and one developed diabetes 10 years post-operatively.
Conclusion
Surgical excision of the focal lesion remains the treatment of choice for focal CHI. However, our data support the possible implementation of medical therapy in select cases.

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OC4.8

Prolactinoma in Childhood and Adolescence – outcomes relating to the size of tumour

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Objective
To describe the clinical presentation, management and treatment outcomes of prolactinomas diagnosed in childhood and adolescence in a consecutive series.
Design and Methods
A retrospective review of medical records of patients with prolactinoma less than 20 years at diagnosis, referred to a tertiary paediatric endocrine service between 1996 and 2018.
Results
Twenty-three patients (14 females) were identified; median age at diagnosis 15.7 years (range 13–19) and median follow up 36 months (range 2–156 months); 13 patients had a macroprolactinoma. Pubertal disorder, galactorrhoea and headache were the commonest presenting symptoms. Although the difference was not statistically significant, there was a definite trend towards larger tumour size at presentation in males as compared to females (21 mm vs 9 mm; $P=0.076$). Seven patients (all macroprolactinomas) had associated pituitary hormone deficiencies at presentation. Co-existing growth hormone excess was present in one patient. The majority (82%) of patients demonstrated good clinical, biochemical and radiological response to dopamine agonist therapy (cabergoline). Six patients underwent surgical resection – cabergoline unresponsive (3), pituitary apoplexy (2), and diagnostic confirmation (1). Patients requiring surgical intervention were invariably macroadenomas greater than 20 mm in diameter at presentation. Patients undergoing surgery had larger tumours ($P=0.008$) and higher serum prolactin concentration ($P=0.046$). Two of these six patients who underwent surgical resection also required Temezolomide and radiotherapy to achieve disease control. New anterior pituitary function deficits were infrequent after surgical resection (17%). One patient was known to be MEN1 positive. Of the remaining patients (9) tested, none were found to have an *AIP or MEN1* mutation.
Conclusions
Prolactinomas are rare below the age of 20 years, occurring mainly during adolescence. Microprolactinoma predominantly occurs in girls and is very effectively treated with cabergoline. Macroprolactinoma occurs predominantly in boys, presents with mass effect and particularly if greater than 20 mm in size, may require multimodal therapy and are more likely to have hormone deficiencies. Due to rarity of these tumours in this age group, paediatric and adolescent patients benefit from being managed in shared/transitional care with the adult endocrine and neurosurgical teams.

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Oral Communications 5

OC5.1

Growth outcomes in adolescents and adults with Silver-Russell syndrome and the effects of childhood growth hormone treatment

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Childhood short stature in Silver-Russell syndrome (SRS) is frequently treated with growth hormone (GH), however final height and long-term body mass index (BMI) data are limited.
Objective
To assess height and BMI in older individuals with molecularly confirmed SRS and compare those previously treated with GH to those untreated.
Methods
Growth data on individuals aged $\geq$13 years with SRS were evaluated from UK, French and German cohorts. Height and BMI standard deviation scores (SDS) were calculated using country-specific reference data.
Results
71 individuals (40 females) aged 13.17–69.71 years (median 22.03) were recruited. Molecular diagnoses: loss of methylation at H19/IGF2 (80.3%), maternal uniparental disomy for chromosome 7 (16.9%), IGF2 mutation (2.8%). 77.5% received GH for a median of 7.10 years (IQR 3.96 to 11.00). The median time since GH cessation was 9.97 years (IQR 2.68–15.94). Median early height SDS in GH-untreated and GH-treated individuals were −2.91 (IQR −3.62 to −2.40) and −3.46 (IQR −5.15 to −2.76) respectively ($P=0.055$). Median height gain from early to final height SDS in GH-untreated and GH-treated individuals were 0.53 (IQR −0.13 to 1.37) and 1.53 (IQR 0.80 to 2.52) respectively ($P=0.006$). The median final height SDS of GH-untreated and GH-treated individuals were −2.74 (IQR −3.36 to −1.13) and −2.22 (IQR −3.66 to −1.16) respectively ($P=0.720$). Median change in BMI from early to final BMI SDS in GH-untreated and GH-treated individuals were 3.58 (IQR 1.85 to 5.18) and 1.95 (IQR 0.76 to 2.69) respectively ($P=0.005$). The median BMI SDS of GH-untreated versus GH-treated individuals were 1.66 (IQR −0.73 to 2.03) and −1.10 (IQR −1.80 to 0.00) respectively ($P=0.002$).
Conclusions
Height gain was significantly greater in GH-treated individuals who (were shorter at treatment initiation but) reached similar final heights to GH-untreated individuals. Historical GH treatment was associated with reduced BMI and reduced gain in BMI, indicating long-term effects.

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OC5.2

Screening for co-morbidities in fibrous dysplasia

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Fibrous dysplasia (FD) is a rare bone disease which usually presents to Endocrinologists as part of McCune albright syndrome or as precocious puberty. A variety of other co-morbidities have been described for FD including renal phophate wasting secondary to an excess of FGF23; abnormal thryoid and growth hormone production and abnormal cortisol production. A large number of children are referred to our Regional Sarcoma Service with lytic bony lesions, many of which are subsequently diagnosed as FD. There is currently no screening programme in place for children with this diagnosis, as is recommended by the FD Foundation. We therefore audited all patients diagnosed with FD since 2009. Of the over 1100 patients suspected to have FD, we were able to conclusively arrive at the diagnosis in 74 patients, 43 Males and 31 females; 19/74 (25%) had polyostotic disease and 55/74 (75%) had monostotic FD. Only 3 polyostotic patients had extra skeletal signs leading to a diagnosis of McCune Albright Syndrome. 3 other patients (2 polyostotic, one monostotic)patients had a clinical presentation of hypophosphataemic rickets. No other abnormalities had been noted. Using the FD Foundation recommendations, patients were screened by Whole Body MRI(WBMRI). 20/55 monostotic and 12/19 polyostic patients were screened with 1/20 and 6/12 patients, respectively, diagnosed with 'additional' lesions. None of the additional lesions found, in either group, has resulted in a change to planned management but has changed advice on ongoing surveillance and physical activity. 38/74 patients have thus far undergone blood testing. 4/38 (11%) were found to have hypophosphataemia that required treatment. 2/15(20%) were in patients with polyostotic disease and 2/23(8%) were in patients with monostotic disease. No one had an endocrinopathy found on screening.

Conclusion

Although patients with FD can have co-morbidities, the prevalence reported in the literature (up to 40%) is not reflected in our prospective screening programme. Hypophosphataemia occurs in a significant proportion (11%) of all FD patients, polyostotic and monostotic. Therefore, testing for phosphate wasting is worthwhile, but screening for endocrinopathy and other skeletal lesions by routine WBMRI, especially in monostotic FD, is of questionable value.

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OC5.3

Can novel stem cell models help unpick the pathogenesis of the Triple A syndrome?

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Triple A syndrome (AAAS) is a rare, incurable, homozygous disorder, characterised by tissue-specific degeneration resulting in adrenal failure and neurodisability. The *AAAS* gene encodes ALADIN, a nuclear pore complex (NPC) protein necessary for nuclear import of DNA protective molecules, important for redox homeostasis. ALADIN's role is not fully characterised: its discovery at the centrosome and the endoplasmic reticulum suggests a role outside the NPC. The interrogation of ALADIN's function is limited by suboptimal disease models not representative of the affected tissue type.

Aim

To generate cellular models of AAAS with isogenic controls and undertake characterisation.

Method

We developed induced pluripotent stem cell (iPSC) models of AAAS using CRISPR-Cas9 gene-editing: 1) Bi-allelic exon 2 deletion (AAAS-KO) and 2) AAAS homozygous patient mutation: a splice donor hotspot mutation p.G14fs (c.43C>A, exon 1) (AAAS-mutant). These are paired with the original healthy wild-type (WT) iPSC line and mono-allelic exon 2 deletion (AAAS-het) as isogenic controls.

Results

Immunoblotting did not detect ALADIN in AAAS-KO or AAAS-mutant cells. There was no difference in cellular proliferation between AAAS-KO compared to WT by cell counting (*P* value 0.24). Immunofluorescence for Ki67 confirmed no significant changes in cellular proliferation (WT: 100% of cells exhibit Ki67, AAAS-KO cells: 88.46%, *P*-value 0.40). RNA sequencing was performed to identify transcriptomal differences between iPSC lines, comparing WT to AAAS-KO, AAAS-mutant and a heterozygous exon 2 deletion. This identified 8 genes with significantly altered transcription (q values <0.05, LogFC values >1.1 and <-1.1). Preliminary analysis suggests an impact of *AAAS* deficiency on genes involved in apoptosis and oxidative stress. We demonstrated that AAAS-KO and AAAS-mutant cells will differentiate along a neurocortical lineage, expressing neuronal transcription factors OTX2, PAX6 and Nestin.

Conclusion

We present a viable iPSC model for the study of ALADIN in a near endogenous environment. These can be differentiated along a neurocortical lineage, to reflect the tissue affected in the Triple A Syndrome. We present a detailed transcriptome analysis, which will inform further functional experiments to clarify the pathogenesis of AAAS.

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OC5.4

Fourteen years' experience of hydrocortisone pump therapy for cortisol replacement in adrenal insufficiency

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Conventional hydrocortisone dosing does not mimic the normal cortisol circadian rhythm making treatment optimisation difficult in patients with adrenal insufficiency. We described the first use of a continuous variable subcutaneous hydrocortisone infusion (CSHI) via an insulin pump to replace cortisol in a patient with congenital adrenal hyperplasia (CAH) to mimic the normal plasma cortisol circadian rhythm. We report the long term experience of CSHI in seven patients with adrenal insufficiency (5M) aged at start of therapy between 14 and 21 years with adrenal insufficiency (2 CAH, 4 Addison, 1 hypopituitarism). Median duration of therapy - 6 years (range 1 – 14). Indications for therapy were rapid clearance (2), gastric problems (2) and loss of energy (1), difficulty managing diabetes (2). Cortisol half-life was calculated from intravenous studies (median value of 67.5 min (range 40–120)). Clearance was used to estimate pump delivery rates to match hourly plasma cortisol concentrations derived from 24 hour plasma cortisol profiles obtained in 80 adults. Cortisol replacement was compared to the normal dataset and in addition in those with CAH, 17OHP and Addison's ACTH. CSHI therapy was well tolerated and over 42 patient-years there was one cannula site problem due to thigh insertion and one allergy to Efcort resolved by Solucortef substitution. There have been no pump failures or hospitalisations and all patients managed sick days using increased infusion rates successfully. Data from the normal subjects were translated into z scores for each hourly measurement so that each time point was 0 ± 1. Compared to the normative set 24h plasma cortisol profiles obtained yearly had a mean z score of -0.2 ± 0.15 indicating a normal circadian rhythm. 17OHP was measurable within the normal range (<5 nmol/l) but was not suppressed. 0800 h ACTH averaged 15 pg/ml and none were suppressed or above the normal range. All patients reported a vast improvement in quality of life, as well as energy levels, reduction in headaches, concentration, stamina and school and work performance. CSHI is the only method currently available to reproduce the cortisol circadian rhythm. The therapy is effective both clinically and economically and improves quality of life.

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OC5.5

New insights into the low dose dexamethasone suppression test in paediatric Cushing's syndrome (CS)

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Background
The low dose dexamethasone suppression test (LDDST) is an important investigation for suspected Cushing's syndrome (CS). The traditional definition of normal suppression of serum cortisol to $\leq$50 nmol/l (0.5 mg 6 hrly $\times$ 48 hrs) comes from a time when biochemical auto analysers did not routinely detect very low values. Previous studies reported 5.1–8.3% of patients with Cushing's disease (CD) suppressed to $<$50 nmol/l at 48 hrs. Many clinicians experienced in the assessment of suspected CS consider that 'normal' individuals suppress to $\leq$20 nmol/l and that values of 20–50 nmol/l represent uncertainty. Current sensitivity and specificity are reported as 90% and 100%, respectively for $\leq$50 nmol/l.
Methods
We reviewed a retrospective cohort of paediatric patients referred to our centre with suspected CS between 1982 and 2018.
Results
Of 82 suspected CS patients, 50 had Cushing's Disease (CD), 8 had primary pigmented nodular adrenocortical disease (PPNAD) and 24 'control' subjects, in whom the diagnosis of CS was excluded following detailed biochemical evaluation and prolonged clinical/auxological follow-up. The serum cortisol remained $>$50 nmol/l in 44/50 (88%) CD patients (29 males, median age 13.31 years, range 5.6–17.8) during LDDST. In contrast, cortisol was $>$20 nmol/l in 49/50 (98%) CD patients. One patient with cortisol $\leq$20 nmol/l during LDDST had a high clinical suspicion of CD and investigations including bilateral simultaneous inferior petrosal sinus sampling confirmed this. The sensitivity and specificity of a LDDST cut off value of $\leq$20 nmol/l is 98%(CI_{95} 89.4–100%) and 96% (78.9–99.9%). None of the eight PPNAD patients (four male, median age 12.5 years, range 10.5–16.9) had cortisol levels $\leq$50 nmol/l during LDDST. Cortisol levels in 23/24 controls (five males, median age 13.9 years, range 4.3–17.0) suppressed to $\leq$20 nmol/l. One control patient: diagnoses of mosaic turners syndrome; high androgens; hypertension and obesity, suppressed to 22 nmol/l.
Conclusion
Changing the LDDST cut off from $\leq$50 nmol/l to $\leq$20 nmol/l improves the sensitivity of the test from 90 to 98% in our paediatric CS patients. This does not greatly reduce the specificity from 100 to 96%. We therefore suggest using serum cortisol of $\leq$20 nmol/l as a new diagnostic cut off value.

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OC5.6

Successes and challenges around cohorted introduction of Burosumab in clinical treatment of X-linked hypophosphataemia (XLH)

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Background
Burosumab (a monoclonal antibody inhibiting elevated FGF23 activity) targets the pathophysiology of XLH better than conventional phosphate and activated Vitamin D and shows encouraging research findings. Whilst marketing authorisation underway, enrolment into a Named Patient Scheme was possible. Delivery of new treatment modalities can present practical challenges. We report our experience of initiating the first UK cohort.
Methods
Seven patients (2M:5F), median age 8.3 (range 2.6–12.1) years met inclusion criteria of physical or radiological evidence of bone disease despite conventional treatment, aged $>$1year and incomplete linear growth. XLH diagnosed median age 4.2 years, all had confirmed PHEX mutation ($n=6$ and $n=1$ in family member). We developed a fortnightly cohorted nurse-led clinic; processes included clear SOP documentation, patient treatment card and monitoring proforma. Conventional medications were stopped 7 days ahead. Fortnightly Burosumab subcutaneously commenced 0.4 mg/kg, venepuncture performed visits 1,2,3,5,7, dose increments of 0.4 mg/kg at monthly intervals until serum phosphate levels normalised. Quality of Life measure EQ-5D-Y administered at baseline and visit 7.
Results
Normophosphataemia achieved in all within 3 months: two patients normophosphataemic by 1 month, 5 patients required dose increase to 0.8 mg/kg at Visit 3, of which two needed further dose increments. No hyperphosphataemia occurred. ALP improved in 6/7 patients (median reduction 103IU/l). Burosumab injection well tolerated, 5 reported mild side effects: injection site reaction ($n=1$), short duration dizziness $\pm$ headaches/malaise ($n=4$). Mean EQ-5D-Y score improved from 60 at baseline to 92.0 at 3 months ($n=6$). Maintenance doses on transfer to homecare administration at 3 months were 0.4 mg/kg ($n=2$), 0.8 mg/kg ($n=3$), 1.2 mg/kg ($n=1$) and 1.6mg/kg ($n=1$) fortnightly.
Conclusion
Burosumab was successful in promptly normalising phosphate and reducing ALP. Implementing this new therapy with a cohorted approach, improved consistency of monitoring, dose optimisation, side effects monitoring and was healthcare resource efficient, although did increase patient travel burden for this initiation. Concordance with treatment was good and well tolerated. The cohorted approach also facilitated social interaction between affected families with this rare bone disease with the emergence of an ongoing informal patient support network.

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OC5.7

A novel GHR pseudoexon mutation causing frameshift and severe postnatal growth failure

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Background
Growth Hormone Insensitivity is usually caused by mutations in the Growth Hormone receptor (*GHR*). Patients present with short stature, high GH levels, low IGF-I levels and typical Laron syndrome facial features. Our centre previously described the first GHR pseudoexon mutation (42700896A$>$G, c.618+792A$>$G). The inclusion of this pseudoexon is predicted to cause in-frame insertion of 36 amino acid residues between exons 6 and 7. This insertion in the dimerization domain of the GHR results in defective trafficking rather than impaired signalling, causing a partial loss-of-function. As such, moderate postnatal growth failure is observed (Height SDS -3.3 to -6.0).
Hypothesis
Pseudoexons outnumber exons by 10-1 and variants in them may be a major contributor to disease burden.
Methods
We designed a custom short stature gene panel that interrogates both coding and non-coding regions to uncover such mutations. In-vitro splicing assays were performed using an exon trap vector (pET01, MoBiTec GmbH, Germany).
Results
We identified a homozygous *GHR* variant (42700940T$>$G, c.618+836T$>$G) in an Italian patient with classical Laron phenotype, severe postnatal growth failure and height SDS -7.5. Both unaffected, non-consanguineous parents were heterozygous for the mutation. This mutation is 44bp downstream of the original pseudoexon mutation and predicted *in silico* to create a donor splice site. Splicing analysis of this variant confirmed inclusion of a 152bp mutant pseudoexon in all transcripts with no evidence of normal splicing in contrast to the wild-type pseudoexon which showed no such inclusion. Inclusion of the pseudoexon will lead to a frameshift and premature truncation of the mRNA.
Discussion
This novel pseudoexon inclusion event will result in a truncated message which will either be destroyed by nonsense mediated mRNA decay or will lead to a truncated protein lacking the transmembrane and intracellular domains responsible for anchoring the protein in the membrane and signalling respectively. Given the undetectable GHBP levels in this patient, the former effect is suspected. This mutation will cause complete loss-of-function, consistent with the severe growth failure observed. This discovery highlights the potential for such splicing events to be more commonly causal for this and other rare diseases.

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OC5.8

Patients with short stature and GH/IGF-1 insensitivity harbour copy number variants causing a Silver-Russell-like phenotype

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Introduction
Our Centre receives international referrals for genetic analysis of children with short stature (SS) and features of GH/IGF-1 insensitivity. Copy number variation (CNV) hasn't previously been investigated in GH/IGF-1 insensitivity. We hypothesised CNVs contribute to the phenotype in our undiagnosed cohort.
Experimental design/methodology
CGH was performed with oligonucleotide array using ~60,000 probes in 60 patients (38 M, mean age 7.0 yrs (range 1.1–16.5), mean height SDS −3.87 (range −1.58 to −7.44)).
Results
We identified CNVs in 10/60 (17%) patients (8M), mean height SDS −3.70 (range −1.6 to −5.7). 7/10 and 3/10 patients had likely pathogenic CNVs and CNVs of uncertain significance, respectively. Patients 1–7 have features of Silver-Russell Syndrome (SRS), scoring 2–3/6 on the Netchine-Harbison Clinical Scoring System. Patients 1–6 have CNVs previously associated with SRS phenotypes. Causative genes within many CNV regions below have yet to be established.

Table 1 CNVs identified in our patients

Patient	Age (years)	Height SDS	Clinical details	CNV
1	12.8	−3.6	Small triangular face, high arched palate, feeding difficulties	1q21 deletion
2	10.1	−1.6	Feeding difficulties, dyslexia	1q21 deletion
3	9.1	−3.7	Clinodactly, feeding difficulties	1q21 deletion
4	11.3	−5.1	Triangular face, high pitched voice	12q14 deletion
5	1.9	−5.7	Low set ears, triangular face, SGA	7q21 deletion, 7q31 deletion
6	14.4	−2.7	SGA	7q21 duplication, Xp22 duplication
7	2.8	−4.9	Triangular face, frontal bossing, feeding difficulties	15q11 deletion
8	17.0	−4.0	Learning difficulties, delayed puberty	5q12 deletion
9	2.7	−2.0	Adrenal insufficiency, SGA	7q36 duplication
10	2.5	−3.6	Short limbs	3p22 deletion, 15q13 duplication

Conclusion
Our cohort was enriched for rare CNVs. Interestingly, 7/10 patients with CNVs had features of SRS, a heterogeneous syndrome with no genetic cause identified in 40% patients. Consistent with previous reports, the SRS phenotype in our CNV patients appears milder than classic 11p15LOM/upd(7)mat cases and only 2/7 with SRS features were born SGA. Our study is the first to report CNVs in GH/IGF-1 insensitivity patients and contributes to the emerging SRS-like phenotype. Our findings emphasise the importance of CNV testing in SS patients, especially those with SRS features.

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OC5.9

Diazoxide-induced pulmonary hypertension: UK multicentre retrospective study on the risk factors, monitoring approach andmanagement recommendations

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Objectives
Diazoxide is first line treatment for hypoglycaemia due to hyperinsulinaemic hypoglycaemia (HH). Although sporadic cases of pulmonary hypertension (PH) have been reported, no HH cohort has been systematically characterised to understand severity and risk factors for diazoxide-induced PH.
Methods
To investigate the onset, progress and associated factors in PH, patients with HH who developed diazoxide-induced PH in 4 regional centres were retrospectively reviewed. PH diagnosis was based on clinical and/or echocardiography evidence. Child and treatment-related risk factors were analysed for association. The time intervals from diazoxide initiation to onset and resolution of PH were also recorded.
Results
Twelve cases were identified (5M:7F). HH was diagnosed at median (range) 12 (1,180) days, with diazoxide started 3 (1,76) days from diagnosis, reaching highest dose of 8.0 (2.5,20) mg/kg/day. Only 3 (25%) patients had mutations in *ABCC8/KCNJ11* establishing genetic causation. Total fluid intake was 170 (100,180) ml/kg/day prior to treatment. The majority developed PH within 2 weeks of diazoxide [12 (2,90) days], with 3 patients requiring intensive care ventilation (2 requiring high frequency oscillation). Two-thirds of (8/12) patients had baseline echocardiography before initiation of diazoxide. Diazoxide dose reduction did not ameliorate PH but complete withdrawal led to PH resolution at a variable time of 32.5 (3,985) days. In 3 patients, PH has yet to resolve after 6 months. Risk factors for the development of PH included low birthweight in 6 (50%) and fluid intake exceeding 130 ml/kg/day in 10 (83%) patients. Eight (67%) patients also had congenital heart disease (CHD). The presence or absence of CHD did not influence the time to develop PH ($P=0.37$) or time for PH resolution ($P=0.99$) respectively.
Conclusion
PH is a serious complication of diazoxide therapy in HH occurring at an unpredictable time from initiation of treatment. We recommend vigilance for PH in low birthweight infants with fluid intake exceeding 130 ml/kg/day. PH-specific echocardiography should be performed before diazoxide treatment to identify underlying CHD, followed by weekly monitoring for at least the first 2 weeks. If PH is identified, diazoxide should be discontinued to facilitate PH resolution.

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Oral Communications 6

OC6.1

A retrospective regional analysis of outcomes during transition of young people with type 1 diabetes

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Objectives
Transition from paediatric (PC) to adult diabetes care (AC) is a vulnerable period for young people (YP). The West Midlands (WM) Regional Paediatric Diabetes Network conducted a region-wide study of Diabetes transition outcomes to identify 1. Areas of good practice, 2. Risk factors for poorer outcomes,

3. Regional objectives for services and 4. Provide baseline data against which future performance can be measured.
Methods
Retrospective regional audit of follow up and HbA1c 12 months pre and 24 months post transfer in YP transitioning between January 2012 and December 2013.
Results
Data was submitted by 9 of 13 (69%) Trusts, accounting for 298 YP moving from PC to transition clinic (TC), and 195 from TC to AC. 41/298 (13.8%) YP were lost to follow up (FU) in TC (range 0–29%). 41/195 (21%) were lost to FU within 2 years of AC (range 0–40%). Median age at move to AC was 17.8 years, range 16 - 19.84 years. 22%, were seen in AC within 3 months of their last TC visit. For 45% and 13% their first AC visit occured 6–12 and >12 months respectively, following their last TC. Pre and post HbA1c data was available on 144 YP (73%) transferring from TC to AC. Median HbA1c was 75 (Trust range 64–83) mmol/mol in the year prior to AC and 78mmol/mol (Trust Range 63.5 to 89.5) in first 2 years of AC. Lag time between the TC and first AC visit did not correlate with HbA1c. YP in TC with HbA1c <53 (7.5%) deteriorate ($P=0.028$), and HbA1c >9.0% improve ($P<0.00009$) on move to AC. Age at move to AC positively correlates with fall in HbA1c ($R=-0.201$, $P=0.048$).
Conclusion
WM Trusts need to focus on
1. Reducing high lost to FU rates of 1 in 5 YP (up to 1 in 2.5 in some Trusts)
2. Reducing lag time from TC to first AC.
3. Careful consideration could be given to transferring some YP in TC with HbA1c > 9.0% to AC at an earlier point.
4. Further studies should look at impact of age and deprivation on rates of attrition following move to AC.

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OC6.2

Perceptions of diabetes education: a questionnaire-based survey of 117 patients and families

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Background
Diabetes is a primarily self-managed condition, and education to patients and families is an essential component of a diabetes service. In line with accepted UK practice, our diabetes team provides a comprehensive education program at diagnosis and regularly thereafter.
Methods
From October 2017 to January 2018, all patients attending diabetes clinic were offered a pseudo-anonymised mixed methods survey, covering experience of education, barriers to education attendance, and ideas to improve our education provision. The respondent's HbA1c, collected on the same day, was recorded.
Results
Of the 117 surveys returned (51% of our population), 46% were completed by patients, 48% by parents/carers, and 4% by both together. Of the respondents, 59% had attended an annual education clinic (mean HbA1c 64 mmol/mol). The 41% who hadn't attended had a mean HbA1c of 68mmol/mol. Those who chose not to attend because they 'already know about diabetes' had an HbA1c ranging from 42–104 mmol/mol, with a mean of 61 mmol/mol [95%CI=52–70 mmol/mol]. Most respondents indicated confidence managing their diabetes: 85% confident/very confident, 1% underconfident. In the qualitative analysis, several unexpected themes emerged. First, respondents indicated that meeting other children and families was what they most valued about education clinic. They suggested peer-led education, sessions delivered by young adults who had recently transitioned, and more socialising opportunities. Second, respondents requested information about research such as novel technologies, artificial pancreas systems, and the search for a cure. The third theme that emerged was mental health, both as a barrier to and a consequence of diabetes management. Finally, respondents suggested more technological approaches to education provision such as Facebook, YouTube videos, emails and webinars.
Discussion
There continue to be unmet needs in diabetes education, and patients' and families' priorities may differ from the diabetes teams'. Peer support and peer education should play larger roles, and broadening education clinics to include topics such as 'advances in diabetes research' may widen their appeal. While some of this data is unit-specific, much of it could be applied UK-wide to make education more patient-focused.

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OC6.3

Has the reduction in maintenance fluid rates following introduction of 2015 BSPED-recommended diabetic ketoacidosis guidelines impacted on complication rates?

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Introduction
In August 2015, a revision of the BSPED-recommended guideline for the management of diabetic ketoacidosis (DKA) was published. A key difference from the previous guideline was a reduction in maintenance fluid rates, with the aim of reducing the incidence of cerebral oedema. Since implementation of these national guidelines, there have been reports within regional networks of an increased incidence in mild acute renal impairment and hypokalaemia. This retrospective audit aimed to compare the incidence of these complications pre- and post-implementation of the guidelines.
Methods
Databases were reviewed for all children newly-diagnosed to have diabetes who presented in DKA, in the 3 years prior to and following implementation of the latest BSPED DKA guidelines at the Royal Manchester Children's Hospital. Data was collected on potassium (K), urea (Ur) and creatinine (Cr) at presentation and lowest K, peak Ur and Cr during admission.
Results
Twenty four children presented with DKA prior to guideline implementation and 23 following guideline implementation. There was no significant difference in mean lowest K (3.3 mmol/l pre, 3.1 mmol/l post, $P=0.32$) or mean difference between admission and lowest K (−0.9 mmol/l pre, −0.9 mmol/l post). Hypokalaemia, as defined by the BSPED DKA guideline (<3.0 mmol/l), during admission significantly increased since new guideline implementation – 21% (5/24) pre, 48% (11/23) post ($P=0.05$). There was no significant difference between mean peak Ur (6.5 mmol/l pre, 5.6 mmol/l post, $P=0.40$), or mean peak Cr (47 mcmol/l pre, 52.3 mcmol/l post, $P=0.35$). There was no mean difference between admission and peak Ur (+0.2 mmol/l pre, +0.3 mmol/l post), or between admission and peak Cr (+1.7 mcmol/l pre, +6.3 mcmol/l post, $P=0.13$).
Conclusion
Although there was no appreciable difference between the two groups in the lowest K or difference between admission K and lowest K, there is noted to be an increase in incidence of hypokalaemia during admission since the new DKA guidelines were introduced. In light of recent evidence that suggests the rate of intravenous fluid administration does not influence neurological outcomes, perhaps the current guidelines need review to reduce the incidence of hypokalaemia.

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Oral Communications 7

OC7.1

DeAPP (Diabetes Education APP): using flipped learning to deliver structured education in newly diagnosed type 1 diabetes patients

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Background
At diagnosis of diabetes is a critical time in the life course of diabetes. This a critical time for patient take on knowledge and using it (ref). Utilisation of this information is suboptimal due to logistical factors such as ward environment, time constraints of staff, psychological impact of the diagnosis. Current models of education are mainly didactic with limited impact in some patients.
Aims
In collaboration with demontfort design unit, we aimed to develop a structured education program combining APP technology and kinaesthetic learning resources to deliver flipped learning. Patients learn 1st the theoretical knowledge before healthcare professionals evaluate and re-enforce patients learning for more effective management of their diabetes.
Methods
East Midland CYP education subgroup (CYPES) held focus groups with healthcare professionals,parents, patients to formulate a curriculum and lesson plans. CYPES presented to Demontfort Design Unit who synthesised these according to age, numeracy, literacy and language. Developing video storyboards with scripted animation, alongside kinaesthetic learning resources. From which they developed a mobile optimised APP to host vimeo animated videos and other

educational content. Patients sequentially view videos covering the curriculum with email confirmation to the team on finishing each lesson. The team then completes a process of flipped learning testing knowledge & utilisation using the learning resources that are then signed off as record of competency. DeAPP is free to download in i-OS and android devices.

Results

Five pilot East Midlands paediatric diabetes units trialled the structured education program with the following outcomes. 350 registrations (102 from pilot centres). Of those registered, 56 have completed all 12 sessions. Patients rated aspects of the app on a scale of 0–5, with consistent high ratings for usefulness, ease and quality/content. Stating they were likely to use the App once discharged home. Pilot data $n=11$: quantitative outcome measures (Table 1), This APP based education platform can deliver structured education using flipped learning. Allowing patients to self-learn core theoretical knowledge prior to health professional testing utilisation. Outcomes are at least comparable to existing structured education at diagnosis.

Table 1

Measure	Average	Range
Kaufmann competency	4.1	2–6
Paid score	10.2	5–14
Hypo scores	<4	0–3

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OC7.2

Provision of psychology services for children and young people with diabetes: a national survey

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Children &Young people (CYP) with Diabetes Mellitus (DM) have increased rates of depression, anxiety, psychological distress and eating disorders than their healthy peers. Psychological factors and the patient's health beliefs are important determinants of self-care behaviour. Randomised control trials have confirmed that Psychological interventions can significantly lead to improvement in measures of psychological well-being. Routine psychological support is advocated as a normal part of a paediatric diabetes service.

Objective

To assess the current level of provision of psychology services for CYP with diabetes mellitus and how integrated the Psychologists are with the rest of paediatric diabetes multidisciplinary team (MDT) in United Kingdom.

Method

Clinicians working in 152 NHS trusts and health boards in the United Kingdom were invited via email to complete an online survey (April 2018–June 2018).

Results

Responses were received from 72.3% (110/152) NHS trusts and Health boards looking after approximately 20,684 CYP with DM. 81.5% have a psychologist as part of the MDT. The median number of whole time equivalent psychologist (WTE) was 0.5. The ratio of WTE Psychologist to number of CYP cared for in the service varied from 1:75 to 1:3,600 (Median 1:460). 49.5% of Psychologists routinely attend all DM clinics. 52.1% see all newly diagnosed patients at presentation. 40.3% accept self-referrals directly from CYP or carers. 87.7% see CYP outside of DM clinics in separate psychology sessions. 58% contribute to training other members of the MDT while 47% contribute to CYP group structured education sessions. 84.1% of services undertake annual assessment of psychological wellbeing using various tools with 'Well being in Diabetes Questionnaire' being the most commonly used (35.9%). Units receiving BPT were significantly more likely to have a Psychologist as part of MDT (85.7% Vs 50%) $P<0.05$.

Conclusion

Compared to the 2010 National survey, there has been a significant increase in the provision of Psychological services for CYP (21% VS 81.5%) $P<0.05$. This appears to be related to increased funding for diabetes services following introduction of best practise tariff.

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OC7.3

The determinants of skeletal morbidity and fractures in children with type 1 diabetes

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Objective

The pathophysiology of the increased fracture risk in Type 1 Diabetes (T1D) remains unclear. Given that childhood and adolescence are important physiological periods for optimal bone development, we performed a multi-modality assessment to determine the effects of T1D on bone health.

Methods

Thirty two affected children at a median (range) age of 13.7 years (10.4, 16.7), were recruited for detailed assessment of bone health. Serum bone alkaline phosphatase (BAP) and c-terminal telopeptide of type 1 collagen (CTX) as well as DXA total body (TB) and lumbar spine (LS) bone mineral content (BMC) adjusted for bone area were converted to SDS. 3T MRI was performed to assess proximal tibia bone microarchitecure and vertebral marrow fat fraction (%) and compared to 26 healthy controls.

Results

In T1D, BAP SDS and CTX SDS were -0.6 ($-2.5, +2.1$) and -1.1 ($-2.5, +0.5$) and TB and LS BMC SDS were -0.1 ($-1.1, 0.9$) and -0.3 ($-1.0, 1.8$), respectively. Trabecular volume (appBV/TV) and trabecular number (appTbN) were lower in cases with corresponding higher trabecular separation (appTbSp) compared to controls at 0.55 (0.47, 0.63) vs 0.59 (0.47, 0.63) ($P=0.024$), 1.67 (1.56, 1.93) vs 1.82 (1.56, 1.99) ($P=0.004$) and 0.27 (0.21,0.32) vs 0.24 (0.20,0.33) ($P=0.001$), respectively. The marrow fat fraction in cases and controls was similar at 23% (11, 66) and 20% (8, 61), respectively ($P=0.25$). T1D cases with poor glycemic control HbA1c>75 mmol/mol had lower BAP SDS compared to those with good control HbA1c<58mmol/mol ($P=0.009$). BAP SDS were also lower in children with acidosis at initial presentation ($P=0.017$) and higher in children on continuous subcutaneous insulin infusion ($P=0.025$). Fractures were encountered in 10/32 (31%) cases after diagnosis of T1D and 5/26 (19%) controls ($P<0.001$). T1D children who fractured had poorer glycaemic control ($P=0.007$) and lower TB BMC SDS ($P<0.001$). There was no significant difference in bone microarchitecture or marrow adiposity between the fracture groups.

Conclusion

Children with T1D display a low bone turnover state with reduced bone mineralisation and poorer bone microarchitecture. Bone formation was affected by glycemic control, acidosis at T1D presentation and insulin delivery whilst fractures were associated with bone mineral status.

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OC7.4

Parental language proficiency and glycaemic control in children with type 1 diabetes

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Introduction

Effective communication between care providers and parents/carers is fundamental for the management of children with Type 1 diabetes. National guidelines highlight the importance of communicating effectively with parents of limited understanding of English. This study evaluates whether parental language proficiency is related to glycaemic control in a paediatric diabetes clinic serving an inner city multi-ethnic population.

Method

Routine data was collected between 1/4/17–31/3/18 at a single London centre from patients diagnosed with Type 1 Diabetes for >1 year. Data included demographics (age, gender, duration of diabetes, deprivation scores), insulin regimen, psychological wellbeing scores and HbA1c. English language proficiency of the main parent/carer for diabetes care was ranked by the diabetes team as basic (group 1: requires interpreter), independent (group 2: manages

without interpreter but not fluent) or proficient (group 3: native or fluent in English as second language). HbA1c was compared and adjusted for confounders. Statistical analysis: ANOVA, ANCOVA, *t*-test and c-Square, using SPSSv24 at 5% significance.

Results

Ninety-five (m:f=45:50) patients were included and categorised into group 1($n=18$), 2($n=9$), and 3($n=68$). Their age ranged between 3.4 and 19.7 years (Median=14.7), diabetes duration ranged between 1 and 16.3 years (Median=5.4) and HbA1c ranged between 43 and 130 mmol/mol (Median=69.4). Within group 1, Somalian (39%) was the most commonly spoken of the nine different non-English languages. HbA1c scores (geometric means) were significantly higher in group 1 (84.6 mmol/mol) compared with groups 2 (70.5 mmol/mol, $P=0.04$) and 3 (68 mmol/mol, $P=0.01$). No significant difference was found between groups 2 and 3. Despite significant differences in deprivation scores between groups, ($P=0.001$), when controlled for, HbA1c remained significantly different between groups (group 1 vs 2: $P=0.01$, 1 vs 3: $P=0.011$). No group differences in gender, age, duration of diagnosis, psychological wellbeing scores. There were more pump users in group 3(32%) vs 1(6%), but no differences in HbA1c scores were identified.

Conclusion

Language proficiency is identified as a potential barrier to optimal glycaemic control. Targeted measures such as language-specific education material/activities, support groups and key workers should be considered.

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OC7.5

Diabetes control is worse in children and young people with type 1 diabetes requiring interpreter support

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Introduction

Language barriers can pose a significant barrier to successful education of children and young people (CYP) with type 1 diabetes (T1DM) and their families, potentially influencing their glycaemic control.

Methods

Retrospective analysis from diagnosis to 18 months post diagnosis of glycaemic control in 41 CYP with T1DM requiring interpreter support (INT) under care of our diabetes centre based within a multi-ethnic community. Median HbA1c at 0, 3, 6, 9, 12 and 18 months following diagnosis were compared to 100 age-, sex- and mode-of-therapy-matched controls who did not require interpreter service. English indices of deprivation are based on the 2015 census and were retrieved from: www.gov.uk/government/statistics.

Results

The main languages spoken were Somali (27%), Urdu (19.5%), Romanian (17%) and Arabic (12%), but also Polish, Hindi, Tigrinya, Portuguese, Bengali and sign language. Overall deprivation was worse in the INT group according to Index of Multiple Deprivation (IMD [median]: INT 1.642; control 3.741; $P=0.001$). The median HbA1c was higher at diagnosis in the control group (9.95 versus 9.0%, $P=0.046$) but was higher in the INT group after diagnosis: the median HbA1c at 18 months post diagnosis was 8.3% (INT) versus 7.9% (controls) ($P=0.014$). There were no hospital admissions required due to diabetes-related complications in both subgroups.

Summary and conclusions

Glycaemic control is worse in CYP with T1DM who face language barriers in our centre. Socioeconomic deprivation may confound these findings but indicate that this is a disadvantaged subset of patients regardless. In order to improve diabetes care for CYP with language barriers, we propose that health care providers develop strategies to provide tailored support, including provision of diabetes-specific training for interpreters. Equally, patients and their families should be supported to acquire language skills for ongoing diabetes education. The findings of this study suggest that equally poor health outcomes for CYP with language barriers and *any*chronic condition is a broader concern. This highlights the need for a sustained medical and political effort toward the effective integration and support of CYPs from disadvantaged backgrounds.

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OC7.6

Type A Insulin Resistance Syndrome due to an *INSR* mutation Presenting with diabetes mellitus evolving to hyperandrogenism and PCOS

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Background

Mutations in the insulin receptor (*INSR)* gene are rare and cause a spectrum of severe insulin resistance syndromes including Donohue syndrome, Rabson Mendenhall syndrome, and Type A Insulin Resistance Syndrome (IRS). We describe a young female with a heterozygous *INSR* mutation, who presented with antibody positive diabetes mellitus (DM) and subsequently developed features of Type A IRS.

Case Report

A 12 year old Jamaican girl with a BMI of 25 kg/m^2 presented with polyuria, polydipsia and hyperglycaemia (blood glucose 18 mmol/l). HbA1c was raised at 85 mmol/mol, urinary ketones were negative. Antibodies to islet antigen-2 were positive (0.56 U/ml; normal range: 0–0.35 U/ml), and antibodies to glutamic acid decarboxylase and insulin were negative. She was diagnosed with Type 1 DM and started on a basal-bolus insulin regime. She previously had precocious puberty, treated with GnRH analogues. She achieved menarche at 13 years with irregular cycles. Over 2 years, she developed hirsutism, acanthosis nigricans, and postprandial hypoglycaemia, with no evidence of lipodystrophy. Biochemical investigations showed raised serum C-peptide (854 pmol/l), LH (29.1 IU/l), and testosterone levels (3.6 nmol/l), with normal lipids. Ultrasound pelvis revealed enlarged ovaries with multiple peripheral follicles suggestive of PCOS. Family history included DM affecting mother, maternal uncle and maternal grandfather. Targeted next generation sequencing of the monogenic diabetes genes revealed a heterozygous missense *INSR* variant p.(His1157 Gln), c.3471T>G in the patient and affected mother. The p.His1157 residue is present within the catalytic loop of the tyrosine kinase domain of the *INSR*. A different missense variant affecting the same residue, p.(His1157Arg), has been previously associated with Type A IRS. The patient was started on metformin and weaned off insulin therapy. Her menstrual cycles then normalised and glycaemic control improved (HbA1C 36 mmol/l).

Conclusion

This is a novel description of a p.His1157Gln mutation in *INSR* causing Type A IRS. Our findings highlight the role of puberty in the manifestation of insulin resistance. This case also emphasises the importance of exploring an *INSR* defect in slim patients with DM and features of insulin resistance in the absence of lipodystrophy and normal lipids.

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OC7.7

Knowledge and confidence of paediatric middle grade doctors in managing out of hours diabetes advice calls

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Background

Paediatric diabetes is predominantly an outpatient based specialty, limiting the training opportunities available to paediatric trainees. At our centre, out of hours diabetes advice calls are managed by paediatric specialty trainees working on the middle grade rota, with 24 hour support from an oncall paediatric diabetes consultant. Feedback locally from families has highlighted the quality of out of hours advice as an area of concern. We aimed to assess the knowledge and confidence of paediatric trainees in managing out of hours advice calls to help inform training and service provision.

Methodology

The study took two parts. Firstly all paediatric trainees at level ST4+ were asked to complete an anonymous questionnaire, with six scenarios covering common advice calls. Model answers were agreed by the diabetes team. Answers were marked by two independent diabetologists. The scoring system gave separate

marks for knowledge and for safety. The second part involved a questionnaire for trainees who responded to advice calls during a three month study period, aiming to assess confidence in dealing with such calls. Timing of advice calls was recorded by the hospital switchboard.
Results
Eighteen of twenty-eight (64%) trainees completed the scenarios. Knowledge was variable, with technology based scenarios generally scoring poorly (average knowledge score for lost pump handset scenario 22% versus 63% for sick day rule scenario). Trainees however tended to act safely (average safety score 87%). There was no correlation between knowledge and safety. Sixteen out of hours advice calls were made during the 3 month study period. Questionnaires were completed for 75% of the calls. All trainees felt confident in managing the call and 92% felt they had adequate training to manage the call.
Conclusions
This project demonstrates a discrepancy between registrar confidence and family satisfaction with out of hours telephone advice. The knowledge base of paediatric trainees in dealing with common diabetes advice scenarios is very variable. We discuss the approach we are taking to the challenges of providing diabetes training to paediatric trainees and how this should be balanced with patient safety and satisfaction.

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OC7.8

Continuous glucose monitoring with regular clinical review of glycaemic control in children with type 1 diabetes experiencing frequent unpredictable hypoglycaemia

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Introduction
Optimal glycaemic control can be extremely challenging to achieve in children and adolescents with Type 1 Diabetes (T1D) who have labile glycaemic control with frequent hypoglycaemia despite intensive blood glucose monitoring (BGM). Effectiveness of continuous glucose monitoring (CGM) in children/adolescents at high risk of hypoglycaemia has been poorly studied. Frequent patient follow-up and review is recommended to support successful CGM management. This pilot study explored the impact of CGM and regular clinical review on glycaemic control in children/adolescents with T1D experiencing frequent unpredictable hypoglycaemia.
Methods
Children/adolescents aged 2–18 with T1D ($n=10$) wore a CGM device for six weeks. During this period, each participant had four clinical reviews with a Paediatric Diabetes Consultant, who assessed the participant's CGM download, adjusted insulin dosage and offered relevant advice to optimise glycaemic control. Glycaemic outcomes from Week 1 and Week 6 of CGM were compared.
Results
Mean daily glucose was 11.5 mmol/L (SD 1.8) in Week 1 and 9.2 mmol/L (0.8) in Week 6: mean reduction of 2.3 (95% CI −3.4 to −1.3; $P=0.002$). Weekly SD of glucose levels (as a measure of glycaemic variability) decreased by 1.1 over six weeks (−1.5 to −0.7; $P<0.001$). Total weekly time spent with a glucose level between 4 and 10 mmol/L increased by 38.25 hours (25.99 to 50.51; $P<0.001$). This was accompanied by a mean reduction of 8.17 hours in the total weekly time spent with a glucose level <4 mmol/L (−11.2 to −5.13; $P<0.001$) and 1.42 hours in the total weekly time spent with a glucose level <2.8 mmol/L (−2.23 to −0.59, $P=0.004$). Additionally, weekly time spent with a glucose level >10 mmol/L decreased by 30.08 hours (−43.61 to −16.54; $P=0.001$).
Conclusion
CGM with regular clinical review over six weeks significantly improved glycaemic control and reduced hypoglycaemia in children/adolescents with T1D. These are important and meaningful clinical outcomes. Larger and longer studies are required to examine longer term impact of CGM on glycaemic control and avoidance of hypoglycaemia in this vulnerable group. These improvements may also have a positive impact on other outcomes including quality of life and sleep quality.

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Oral Communications 8

OC8.1

Five year outcomes in a cohort with hypoglycaemia due to congenital hyperinsulinism

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Background
Congenital hyperinsulinism (CHI) is one of the commonest causes of recurrent hypoglycaemia due to excess production of insulin in infancy and results in neurological impairment in a third to a half of patients. The treatment of CHI is often complex and complicated by side effects; the medium-term effects of such treatment are not known.
Aim
To describe five year clinical outcomes in a cohort of infants with CHI.
Methods
Data from 37 infants (26 males) diagnosed and treated for CHI in 2011- 2012 at a single centre were reviewed. Five year outcomes included auxology, feeding, treatment and neurodevelopment.
Results
Small for gestational age was a common diagnostic association with birth weight <2 SDS. CHI was transient in 32 (86%) patients with the rest requiring persistent treatment. At one year, 20 (54%) patients treated with diazoxide reduced and stopped treatment. Five patients underwent 18-fluoro-DOPA PET-CT scanning which identified focal CHI, treated by focal lesionectomy in one patient only. Two patients required subtotal pancreatectomy, while the majority were successfully managed by medical therapy. Auxology parameters normalised by age one year, with height and weight SDS < −2.0 SDS in only at 8% and 21% respectively. In this cohort, only 4 (11%) patients had abnormal feeding which required either feeding through nasogastric or gastrostomy tubes. However feeding remained problematic in 3 patients as late as the 5 year review. Neurodevelopmental concerns (speech delay/cognitive dysfunction) were present in 9 out of 32 patients (28%) examined.
Conclusion
The majority of patients in a CHI cohort were born small for gestational age, responded to medical therapy, improved growth and had disease resolution in clinical review. Neurodevelopment was abnormal in a third of patients.

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OC8.2

The effect of GnRHa treatment on bone density in young adolescents with gender dysphoria: findings from a large national cohort

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Background/Aims
More young people with gender dysphoria are undergoing hormonal intervention with GnRHa treatment. The impact on bone density is not known in the very young transgender adolescents, with guidelines mentioning that Bone Mineral Density (BMD) should be monitored without a suggestion on how. This study aimed to investigate whether there were any changes in BMD or Bone Mineral Apparent Density (BMAD) whilst on GnRHa therapy.
Methods
A retrospective analysis of 70 transgender subjects aged 12–14 years who were referred to a national centre for the management of gender dysphoria (2011–16) and had had yearly DEXA scans. A longitudinal analysis ($n=31$) where subjects had had scans over 3 years and a cross-sectional analysis ($n=70$) were performed for BMD differences between each scan.
Results
Although there was a decline in age-related Z-scores, there was no significant change in BMAD after one year on GnRHa and no significant changes between DEXA scans for tBMD or BMAD when analysed cross-sectionally or longitudinally over 3 years.
Conclusion
We have shown that there is no actual change in BMAD or tBMD in young transgender adolescents on long term GnRHa therapy, and certainly no true fall as

initially suspected. We suggest that yearly DEXA scans may not be necessary. We also suggest that reference ranges may need to be re-defined for this patient cohort.

Characteristic	Scan 1	Scan 2	Scan 3	P^a	P^b	P^c
Transgirls (n)	31	31	10			
Age	13.2	14.4	15.8			
Spine tBMD [kg/m^2] (SD)	0.867 (0.141)	0.866 (0.126)	0.878 (0.130)	0.952	0.395	0.202
Spine tBMD Z-Score	0.130 (0.972)	−0.650 (1.182)	−0.890 (1.075)	0.001	0.000	0.203
Spine BMAD [g/cm^3] (SD)	0.235 (0.030)	0.233 (0.029)	0.241 (0.029)	0.459	0.865	0.355
Transboys (n)	39	39	21			
Age (y)	12.6	13.8	15.4			
Spine tBMD [kg/m^2] (SD)	0.695 (0.220)	0.711 (0.205)	0.731 (0.209)	0.107	0.058	0.056
Spine tBMD Z-Score	−0.715 (1.406)	−1.610 (1.462)	−2.000 (1.384)	0.000	0.000	0.035
Spine BMAD [g/cm^3] (SD)	0.196 (0.035)	0.201 (0.033)	0.198 (0.033)	0.074	0.526	0.580

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OC8.3

Attitudes toward fertility and reproductive health among transgender adolescents

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Introduction
Utilization rates of fertility preservation among transgender adolescents (TA) are low. Few studies have addressed the reproductive desires of this population. The aim of this study was to assess TA parenthood goals, attitudes about fertility preservation (FP) and perceived barriers to successful gamete banking.
Methods
Transgender adolescents who attended the Gender Identity Development Service (GIDS - endocrine clinic) between March and June 2018, were invited to complete an online survey based on a modified version of The Transgender Youth Fertility Attitudes Questionnaire (TYFAQ).
Results
The questionnaire was answered by 40 TA (27 trans-males): 8 (20%) were younger than 16 years old and 32 (80%) were 16 years and older. 35 individuals (87.5%) received pharmacological therapy for their gender: GnRH analogue (57.1%), combination of GnRH analogue and cross sex hormones (28.57%) or contraceptive pill (2.85%). 23 TA (57.5%) expressed their positive desire of having children either biologically related (22.5%) or adopted (35%) and only 6 TA of 14 who did not want to have children or were unsure about it, acknowledged that their decision could change when older. Regarding fertility implications of gender dysphoria treatment 40 TA strongly agreed (42.5%) or agreed (57.5%) that counselling was important. Information given by psychologist, endocrinologist, general practitioners and fertility units was rated good or very good by 34 (89.5%), 28 (75.7%), 13 (37.1%) and 9 (28.1%) individuals respectively. 39 participants (97.5%) reported a good understanding of available FP methods but utilization rates were low among the whole group: 5 TA (1 trans-male and 4 trans-females). Barriers to access FP in descending order were: incongruence between perceived gender and biological parental role in trans-males and discomfort with FP procedures in trans-females, invasiveness of procedures for trans-males and cost for trans-females and delay of pharmacological intervention for both groups.
Conclusions
More than half of TA expressed interest in parenthood options and agreed that FP counselling was relevant. Unfortunately FP utilisation rate in this population is low. Guidelines and pathways design should consider TA unique fertility and reproductive health needs.

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Poster Presentations

Adrenal

P001

A Cochrane Review of glucocorticoid replacement regimens in the treatment of 21-hydroxylase deficiency congenital adrenal hyperplasia

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Congenital adrenal hyperplasia (CAH) is an autosomal recessive condition which leads to glucocorticoid deficiency. During childhood, aims of treatment are to prevent adrenal crisis and to achieve optimal adult height and normal puberty. In adults, aims of treatment are to prevent adrenal crisis, ensure normal fertility and avoid long-term consequences of glucocorticoid use. Current regimens with glucocorticoids cannot optimally replicate the normal physiological cortisol level. Overtreatment or undertreatment is often reported and there is no current standard treatment for CAH. It remains unclear which treatment regimen is most effective.

Objective

This Cochrane review (protocol published) aims to determine the efficacy of different glucocorticoid replacement regimens of CAH.

Methods

We included any RCT or quasiRCT comparing different glucocorticoid replacement regimens in the treatment of CAH due to 21-hydroxylase deficiency in children and adults. GRADE was used to assess quality of the evidence.

Results

The initial search identified 297 records which identified 20 publications for further examination. After screening, we included five RCTs with 101 people with CAH. The number of participants in each trial varied from 6 to 44 with participants' ages ranging from 1.2 to 21 years. The majority of the trials we included were small and many had methodological weaknesses. The number of trials assessing different glucocorticoid regimens varied as well as the trial durations. Although 17OHP and androstenedione are frequently used to monitor treatment, there is a great amount of variability in the measurements. Overall, we judged trials to be moderate to high risk of bias across many domains.

Conclusions

There is insufficient evidence to indicate which glucocorticoid replacement regimen results in better outcomes. There were no trials on modified-release formulation of hydrocortisone or use of 24-hour circadian continuous subcutaneous infusion of hydrocortisone. This review identified the need for well-designed, adequately-powered trials to assess the efficacy of different glucocorticoid replacement regimens in the treatment of CAH.

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P002

Borderline peak plasma cortisol following Synacthen stimulation – single-centre analysis of three years' data

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Introduction

Diagnostic cut-offs for plasma cortisol on Short Synacthen Test (SST) are controversial, made more complicated by modern assays and paediatric normative values extrapolated from adult data. Some advocate a division between biochemical and clinical AI, with different cut-offs and management strategies. For asymptomatic children, with a low-index of suspicion, and borderline SST results our department has evolved a tendency to advise hydrocortisone replacement in times of stress only. We analysed three years of SST data, examining the cases with borderline peak cortisol results for aetiological links and subsequent management strategies.

Methods

Retrospective analysis of all SST performed between September 2014 and 2017 was undertaken. Plasma cortisol samples were analysed on the Abbott Architect i1000 immunoassay (CVs $<5\%$). Our diagnostic threshold for a 'pass' for both high (HDT) and low-dose SST (LDT) is 450 nmol/l. 'Borderline' peak cortisol was considered to be 300–449 nmol/l and this group was further subdivided into 300–349, 350–399 and 400–449 nmol/l for analysis in terms of demographics, test indication, dose of synacthen and resultant management plan.

Results

433 SSTs were performed, 74 (41M) of whom had a borderline peak cortisol (16.7%). The proportion of borderline tests remained similar each year, despite an increasing trend towards HDT over LDT. Management of patients with borderline peak cortisol varied, however there was a tendency to reduce or stop replacement glucocorticoids with higher results, particularly after a HDT. Steroids were more likely to be started or continued with lower borderline values. Patients with known AI were more likely to have their steroids continued or SST repeated at lower peak cortisols and weaned at higher peak cortisols. Those without established AI were less likely to have glucocorticoid replacement commenced if higher borderline value, particularly following a LDT.

Conclusions

There was significant variation in the management of borderline SST results with the same cortisol result warranting commencement of regular replacement for one physician and stopping replacement for another. There is a paucity of research in this area and studies to examine both the natural course of children with borderline SSTs and whether stress cover represents pragmatic but safe management are warranted.

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P003

Differences in hydrocortisone absorption during the 24 hour period in patients with adrenal insufficiency

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Hydrocortisone therapy should be individualised in patients with adrenal insufficiency to avoid over and under replacement. We assessed hydrocortisone absorbtion at different times of day which may impact on treatment regimens. We assessed the oral absorption of hydrocortisone in 48 patients (21M) aged between 6.1 and 20.3 years with congenital adrenal hyperplasia due to P450c21 deficiency. Hydrocortisone dosing ranged between 11.5 and 22.6 mg/m^2 per day in three or four doses. Each patient underwent a 24 h plasma cortisol and 17-hydroxy-progesterone (17OHP) concentration profile with the morning dose used to calculate absorption parameters. Parameters derived were maximum plasma concentration (C_{max}), time of maximum plasma concentration (t_{max}), the cortisol concentration leading to 50% inhibition of 17OHP) (IC_{50}) and time to attaining plasma cortisol concentration less than 100 nmol/l (100 nmol/l was the IC_{50} value). C_{max}, t_{max} and IC_{50} were derived using conventional pharmacokinetic techniques from the absorption profiles. In a further 6 patients sampling was undertaken at 30, 60 and 120 minutes after the first (06.00–07.00 h) and last (23.00–00.30 h) dose of the day. The C_{max} for the 48 patients was 780.7 ± 61.6 nmol/l and t_{max} 66.7 (range 20–118) min. The IC_{50} for plasma cortisol suppression of plasma 17OHP was 100 nmol/l. Time taken to a plasma cortisol concentration less than 100 nmol/l was 289 (range 140–540) min. In the six patients who had studies morning and evening the evening dose C_{max} was significantly less than the morning dose ($P=0.01$) which reflected the lower dose overall given in the evening compared to the morning. Despite the reduction in C_{max},t_{max} was prolonged with the evening dose compared to the morning peak (detected in most of the patients at 30 minutes). In the evening t_{max} occurred usually after 60 minutes and was associated with a longer time to a cortisol concentration less than 100 nmol/l than the morning peak ($P=0.01$). Absorption of hydrocortisone varies throughout the 24 hour period probably due to alterations in clearance. To determine the true peak and exposure to cortisol frequent sampling around a dose is required. Dosing regimens need to be incorporate these observations.

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P004

Adrenocortical function in infants admitted to PICU

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Background

Hypocortisolaemia is common in neonates[1] and infants following cardiac surgery.[2] In critically ill children with other pathologies, hypocortisolaemia may result from accelerated cortisol metabolism and reduced protein binding. However, the timing and frequency of normalisation of cortisol concentrations following infantile critical illness is poorly described.

Objective

To describe the natural history of hypocortisolaemia in critically ill infants admitted to a single paediatric intensive care unit (PICU).

Methods
Retrospective observational study of infants admitted to PICU from 2016–2018. If random cortisol was <450 nmol/l during critical illness a low dose short Synacthen test (LDSST) was performed on recovery. Results were classified based on basal and peak cortisol concentrations: Normal (basal > 100 nmol/l, peak >450 nmol/l); suboptimal (basal > 100 nmol/l, peak 350–450 nmol/l), abnormal (basal < 100 nmol/l, and /or peak <350 nmol/l).
Results
Data from 63 infants (40M, 23F), mean age 2.4 months (range 1 wk to 10 m), were analysed. 30 patients (47.6%) had cardiac malformations, 11 (17.5%) abdominal pathologies, 5 (8.0%) sepsis, 4 (6.3%) brain pathologies, 3 (4.7%) spina bifida, 3 (4.7%) respiratory pathologies and 7 (11.0%) other pathologies. During critical illness random cortisol was <450 nmol/l in 57/63 infants (90%): undetectable in 25 (43.8%); 50–350 nmol/l in 28 (49%), and 350–450 nmol/l in 4 (7%). 49 infants (86%) underwent a LDSST which was normal in 33 infants (67.3%) in whom random cortisol was <50 nmol/l in 23 (47%) and 50–350 nmol/l 10 (20.4%) during critical illness. 15 patients (30%) with abnormal ($N=11$) or suboptimal ($N=4$) LDSST were treated with hydrocortisone for < 6 months in 5 patients (33.3%) and > 6 months in 10 patients (66.7%).
Conclusions
Hypocortisolaemia persisted for longer following critical illness than reported previously in other infant cohorts.[1] Greater understanding of the mechanisms of hypocortisolaemia during and following critical illness should enable more accurate prognosis, diagnosis and management.
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P005

Sphingosine-1-phosphate lyase (SGPL1) deficiency is associated with mitochondrial dysfunction
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Introduction
Loss of function mutations in *SGPL1*, a key component of sphingolipid metabolism, are associated with accumulation of sphingolipid intermediates giving rise to a multisystemic disease incorporating primary adrenal insufficiency (PAI) and progressive renal and neurological disease. Sphingolipid accumulation is implicated in mitochondrial pathology.
Objective
To investigate the impact of SGPL1 deficiency on mitochondrial morphology/function.
Methods
Cell lines: Primary cell cultures of dermal fibroblasts from patients with *SGPL1* deficiency (Patient 1 - **p.F545del; PAI, later onset renal/neurological compromise**; Patient 2 - **p.S65Rfs*6G; PAI, early onset renal/neurological compromise**) and a CRISPR *SGPL1*- knockout HeLa cell line. The following were investigated: steroidogenic capacity (ELISA of cortisol from progesterone stimulated fibroblasts); mitochondrial architecture (confocal microscopy); oxidative phosphorylation rate (Seahorse XF Extracellular Flux Analyser) and expression levels of fusion and fission genes, *MFN1/2* and *DRP1* respectively (RT-qPCR).
Results
Cortisol production was significantly reduced in patient fibroblasts vs controls (**p.F545del**; $P<0.05$; **p.S65Rfs*6G**; $P<0.001$, $n=3$). Total mitochondrial volume in patient fibroblasts and *SGPL1*-KO-HeLa cell lines vs controls was reduced: (**p.F545del**; $P<0.05$; $n=20$; **p.S65Rfs*6G**; $P<0.001$, $n=20$, *SGPL1*-KO-HeLa, $P<0.01$; $n=20$). Additionally, the number of fragmented mitochondria was increased in **p.S65Rfs*6G** vs control ($P<0.0001$; $n=20$). The respiratory flux profile of **p.F545del** fibroblasts was unaltered, however, **p.S65Rfs*6G** fibroblasts showed a significant reduction in non-mitochondrial respiration ($P<0.01$, $n=3$), maximal respiration ($P<0.05$), ATP production ($P<0.05$) and spare respiratory capacity ($P<0.05$). Mitochondrial morphology differed; *SGPL1*-KO-HeLa and **p.F545del** had elongated, hyper-fused mitochondria whereas **p.S65Rfs*6G** had rounded, fragmented mitochondria. Accordingly, *MFN1/MFN2* expression were upregulated in *SGPL1*-KO- and **p.F545del** fibroblasts ($P<0.0001$; $n=3$) and downregulated in **p.S65Rfs*6G** ($P<0.0001$; $n=3$). However, *DRP1* was uniformly downregulated in *SGPL1*-KO-HeLa and patient fibroblasts ($P<0.0001$, $n=3$).
Conclusion
Aberrant sphingolipid metabolism in SGPL1 deficiency leads to disruption of mitochondrial morphology/function with a reduction in mitochondrial volume and an impact on steroidogenesis. Decreased *DRP1* expression suggests an imbalance tilted towards reduced fission. The degree of SGPL1 deficiency or other genetic modifiers may account for differences seen. Further work is required to characterize the potential multi-systemic effects of mitochondrial dysfunction in SGPL1 deficiency.
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P006

Questionnaire survey identifies timing of last dose of hydrocortisone as important determinant of side effects
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The aim of cortisol replacement in adrenal insufficiency is to mimic the normal cortisol circadian rhythm. Timing of the last dose varies. Paediatric practice doses as close to midnight or after as possible compared to no dose after 18.00 h in adults. Using a detailed questionnaire, we ascertained side effect prevalence in 226 patients with adrenal insufficiency (77 CAH, 82 Addison, 67 hypopituitarism) and compared frequency of problems with timing glucocorticoid replacement. Age range differed between the groups with 88% CAH under 20 years and 67% of Addison and 81% hypopituitary over 20 years. Hydrocortisone was used by nearly all individuals with thrice (58% of total) and four (24.3%) times daily regimens commonest. 59% took their first dose between 06.00 and 07.00 h with no difference between the groups. Timing of the last dose differed between groups: 60% CAH; 7.3% Addison; 17.9% hypopituitary; between 22.00 and 01.00h $P=0.01$). 54% Addison and 44.7% hypopituitary took last dose between 17.00 and 19.00 h. A greater proportion of Addison patients had side effects of dizziness (55%), low blood glucose (67%), low blood pressure (64%), headaches (54%), hyperpigmentation (78%), stretch marks (51%) and gastritis (48%) than the CAH (12, 8, 0, 18, 11, 16, 20% respectively) and hypopituitary (33, 25, 21, 29, 11, 33, 32% respectively) groups ($P<0.01$). Osteopenia/porosis was lowest in CAH (0.9%) and similar between the Addison (9.8%) and hypopituitary groups (9.3%). The number of Addison patients that had trouble getting off to sleep was greater (48%) than CAH (25%) and hypopituitary (26%) groups. Overall, there was no effect of dose timing on ability to get to sleep. The major factor associated with an increased prevalence of side effects was taking the last hydrocortisone dose early in the evening ($P=0.01$). These data demonstrate a high prevalence of side effects in Addison and hypopituitary patients compared to CAH. The difference appears to be explained by the timing of the last dose of steroid. There did not appear to be any benefit on sleep onset from taking the dose earlier. Hyperpigmentation probably reflects unrestrained ACTH secretion from midnight onwards and stretch marks due to over exposure to hydrocortisone between 06.00 and 18.00 h.
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Bone

P007

Impact of type 1 diabetes mellitus on skeletal integrity and strength assessed by HRpQCT
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Introduction
Adults with Type 1 Diabetes Mellitus (T1DM) are at risk of premature osteoporosis and fractures. The onset of T1DM typically starts during childhood and adolescence thus the effects of diabetes on the skeleton may be established in this period. Studies in children primarily use DXA to evaluate the effects of

T1DM on bone with conflicting results. We present the first study in children assessing the impact of T1DM on skeletal microstructure and strength, using HRpQCT (High Resolution peripheral Quantitative Computed Tomography).
Methods
We recruited 22 patients aged 12–16 years with T1DM who were matched by age and gender with healthy controls. Recruits underwent a standard medical and fracture history; diabetic therapy and control was assessed in T1DM patients. Paired t-tests were applied to assess differences in total body and lumbar DXA parameters, cortical and trabecular microstructural parameters (assessed by HRpQCT) and skeletal strength assessed by microfinite element analysis.
Results
There was no significant difference in the total body and lumbar spine bone mineral density between T1DM and control pairs. Tibial trabecular thickness was lower in T1DM patients (−0.005 mm; CI −0.01,−0.001, $P=0.029$). There was a reduction in trabecular loading at the radius (Tb.F/TF distal: −6.2; CI −12.4, −0.03, $P=0.049$) and tibia (Tb.F/TF distal: −5.2; CI −9.2, −1.2, $P=0.013$), (Tb.F/TF proximal: −5.0; CI −9.8, −0.1, $P=0.047$). Regression models demonstrated a reduction in tibial stiffness (kN.mm, $P=0.03$) and tibial failure load (kN, $P=0.03$) with higher HbA1C before and after adjusting for age and gender.
Conclusion
Alteration of tibial trabecular microarchitecture is associated with an alteration in tibial loading properties. Similar loading alterations at the radius also appear to emerge in children with T1DM. Poor diabetic control may contribute to reduced tibial bone strength. Larger patient cohorts are required to determine if T1DM results in changes in skeletal integrity driven by duration and control of T1DM in childhood.

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P008

Incidental morphological findings on bone age radiographs: their importance in clinical diagnosis

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Background
X-rays of the hand and wrist are routinely performed to evaluate bone age (BA) in children with endocrine and growth disorders. BA is used essentially to assess growth potential, but the BA x-ray can reveal additional morphological abnormalities. Incidental findings on the BA x-ray can aid clinical diagnosis and prompt appropriate further investigations to establish the child's final diagnosis.
Methods
A 10-year retrospective review of 1535 BA x-rays performed at a single teaching hospital was conducted. The age range of the patients was 2–17 yrs, and 60% were male. Bone age is routinely reported using Greulich and Pyle methodology. From this cohort, x-rays were identified where morphological abnormalities were reported and the incidence and nature of the abnormalities was determined. The x-ray findings were correlated with the original x-ray request details, clinical notes and subsequent diagnosis.
Results
99 (7%) of the x-rays were reported showing additional morphological abnormalities. Abnormalities such as clinodactyly, Madelung deformity and short phalanges were noted, as well as more diffuse abnormalities such as osteopaenia or osteosclerosis. Many suspected diagnoses were supported by the additional findings on the bone age radiograph. However, in nine cases the bone age x-ray alone pointed to a previously unsuspected diagnosis and prompted further imaging including skeletal survey ($n=7$) and bone lesion characterization ($n=2$) to establish the correct final diagnoses.
Conclusion
This large retrospective study demonstrated that 7% of BA x-rays showed incidental morphological abnormalities. In 9 (9%) of these cases, the findings pointed to a previously unsuspected diagnosis. Recently there has been a focus on the use of automated BA assessment software in place of radiologist reporting. We believe that ongoing paediatric radiologist review of BA x-rays (and close working between radiologist and paediatric endocrinologist) is essential to identify additional morphological abnormalities and prompt appropriate further investigations, which can prove crucial to the accurate diagnosis of the patient's underlying condition.

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P009

A case of persistent hypercalcaemia, following accidental denosumab administration

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Introduction
Denosumab, a human monoclonal antibody that inhibits activation of osteoclasts provides sustained suppression of bone turnover in osteolytic bone disease. Denosumab has rarely been associated with late hypercalcaemia following therapeutic administration for bone tumours in children, bone metastases in adults and in children with Osteogenesis Imperfecta Type VI.
Case report
A male child of Indian origin was referred for advice to GOSH from a local hospital at 2.24 years for limping and hypercalcaemia (cCa: 3.32–3.91 mmol/l). Four months before presentation, 60 mg of denosumab were erroneously administered intramuscularly instead of a hepatitis immunization (not at either hospital involved). Following this, the child was reviewed at another hospital with an unremarkable clinical examination and serial bone profile testing which were normocalcaemic (cCa: 2.35 mmol/l). He was started on vitamin D supplements (6000 units OD). After presentation with the limp, calcium concentrations remained markedly elevated (cCa: 3.15 mmol/l), with an appropriately suppressed PTH (<0.7 pmol/l) while 25OH-vitamin D was markedly elevated (299 nmol/l). No signs of malignancy were noted on peripheral blood film and bone marrow aspirate was normal. Provisional diagnosis at this point was vitamin D intoxication. Second line investigations performed were negative for malignancy. Since hypercalcaemia was resistant to hyperhydration and frusemide, pamidronate (0.5 mg/kg iv) was used. Calcium concentrations returned to normal following the second dose (cCa: 2.47 mmol/l). 25OHD rapidly returned to normal while still hypercalcaemic. To elucidate the pathophysiology of hypercalcaemia, N-terminal telopeptide (NTX), as a marker of increased bone turnover, was elevated and $1,25(OH)_2D$ was low. PTHrP was undetectable. Lower leg x-rays showed dense metaphyseal bands (bilateral distal femurs, distal tibias and fibulas), indicating osteoclast inhibition that correlated with the time of denosumab administration.
Conclusions
There have been previously highlighted cases of rebound hypercalcaemia following cessation of Denosumab for therapeutic use. However, this is to our knowledge the first case of resolving late hypercalcaemia thought likely to be secondary to accidental administration of a toxic dose of Denosumab. This case suggests that this rare side effect is pharmacological and not a result of underlying conditions as previously noted.

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P010

Changes in bone mineral density from age 10 to 30 years in individuals with cystic fibrosis

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Background
Osteoporosis and increased fracture risk associated with cystic fibrosis (CF) are becoming more relevant with improved life expectancy in this disease. The evolution of CF-related bone disease remains unclear.
Aims
To evaluate change in bone mineral density (BMD) in individuals with CF from age 10 to 30 y.
Methods
Data from the UK CF Trust registry, which contains anonymised clinical information, was used to evaluate BMD at age 10, 18 and 30 y against the

population mean. BMD z score was adjusted for size by including height z score in linear regressions. Association of BMD with lung function (FEV1%) was evaluated.
Results
Data was available for total body (TB) BMD at 10y $n=62$ (30 male) and 18 y $n=78$ (41 male); for lumbar spine (LS) BMD at 10y $n=75$ (37 male), 18 y $n=148$ (77 male), 30y $n=133$ (72 male). Mean TB BMD z scores at 10y and 18 y were -0.135 and -0.921 respectively. In a one-sample t test against the population mean, TB BMD z score was significantly different at 18 y ($P<0.01$) but not at 10 y. There was a significant relationship between BMD z score and FEV1% at 18 y ($P<0.01$) but not at 10 y. Mean LS BMD z score at 10 y, 18 y and 30 y were -0.167 ($P>0.05$), -0.958 ($P<0.01$) and -0.874 ($P<0.01$) respectively, P values representing significant difference to the population mean. There was a significant relationship between LS BMD z score and FEV1% at 18 y ($P<0.01$) and 30 y ($P<0.05$) but not at 10 y. For the TB BMD cohort, the percentage with a BMD z score of <-2 was 3.23% at 10 y and 25.6% at 18 y; for the LS BMD cohort, this was 2.67%, 20.3% and 21.8% at 10 y, 18 y and 30 y respectively.
Conclusions
There was a trend to decreasing BMD with increasing age in individuals with CF. A relationship between reduced FEV1% and reduced BMD was observed in adulthood. These results highlight the importance of monitoring BMDin CF.
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P011

Congenital hyperinsulism of infancy in a child with autosomal dominant hypocalcaemia type1 due to an activiting calcium sensing receptor mutation

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Introduction
Autosomal dominant hypocalcaemia (ADH) is caused by activating mutations of the calcium sensing receptor (CaSR). Symptomatology ranges from asymptomatic hypocalcaemia to paraesthesia, tetani, laringospasm and, seizures. This is the first report of congenital hyperinsulinism (CHI) in a child with ADH.
Case report
A female infant, born at term from non-consanguineous parents, presented on D2 with persistent asymptomatic hypoglycaemia requiring 11 mg/kg/m in glucose. Investigations showed raised insulin and C-peptide, low beta-hydroxybutyrate and NEFA, consistent with CHI. She was started on diazoxide and chlorothiazide by D15. Diazoxide was stopped thrice, unsuccessfully, and she is currently, at the age of 7 months, on a dose of 3.7 mg/kg/day. On D4 she developed tonic-clonic seizures, with hypocalcemia and hypomagnesemia. She had undetectable PTH and high calcium/creatinine ratio, suggestive of ADH. Hypocalcemic seizures were difficult to control with high doses of alpha-calcidol, calcium and magnesium. At 11 weeks of age she was started on treatment with subcutaneous continuous PTH via a Medtronic pump, after which, seizures improved. From early age, she had difficulties in gaining weight, and had polyuria, raised urea and creatinine, hypokalemia and hyperaldosteronism, in line with a Bartter type V and requires potassium supplementation. Sequencing of *CASR* showed a *de novo* mutation c.2528C>A(Ala843Glu) previously described in ADH with Bartter Syndrome. Functional studies show constitutively active CaSR. No mutations in genes on the extended CHI panel were found.
Conclusions
c.2528C>A(Ala843Glu) *CaSR* leads to severe ADH1 and can cause Bartter Syndrome typeV, likely due to the effect of constitutively active CaSR on the Na:K:2Clco-transporter and ROMK in thick ascending limb of Henle's loop. No link between hyperinsulinism and ADH has been previously described. $CaSR^{Nuf/Nuf}$ mice that harbor an activating CaSR show hyperglycemia due to impaired b-cell function and higher number of a-cells. We hypothesized that, like in other forms of CHI, the active CaSR interferes with regulation of insulin secretion at young age, resulting in CHI, and at later age, results in beta cell defects. Further work is required to understand the relation between CaSR, potassium transport and beta cell function in ADH.
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P012

An unusual case of an infant presenting with Tetany and seizures secondary to phosphate supplementation

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Introduction
Hypocalcemia is a well known adverse reaction of phosphate supplements but rarely reported. We report a case of Infant presenting with hypocalcemic seizures after initiation of phosphate supplements.
Clinical case
A baby Girl was born at 34+4 weeks gestation. She was admitted in NNU for preterm care. The admission was complicated by severe Gastroesophageal reflux disease(confirmed by PH impedance study), anemia and sepsis. She was discharged home on Neocate LCP for a suspected cows milk protein allergy. Following discharge from the Neonatal unit, she developed faltering growth, recurrent chest infections, and rib fractures. Generalised osteopenia with radiological rickets as well as multiple long bone fractures was evident on the skeletal survey. Due to severe reflux and recurrent aspiration pneumonia, PEG was inserted. She was suspected to have a Metabolic bone disease with low phosphate (0.70), raised alkaline phosphatase (1043), normal calcium, Vitamin d (73) and low PTH (8). She was discharged home with 2 mmol/kg BD of phosphate supplement. Unexpectedly, she was admitted at the age of 9 months with a rigidity of extremities, vomiting, irritability and inconsolable cry with a fever. She developed generalized hypertonia with hypoxia needing oxygen. Anterior fontanelle was tense and bulging. She subsequently developed convulsions. Venous gas showed a low ionized calcium of 0.55. She was suspected to have Hypocalcemic tetany. Intravenous calcium replacement was given in form of 10% calcium gluconate followed by maintenance intravenous fluid with calcium supplement. She responded well to the infusion with reduction of tone. The diagnosis was confirmed with a low corrected calcium (1.32), normal magnesium and an elevated phosphate (2.77) on samples obtained prior to treatment. The parents confirmed that the first dose of Phosphate supplement was administered one hour prior to the episode via the PEG.
Conclusion
This case demonstrates the risk of Hypocalcemic tetany with phosphate administration. The first dose of phosphate should be considered to be administered in hospital under supervision particularly with a PEG in situ.
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Gonadal

P013

Pubertal induction among girls with turner syndrome: an audit of practice from 2008–2017

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Background
Pubertal induction with incremental doses of oestrogen replacement is an important component of care offered to hypogonadal patients with Turner Syndrome (TS). Low dose oral ethinylestradiol (EE) has been extensively used in the UK but natural 17-β oestradiol (more physiological, cheaper and easily monitored in blood) is becoming increasingly popular. We undertook this audit to compare the efficacy and acceptability of oral (EE) and patch (Evorel) oestrogen preparations used in our centre.
Subjects and method
A retrospective audit was undertaken analysing the clinical records of all girls with TS who started pubertal induction 2008–2017, excluding those yet to start progestogens ($n=27$). Data is mean ± S.D.
Result
Pubertal induction was started at 13.1 ± 1.8 years and progestogen introduced at 16.1 ± 1.9 years; duration of unopposed oestrogen action was 2.8 ± 0.8 years. Eleven (40.7%) patients used oral EE, 10 (37.0%) patches and 6 (22.2%) changed from one form to the other. Where recorded, 15 (62.5%) were in Tanner stage 1, 7 (29.2%) in stage 2, while 2 (8.3%) were in stage 3 before induction. At introduction of progestogen, 19 (82.6%) were in stage 3 and the rest in stage 4. Height SDS (UK-WHO reference) was -2.3 ± 1.0 at pubertal induction and -1.9 ± 1.0 at completion. Height SDS change during induction was 0.5 ± 1.0. There was no significant difference between oestrogen regimens in height SDS change (oral: 0.4 ± 1.0, patches: 0.8 ± 1.1, $P=0.4$). Pelvic USS was undertaken in 9 (33.3%) before pubertal induction, of which there was a normal prepubertal uterus in 8 and normal ovaries in 1. Six (21.4%) had a pelvic USS at the end of

puberty; 5 had normal sized post-pubertal uterus and 1 remained infantile. Seventeen (63.0%) patients had DEXA at transition, 2 had low bone mineral density (BMD). Both presented at 13 and 16 years with short stature and delayed puberty; both used patches. BMD status was not significantly different between oestrogen regimens ($P=0.5$).
Conclusion
Induction of puberty with oral or patch oestrogen appears to be equally effective in girls with TS. One third of girls who started on patches switched to an oral preparation. Uterine imaging was not consistently undertaken.

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P014

Turners syndrome – clinical presentation, genetics, investigation and management: a 10 year review

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Background
Turner syndrome (TS) is characterised by a wide phenotype and age at presentation. We reviewed our over-12s Turner clinic over a period of 10 years to evaluate pattern of diagnosis, co-morbidities and management.
Subjects and method
Retrospective data analysis of patients with TS who attended the over-12s clinic (2008–2017, $n=28$). Data is median (IQR) or mean $\pm$ SD as appropriate.
Result
The age at diagnosis was 10.4(1.9–15.0) years. Presenting complaints were identified in 18 (64.3%) patients: congenital heart disease (CHD) in 2 of 3 diagnosed at birth; short stature in all 9 diagnosed at 1–13.9years; delayed/arrested puberty in 7 diagnosed $\geq$14 years). Karyotype results were available for 27(96.4%) patients (11 45,XO; 16 mosaic). Those diagnosed at birth had Classic TS (100%) compared to 23% of those diagnosed after infancy. Routine referrals as recommended by the TS Consensus Study Group were made for echocardiogram (21, 75.0%), renal ultrasound (17, 60.7%), dental review (5,17.9%) and to ENT (21, 75.0%). Twenty-five (89.2%) patients had documented comorbidities; ENT disorders ($n=12$), CHD ($n=5$), lymphedema ($n=5$), renal/urological disorders ($n=7$), visual impairment ($n=5$), psychological problems ($n=3$); thyroid dysfunction ($n=3$) and coeliac disease ($n=1$). Raised ALT ($\geq$35 iu/l) in the absence of clinical symptoms of liver disease was seen both pre- and post- puberty (2/26 and 5/25 respectively) and was unlikely to be related to oestrogen therapy. The 2 girls with pre-pubertal raised ALT remained so after puberty. Raised triglycerides (TGL) noted pre-puberty (2/12) persisted (3/22 post puberty). There was no significant difference in the BMI SDS change of either those with normal and raised ALT or TGL. Twenty-six (92.9%) had growth hormone therapy (GHT), duration 3.7 (2.6–5.6) years with an improvement in height-SDS at the end of GHT of 0.3 $\pm$ 1.0. Patients with late diagnosis were relatively shorter at the start of GHT ($\geq$14 years: -2.9 ± 0.6; $\leq$13 years; -2.1 ± 0.7; $P=0.05$) and the final height-SDS difference was significantly different ($P<0.01$).
Conclusion
TS is diagnosed all through childhood with some age specific presentations. Comorbidities result in a significant disease burden and ENT disorders particularly are common. GHT is associated with an overall positive gain in height-SDS.

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P015

Abstract Unavailable.

P016

A review of region-wide consultant knowledge of the management of disorders of sexual development (DSD)

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Background
Disorders of sexual development (DSD) are estimated to occur in every 1 in 4500 births. This project builds upon previous work by the authors to explore the knowledge and management of paediatric junior doctors in a single deanery. The majority of junior doctors stated that they would seek the advice and explanation of paediatric consultant. We therefore attempted to qualify the knowledge and management strategies of the region-wide consultant body with regards to DSD.
Methods
We used an online survey which was distributed to all general paediatric and neonatal consultants in a single deanery. The survey comprised of 10 questions designed to investigate the knowledge of history taking, examination, investigations and management.
Results
A total of 15 consultants completed the questionnaire. 93% of respondents were general paediatricians and 7% neonatologists. Knowledge of key points to record in history and examination findings was high at 80% compliance with national standards. Management of a patient with suspected DSD (eg., hypospadias with unilateral testicle) was highly variable with 74% referral to urology, 13% referral to DSD co-ordinator of the DSD service based at tertiary centre and 13% organising follow-up in the clinic in 2–3 months. Knowledge of ordering investigations in cases of suspected DSD was good with 100% of respondents ordering chromosomal studies, abdominal ultrasound and serial electrolyte samples. However, only 75% of respondents would order 17-OH progesterone. Only 27% of respondents were aware of the regional DSD pathway and co-ordinator. Most (87%) recognised they would appreciate further training on DSD with an online module being the most preferable form of delivery.
Conclusion
This work builds upon previous a previous study which highlighted a lack of knowledge and management in junior doctors with regards to DSD. Given that all respondents in the original study indicated they would involve senior colleagues, this study demonstrates that even at consultant level the management of DSD is still suboptimal. Most professionals indicated that further training would be beneficial to their knowledge and suggested an online module to be the most convenient method of delivering this.

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P017

Paediatric doctors' experience and knowledge of the initial management of neonatal ambiguous genitalia

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Introduction
Neonatal ambiguous genitalia can herald sensitive, time-critical, and life-threatening diagnoses and thus paediatric doctors must be competent in their management. However, ambiguous genitalia are rare, limiting clinical exposure. We assessed paediatric doctors' knowledge of and confidence in managing this condition.
Methods
A questionnaire was circulated to paediatric doctors at six paediatric teaching hospitals. It established doctors' clinical experience of ambiguous genitalia and used a Likert scale to assess their confidence in its management (1=I am very unconfident, 5=I am very confident). A clinical vignette followed by multiple choice questions (MCQ) assessed knowledge of diagnostic tests and differential diagnoses. A response was deemed correct if a right answer was selected or if a wrong answer was not selected. An educational module was designed and the questionnaire re-administered.
Results
Response rate was 100% ($n=42$; 26.2% male; 71.4% ($n=30$) junior trainees, 14.3% ($n=6$) senior, 14.3% ($n=6$) consultants). 61.9% ($n=26$) worked in tertiary centres. 42.9% ($n=18$) had never seen ambiguous genitalia. Junior trainees had seen fewer cases (M=0.9, SD 1.4) than senior (M=2.4, SD=2.2), ($t(14.7)=-2.2$, $P=0.04$). 33.3% ($n=14$) had helped manage a case. 21.4% ($n=9$) had been the first to review an infant with ambiguous genitalia, and 11.9% ($n=5$) the first to inform parents of the finding. On 1 5 Likert scoring, doctors were not confident in the overall management of ambiguous genitalia (M=2.5),

in discussing findings with parents (M = 2.9), or in examining ambiguous genitalia (M = 2.9). Seniority, number of cases seen, and tertiary experience did not significantly influence confidence levels. MCQ responses were correct a mean of 64.0% of the time, and improved to 83.4% when re-tested after the educational session ($P < 0.01$). Seniority, number of cases seen, and tertiary experience did not significantly influence performance. Reported confidence levels did not improve after the educational session.

Discussion

Paediatric doctors, regardless of seniority, have insufficient knowledge and confidence to manage neonatal ambiguous genitalia. This reflects limited clinical exposure. As we cannot rely on experiential learning, paediatric doctors must receive targeted educational sessions on the management of ambiguous genitalia to improve their knowledge of this rare condition.

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P018

XY-DSD due to haematological chimerism in twin pregnancy

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Introduction

Blood chimerism is the condition characterized by the presence of cells from at least 2 zygote lineages in only the lympho-hematopoietic system. It is very rare in humans and is most commonly seen in monozygotic monochorionic twins through placental anastomoses.

Case report

A 12 years old young girl, one of dichorionic dizygotic twins, had a genetic test performed for paternity issues. CGH array showed 46XY genotype (90%) and another genotype at a low level. She had female external and internal genitalia with no evidence of virilisation. Her puberty staging was breast stage: 3–4, pubic hair stage 3 to 4, axillary hair stage 2, menstrual stage 0. There was no clitoromegaly. Her endocrinology has been normal (pubertal LH:5.3 U/L, FSH:3.0 U/L, oestradiol:130 pmol/l, normal prolactin:261 mIU/L, TSH:1.22 mIU/L, anti-mullerian hormone:31 pmol/L, inhibinB:77.1 pg/ml, low testosterone: < 0.5 nmol/L, 17-OH-Progesterone: < 1.3 nmol/L) with normal urine steroid profile. Her pelvic ultrasound showed normal anteverted uterus, endometrial stripe 6 mm and normal ovaries. Her investigations, therefore, excluded androgen insensitivity and inborn errors of steroidogenesis. Further tests included a skin biopsy from the patient and blood tests for genetics on her twin brother. The skin biopsy revealed female genotype which was the same as the low level genotype detected in her blood sample. There was very low level of male genotype (same as her blood and majority of brother's genotype). There was low level of same XX genotype in her brother's blood sample. At her follow up visit she attained menarche.

Conclusions

The results indicated haematologic chimerism due to twin-twin transfusion. Blood chimerism has been reported before in cases of dizygotic monochorionic twins, but there is only one previously described case of XY-DSD in dizygotic dichorionic twins. When an admixture of cells with 46,XX and 46,XY is detected, it should be determined whether the admixture is present in the entire body or limited to the blood. The risk for tumour formation and for passing Y chromosome to her oocytes is unknown and needs to be monitored.

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P019

Adolescents with HH: what outcome do they want from the gonadotropin stimulation process?

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Background

Male adolescents with hypogonadotropic hypogonadism (HH) or delayed puberty start pubertal induction from 12–14 years. Testosterone obtains secondarysexual characteristics and improves psychosocial well being. Gonadotropin releasing hormone (GnRH) or recombinant FSH (rFSH) and human chorionic gonadotropin (hCG) generate testicular growth (fertility) and testicular testosterone production. HCG-rFSH treatment increase testis size and improves the quality of life of HH.

Aim and Method

This retrospective study (2014–2018) examines the pubertal induction results with rFSH + testosterone followed by rFSH + HCG (rFSH + T - rFSH + HCG) in male adolescent with HH in a single clinic.

Results

Seven boys (16.2 y ± 0.7) opted for the rFSH + T - rFSH + HCG treatment (2 still on the treatment). The fertility laboratory was accessed by 4 of the 5 patients who completed the treatment (a patient opted not have sperm analysis). Sperm banking was successful in 3 (1 azoospermic).

Conclusions

In less than 18 months, the rFSH + T - rFSH + HCG treatment enables the duplication of the initial testicular volume in HH. Adolescent interest in the gonadotropin treatment seemed related to obtaining testis enlargement as well as sperm production. Sperm banking decision and success rate are affected by the individual's background condition. The study also confirm that LHRH test didn't add information to the basal gonadotropin measurement. Prospective controlled studies will need not only to compare the gonadotropin treatment in terms of sexual maturation results and treatment length but also to explore the adolescents prospective and pshychophisical needs in order to improve the counselling professionals provide.

Initial Height	166 ± 10.4 cm	Pubertal spurt	8.1 ± 5.7 cm
Initial Weight	69.2 ± 22.1 Kg	Testicular volume increase	5 ± 2 mL
Initial BMI	24.8 ± 6.4 Kg/m2	Final BMI	26.5 ± 8.7 Kg/m^2
Basal FSH	0.5 ± 0.7 U/L	End of treatment FSH	3.4 ± 2.1 U/L
Inhibin B	62.7 ± 7.9 pg/mL	Sperm bank success rate	3/5
LHRH test LH peak	2.8 ± 1.2 U/L	Duration of treatment	1.29 ± 0.73 y
LHRH test FSH peak	1.6 ± 1 U/L		

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Growth

P020

The challenges of managing pituitary gigantism

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Introduction

Pituitary gigantism is a rare but clinically significant paediatric condition. Transphenoidal surgery is the treatment of choice, however medical treatment is often considered as adjuvant therapy.

Case report

A 10.6 year old boy presented with tall stature. With hindsight he was noticeably tall from age 5 years. At 10 years his height velocity was 12 cm/year, prompting referral and further investigation. His height was 178.7 cm (+5.79 sds above mean), and well outside the family target centile range. IGF-1 was elevated at 78.6 nmol/L (10.6-60.8 nmol/l) and an OGTT demonstrated non-suppression of GH (trough value 5.5 mcg/L, normal = < 0.5). His bone age was 11.03 years. The remaining pituitary profile and visual fields were normal. Initial contrast MRI was inconclusive but C11 methionine PET/CT at Addenbrooke's identified a pituitary microadenoma as a potential surgical target. Genetics for AIP, MEN, MEN4 were negative, while results for Carney complex are pending. He has been recruited into an on-going national research project. An MDT clinic held with the patient, his parents, paediatric and adult endocrinologists, neuroradiology and neuro-surgical teams allowed discussion about medical and surgical treatment options.In view of his young age, his prepubertal status, a wish to allow him to settle into his new high school, and his desire to reach a final height taller than his father's own height, it was decided to try medical therapy first with octreotide, a somatostatin analogue. In addition, pubertal induction was commenced and bilateral epiphysiodesis surgery performed. While the initial response to octreotide was positive (IGF-1 43.2 nmol/L, average GH on profiling = 2.0 mcg/L, aiming for < 2.5), four months into therapy it was noted that the IGF-1 was climbing (57.8 nmol/L) and a repeat GH profile was not fully suppressed (average GH 2.8 mcg/L). In view of this the patient proceeded to have successful transphenoidal surgical de-bulking of the adenoma.

Conclusion
Rare cases such as this require the sharing of knowledge, experience and expertise so the best possible care is offered. It is often necessary to work across sites and disciplines. Each case requires an individual approach tailored to the patient and their family.

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P021

Adherence and long-term outcomes of growth hormone therapy in patients from the UK: the easypod connect observational study (ECOS)

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Introduction
The easypod™ Connect Observational Study (ECOS) was a global study with easypod™, an electronic injection device for recombinant human growth hormone (r-hGH; Saizen®). This study aimed to assess adherence and growth outcomes of patients treated with r-hGH via easypod™ in the UK-based ECOS cohort (NCT01263457).
Methods
Patients aged 2–18 years, with ≥3 months of easypod™ data after enrolment into the study comprised the ECOS data analysis set (DAS); ECOS DAS patients with ≥3 months of easypod™ data after initiating easypod™ use comprised the easypod™ DAS. The primary objective was to assess adherence; growth outcomes (Δheight [ΔHt], ΔHt standard deviation score [ΔHtSDS], height velocity [HV], HVSDS), correlation between adherence and growth outcomes (Spearman's product moment), and the impact of adherence on IGF-I were secondary objectives. All analyses were descriptive.
Results
The study included 63 patients; growth hormone deficiency ($n=44$), small for gestational age ($n=8$), Turner syndrome ($n=7$) and other diagnoses ($n=4$). Median age was 12 years with 21 (33%) female. In the ECOS DAS, median adherence was 92.75% over 1 year ($n=56$), 89.70% over 2 years ($n=35$) and 71.90% over 3 years ($n=13$). After 1 year, median results showed ΔHt 7.6 cm, ΔHtSDS 0.42, HV 7.69 cm/year and HVSDS 2.36. Significant correlations were detected between adherence and ΔHtSDS ($n=44$; $P=0.018$) and HVSDS ($n=43$; $P=0.006$) in the ECOS DAS after 1 year. In GH-naïve patients from the easypod™ DAS ($n=42/63$; 67%), median adherence was 93.3% over 1 year ($n=40$), 92.7% over 2 years ($n=35$) and 77.8% over 3 years ($n=22$); after 1 year, median growth outcomes were ΔHt 8.25 cm, ΔHtSDS 0.46, HV 8.55 cm/year and HVSDS 2.01. IGF-I concentrations were normal after 1 year in 17/22 patients with data [77.3%]); 3 (13.6%) had abnormally low and 2 (9.1%) had abnormally high concentrations.
Conclusions
Treatment with r-hGH via easypod™ led to high adherence in this UK ECOS population although slightly lower than in the global analysis. After 1 year, treatment efficacy, IGF-I normalisation and significant correlations between adherence and ΔHtSDS and HVSDS were reported.

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P022

You are what you eat: gonadotrophin independent precocious puberty

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Introduction
Phytoestrogens are derived from plants that are structurally and functionally similar to oestrogens. Their health benefits are widely extolled, although excessive consumption in children may cause adverse effects.
Case 1
A 5.7-year old female presented with a one-month history of breast development and a 3-day history of vaginal bleeding. Prior to presentation, she was taking a health drink containing fennel and sesame seeds, in addition to eating a vegetarian diet high in soya. Examination was B4, P1, A1 with no cliteromegaly, and her height was above her mid-parental target range. Baseline gonadotrophins were suppressed (LH <0.1 IU/L, FSH 0.1 IU/L, oestradiol <92 pmol/L). GnRH stimulation test indicated gonadotrophin independent puberty. Tumour markers were normal, as was her urine steroid profile (USP) and brain MRI. Pelvic ultrasound scan (USS) reported a peri-pubertal uterus with an endometrial stripe and marginally increased ovarian volumes with small follicles. Bone age was advanced by 2.5 years. A diagnosis of pseudo-precocious puberty secondary to high dietary phytoestrogen was proposed. Advice was given to remove the seeds and soya products from her diet. Three months later her pubertal features had regressed.
Case 2
A 3-year old Malaysian female presented with a 1-month history of breast development and 1-week history of vaginal bleeding. Examination was B3, P1, A1, with oestrogenisation of the labia and clitoromegaly, but no cutaneous lesions. Baseline gonadotrophins were suppressed with an elevated oestrogen of 493pmol. USP and tumour markers were normal. GnRH test excluded central puberty. USS showed a pubertal uterus, and bone age was advanced by 18 months. MRI of head and adrenals were normal. On further questioning, the gonadotrophin-independent precocious puberty was thought to be secondary to her parents' phytoestrogen containing herbal extract (Kacip Fatimah) which she had been intermittently taking. Once this was stopped, all pubertal features regressed.
Conclusions
Phytoestrogens are widely available and their increased consumption may play a role in earlier pubertal development. These cases highlight the importance of a thorough history of diet and non-prescription supplements when assessing premature pubertal changes.

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P023

Optimising diagnostic performance of IGF-I and IGFBP-3 measurement: importance of reference range and cut-off value

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Background
The diagnosis of growth hormone deficiency (GHD) is based on a combination of clinical suspicion supported by growth hormone stimulation testing. IGF-1 and IGFBP-3 are used as supportive markers. Reports over the last decade have examined the performance of IGF-I and IGFBP-3 in the diagnosis of GHD. It is important that each unit evaluates the utility of these markers in the assay used by their laboratory based on relevant normative data.
Aim
To evaluate the diagnostic accuracy of IGF-I and IGFBP-3 serum levels in relation to the diagnosis of GHD in short children using updated reference ranges with different cut offs.
Methods
Data from every short child in our unit, who had been investigated for short stature with GH stimulation testing and measurements of IGF-1 and IGFBP-3 between March 2017 and January 2018, were evaluated. Their performance in relation to the diagnosis of GHD was examined using updated IDS-iSYS reference ranges for both at a cut off value of −2 SDS and cut-off levels of −1.6 SDS for IGF-1 and −1.8 SDS for IGFBP-3 (based on levels in previous studies).
Results
Seventy-three patients (44 males) fulfilled the entry criteria. 30 patients were classified as GHD based on either two failed stimulation tests or a single failed test with abnormal pituitary imaging. Using the updated reference ranges, IGF-1 had a sensitivity of 55% and a specificity of 83%. IGFBP-3 had a sensitivity of 35% and a specificity of 90%. The sensitivity for IGF-1 increased to 77% and the specificity reduced to 64% when using −1.6 SDS as a cut off value. Similarly, the sensitivity of IGFBP-3 using −1.8 SDS increased to 52%, but the specificity reduced to 88%.
Conclusion
IGF-I and IGFBP-3 at levels below −2 SDS increase the likelihood of confirming GHD. Modifying the cut-off values improves concordance with the diagnosis of GHD, but increases false positives. However it must be recognised that these 'tried and tested' markers are only modestly accurate markers of GH status as defined by stimulation testing.

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P024

Genotype–phenotype correlation in patients with homozygous *GHR* pseudoexon (6Ψ) mutation

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Objectives
The homozygous *GHR* pseudoexon (6Ψ) mutation leads to aberrant splicing of the *GHR* gene with clinical and biochemical heterogeneity. We investigated whether the phenotypic variability could be explained by transcript heterogeneity i.e. ratio of abnormal (6Ψ *GHR*) to normal (WT *GHR*) transcripts and/or the presence of concurrent defects in other short stature (SS) genes.
Methods
6 Ψ *GHR* and WT *GHR* mRNA transcripts from 4 6Ψ patients' fibroblasts (height SDS −3.6, −5.9, −4.2 and −3.8) and 1 control subject were investigated by reverse-transcriptase PCR (RT-PCR) using intron skipping primers. Transcripts (mean ± SD) were quantified by qRT-PCR and double delta CT analysis (5 experimental repeats) and compared using ANOVA with Bonferroni correction. In eleven 6Ψ patients, 63 genes known to cause SS were analysed by targeted sequencing.
Results
RT-PCR confirmed the presence of WT transcript (193 bp) in 6Ψ patients and control. 6Ψ transcript (217 bp) was seen in all 4 6Ψ patients but not control. Direct sequencing verified predicted mRNA sequences. 6Ψ transcript expression was significantly different amongst patients (1 ± 0, 0.334 ± 0.032, 0.549 ± 0.005, 0.960 ± 0.071) P values < 0.001, except between patients 1 & 4. The mean 6Ψ:WT transcript ratios (40.33, 72.74, 47.39) correlated negatively with height SDS ($R = 0.99$, P value 0.079) in 3 out of 4 6Ψ patients. Genetic analysis of 11 6Ψ patients revealed 9 deleterious variants in 6 genes. However, there was no correlation between the number of gene hits and degree of short stature in individual 6Ψ patients.
Conclusion
Varying amounts of 6Ψ and WT *GHR* transcripts were identified in 6Ψ patients, with no 6Ψ transcript identified in the control. A higher 6Ψ:WT *GHR* transcript ratio correlates with the severity of short stature in 3 patients. Genetic changes in other known SS genes do not appear to account for the phenotypic variation. A combination of genetic defects in multiple, unknown genes and/or environmental factors may contribute to the phenotypic variability in height seen in the 6Ψ patients.

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P025

The phenotype and cardio-metabolic associations of Silver-Russell syndrome in an older cohort and the effects of childhood growth hormone treatment

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The classical features of Silver-Russell syndrome (SRS) appear to become less pronounced with increasing age. Small-for-gestational-age (SGA) birth is associated with adult metabolic syndrome. SRS is associated with SGA but the adult sequelae and long-term effects of childhood growth hormone (GH) treatment are unclear.
Objective
To determine the phenotype and cardio-metabolic profile in older individuals with SRS and compare individuals previously untreated with GH to those treated.
Method
UK participants aged ≥13 years with molecularly confirmed SRS were invited to a study appointment involving a medical history, examination and investigations. Height, weight and head circumference measurements were converted to standard deviation scores (SDS) using UK reference data.
Result
33 individuals (18 females) aged 13.32-69.71 years (median 29.58) were recruited. Loss of methylation at H19/IGF2 was diagnosed in 81.8%; maternal uniparental disomy for chromosome 7 in 18.2%. 69.7% had previously been treated with GH. Median height SDS was −2.67; median weight SDS −1.72; median body mass index SDS −0.53; and median head circumference SDS −0.95. Height SDS ≤−2 was present in 60.6%. Asymmetry and relative macrocephaly were present in 66.7% and 57.6% respectively. Blood glucose concentration ≥6.1 mmol/L was present in 20.0% (6/30); type 2 diabetes mellitus ($n = 3$), impaired fasting glycaemia ($n = 2$) and impaired glucose tolerance ($n = 1$). Treatment for hypertension ($n = 2$) and hypercholesterolaemia ($n = 2$) was observed. 15.4% (4/26) met criteria for diagnosis of metabolic syndrome. Hypertriglyceridaemia was present in 16.1% (5/31) overall; in 44.4% (4/9) in GH-untreated versus 4.5% (1/22) of GH-treated individuals ($P = 0.017$). Median waist-to-hip ratios in females and males aged ≥18 years were 0.83 and 0.93 respectively.
Conclusion
Relative macrocephaly in older individuals with SRS was less prevalent than in childhood. Metabolic syndrome and hypertriglyceridaemia were more prevalent than previously reported. Historical GH treatment was associated with improved triglyceride levels, suggesting a beneficial longterm effect after treatment discontinuation.

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Miscellaneous Endocrinology

P026

Using a testicular simulation model as an educational tool to improve testicular volume estimations

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Background
Measuring testicular volume (TV) by orchidometer is a standard method of male pubertal staging. Previously we have developed a simulation model for TV estimation with different sized silicon testes housed in latex scrotum and displayed on paediatric mannequins. When used in a study of 215 paediatric endocrinologists TV was measured accurately on only 33% of occasions. Intra-observer reliability was also lacking with participants giving different estimations for the same size testicle on 61% of occasions. We have investigated whether training naïve medical students, using a workshop involving our simulation models, could improve the accuracy and reliability of TV estimation.
Method
All participating preclinical medical students watched a 5min video to represent standard undergraduate training in male pubertal assessment. Volunteers were then randomised directly to assessment or to attend a workshop consisting of a more in-depth video and five stations contextualising and practicing the skills required for accurate and reliable TV estimation, prior to assessment. The workshop was designed to promote skill acquisition through the four different learning modalities. The assessment consisted of three child mannequins displaying testes of 3ml, 4ml (twice), 5ml, 10ml and 20ml. To assess intra-observer reliability, the effect of repeated examinations on accuracy and the effect of time on skill retention, participants were asked to return a fortnight later for repeat assessment.
Results
Ninety students participated (55F), 46 of whom attended the workshop and were considered 'trained'. Of the total number of estimates across both assessments (1020), 31% in the trained group were correct, compared to 26% in the untrained group. Both groups had a tendency to overestimate (40% trained, 48% untrained). The trained group were more accurate (estimating the correct TV or one size away), 77% versus 65%, and the untrained group significantly more inaccurate (estimating 3 or more sizes away) 14% versus 3%. On reassessment the trained group improved their overall accuracy whereas the untrained group marginally worsened.

Conclusion
Overall TV estimation accuracy was poor. Workshop style training improved accuracy and retention of skill acquisition and could be considered as a learning tool for those new to the specialty.

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P027

Audit of transition pathway to adult services for girls/young women with turner syndrome

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Introduction
Children and young people with Turner Syndrome have regular follow up with a paediatric multidisciplinary team to monitor growth, puberty and cardiac comorbidities. As these young women transition to adult care, they need ongoing follow-up for surveillance of potential morbidity and reproductive issues. Following publication of the International Turner Syndrome Consensus Group guidelines on transitional care, a review of current clinical practice in our tertiary centre was undertaken.
Method
Young women who had previously transitioned to adult services were identified through clinical databases in a tertiary paediatric centre. Data was collected on transition pathways such as attendance at joint clinics, cardiac investigation, BMI and blood pressure measurements and continuing adult specialist care. These clinical parameters were chosen in keeping with the consensus guidelines. It was anticipated that some women would transition to local clinics and adherence to the guidelines was explored. Full institutional audit approval was granted.
Result
16 women transitioned to adult care. 5 continued in the trust whilst 11 were followed up by regional adult teams. The 5 who remained within the trust were transitioned to an adult Turner clinic. 80% attended a joint transition clinic that included a paediatric endocrinologist and gynaecologist. An adult endocrinologist was present in 60% of clinics. All women underwent a cardiac investigation around the time of transition and were followed up in an adult clinic. 80% of women had height, weight, body mass index and blood pressure measured at the time of transition. The 11 women who transitioned to six regional clinics were managed through a variety of clinical pathways, one of which involved a specific adult Turner clinic.
Conclusion
This audit has mapped the various pathways of care for young women with Turner Syndrome within the region. It describes the points of care, particularly cardiac investigation, which are being delivered, either through a tertiary centre or locally. A patient-held information document and checklist of required follow-up are under development to help ensure that adherence to the transition consensus guidelines is maintained.

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P028

A 10 year experience of the management of severe hypocalcaemia associated with thymus transplantation in a United Kingdom tertiary centre

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Background
Thymus transplantation is undertaken for conditions associated with severe immunodeficiency. These comprise various genetic and syndromic associations including 22q deletion syndrome, CHARGE association, diabetic embryopathy, and other rarer conditions. Some of these conditions are associated with hypoparathyroidism and therefore hypocalcaemia. There are no established guidelines on the management and prevention of hypocalcaemia during the transplant period.
Case Series
29 patients underwent thymus transplantation in our centre between 2009–2018 (age 2 months-2 years, 9 female). The underlying diagnoses included 22q11.2 ($n=17$, 1 only phenotypically 22q11.2), CHARGE association ($n=8$), diabetic embryopathy ($n=2$), *FOXN1* mutation ($n=1$), and *TBX1* mutation ($n=1$). 93% had hypoparathyroidism prior to transplant. 79% had hypocalcaemia (defined as corrected calcium (cCa) <2.0mmol/L) during admission. The mean nadir in the entire cohort was cCa $=1.7$ mmol/L (1.2–2.4 mmol/L). This occurred from 45 days pre-transplant to 35 days post-transplant (mean $=$ day $+1$ post-transplant). 55% of patients required intravenous calcium during admission, and 35% required continuous calcium infusions. A diagnosis of 22q11.2 was associated with a slight increase in likelihood of requiring intravenous calcium (Likelihood Ratio $=1.4$, 63% of patients with 22q11.2 compared to 46% with alternate diagnosis). The mean duration of intravenous treatment was 4.7 days (1–39 days) and calcium requirements varied from 0.7–2.4 mmol/Kg/day (mean $=0.7$ mmol/Kg/day.) Associated complications included prolonged length of stay [median $=28$ days (11–255)], admission to intensive care (24%), hypocalcaemic seizures (14%), nephrocalcinosis (20% of those who underwent sonographic evaluation), infection (68%), mortality (10%).
Conclusion
This cohort is at significant risk of hypocalcaemia due to transplant conditioning, hypoparathyroidism, surgery itself and post-operative reduced enteral absorption. This case series highlights the variability of severe hypocalcaemia in patients undergoing thymus transplantation. Our practice has evolved over time to include prophylactic intravenous calcium infusions in patients with borderline hypocalcaemia at the start of conditioning. Further studies are warranted to evaluate whether early pre-operative intravenous calcium therapy reduces hypocalcaemia related post-operative complications. The lack of standardised evidence-based guidelines for managing these patients has important implications for morbidity, mortality and healthcare cost.

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P029

Using CRISPR/Cas9gene editing to study the molecular genetics of congenital hyperinsulinism

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Background
Congenital Hyperinsulinism (CHI) is characterized by the unregulated secretion of insulin in the presence of hypoglycaemia. The mutations in ABCC8 and KCNJ11, which encode the sulfonylurea receptor 1 (SUR1) and potassium inward-rectifying 6.2 (Kir6.2) subunits of ATP-sensitive potassium channel (K channel), are the most common identified cause of the condition.
Aims
The aim is to use the novel CRISPR/Cas9 gene editing technique to create a KO mouse cell model of Congenital Hyperinsulinism. Such cellular models would play a key role in the elucidation of the function of the two genes of interest-ABCC8 and HADH. In addition, this cell model would be used to develop and screen for novel therapeutic drugs.
Methods
Several CRISPR sgRNAs were designed to target both genes in order to generate the KO cellular model. Optimisation of the delivery of CRISPR/Cas9 system included the evaluation of different formats such as plasmid DNA, mRNA and RNP complex using a reporter gene. As a pilot, optimisation of ELISA using wild type (WT) Beta TC6 cells to demonstrate glucose-stimulated insulin secretion (GSIS) has been undertaken.
Results
Progress so far has addressed the optimisation of transfection conditions to deliver CRISPR/Cas9. Several sgRNAs have been designed for the disruption of the *Abcc8* and *Hadh* genes. In addition, the optimisation of the ELISA insulin assay in wild type Beta TC6 cells has demonstrated a dose dependent GSIS which can be used as a standard to compare the GSIS from the KO cell model.
Conclusions
The results of our study so far has demonstrated the potential of the 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 *Abcc*8 gene; create a KO allele of *Hadh* gene in the Beta TC6 cell line and further, use the newly generated KO mutant cells to analyse the function of these genes and furthermore, to test and develop novel therapeutic drugs for CHI.

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P030

Fertility preservation for transgender adolescents: The parent's view

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Background
Fertility preservation (FP) amongst transgender adolescents (TA) is receiving more attention as individuals are transitioning at younger ages. Parents have a key role at exploring options for their children and are usually the ones responsible for consenting to interventions. Our aim was to explore parent's attitudes regarding their offspring parenthood goals, FP counselling and perceived barriers to successful gamete banking.
Methods
Parents of TA who attended the Gender Identity Development Service (GIDS - endocrine clinic) between March and June 2018, were invited to complete an online survey based on a modified version of The Transgender Youth Fertility Attitudes Questionnaire (TYFAQ).
Results
32 parents answered the questionnaire: 22 (68.75%) respondents described their children as trans-males, 9 (28.1%) as trans-females and 1 parent as gender fluid (3.1%). 16 TA (50%) were younger than 16 years old and 28 TA (87.5%) received pharmacological treatment for gender dysphoria. 13 parents of TA (40.6%) indicated their own desire of having grandchildren biologically related but only 9 (28.1%) agreed would feel disappointment if their children could not reproduce. 50% of respondents agreed that their children decision about FP could change when older. Regarding fertility implications of gender dysphoria treatment, 20 individuals (62.5%) strongly agreed and 11 (34.3%) agreed that counselling was important. Information given by psychologist, endocrinologist, general practitioners and fertility units was rated good or very good by 19 (59.37%), 16 (50%), 5 (15.6%) and 9 (28.12%) individuals respectively. 14 respondents had not received any information prior their first appointment at GIDS. Parents reported a very low FP uptake among their offspring (1 trans-female). Their perception about the most common barriers to access FP in descending order were: delay to start pharmacological intervention, funding issues, discomfort with FP procedures and incongruence between perceived gender and biological parental role.
Conclusions
Parents in our cohort expressed similar attitudes to those of their children regarding fertility and FP. Overall they did not emphasize the importance of their child having biological children but agreed that that FP counselling was relevant. Parent's expectations seem to adjust to their children's life course and wishes.

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P031

Gonadotropins and free testosterone in obese adolescent males: relationships to depressive symptoms

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Introduction
One tenth of children worldwide are obese and disturbance in pubertal progression is one of the unpleasant health consequences of adolescent obesity. Data on pubertal hormones in obese adolescents are scarce and contradictory.
Methods
This study was a cross-sectional, case-control study conducted on 120 participants; 60 randomly chosen obese adolescent males and 60 age and sex matched controls. All participants had measurements of their weight, height, waist circumference and calculation of their body mass index (BMI), waist height and waist hip ratios. Pubertal status was assessed by Tanner staging. Assessment for depression was carried out using the Center for Epidemiological Studies Depression Scale for Children (CES-DC), Children's Depression Inventory (CDI), and Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). Laboratory investigations included free testosterone (fT), estradiol, follicle stimulating hormone (FSH), and luteinising hormone (LH) measurement for all cases and controls.
Results
Obese adolescents had significantly lower testicular volumes, higher FSH, LH, fT, and estradiol compared to lean controls. fT correlated negatively in cases with the BMI ($P<0.001$), waist circumference ($P=0.009$), waist height ratio ($P=0.003$), waist SDS ($P=0.017$) and waist height ratio SDS ($P=0.006$). However, fT didn't show any significant correlations with the aforementioned parameters in controls. Cases differed significantly from controls regarding the presence of depression, presence of depressive symptoms and absence of depression ($P< 0.001$ for each category). Comparison between presence and absence of depressive symptoms (according to the MINI KID module A) regarding the mean free testosterone level showed that the following symptoms were significantly different between cases and controls: feeling depressed ($P=0.036$), loss of interest ($P=0.032$), eating disorders ($P=0.000$), sleeping disorders ($P=0.003$), feeling restless ($P=0.000$), feeling tired ($P=0.002$), feeling guilty ($P=0.000$) and Suicidality ($P=0.000$).
Conclusion
In adolescent males, obesity was associated with lower testosterone levels which were associated with higher incidence of depression and depressive symptoms.

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P032

Are caucasian children at risk of sub-optimal vitamin D levels?

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Background
Low vitamin D levels have been linked to stunted growth, lower bone mineral density and health. Optimal levels of vitamin D are not adequately defined and guidance regarding supplementation is limited.
Aim
To identify vitamin D levels in a cohort of Caucasian children aged 0–16 years, and describe how preterm birth, obesity, age and malabsorptive conditions correlate with sub-optimal levels.
Methods
We obtained 368 25(OH)D test results conducted over 8 months from electronic records at Royal Cornwall Hospital. 314 results were screened for demographic and clinical factors, and vitamin D status. Vitamin D levels are defined as deficient at <25 nmol/l, insufficient between 25–50 nmol/l and sub-optimal between 50–75 nmol/l.
Results
Insufficient vitamin D levels or lower were identified in 40.46% of the cohort and 75.19% had sub-optimal levels or lower. The mean vitamin D level across the cohort was 58.27 nmol/l. Mean vitamin D levels were 70.41 nmol/l in children aged 0–4, 58.30 nmol/l in children aged 5–10 and 50.26 nmol/l in children aged 11–16 ($P<0.0001$). In overweight children, there was a weak negative correlation of -0.2 between BMI and vitamin D levels. 9.68% of children born preterm had vitamin D deficiency compared to 4.17% of children born at term. Optimal levels were found in 35.48% of preterm children and 24.31% of those born at term. There was no significant difference in insufficient or lower vitamin D levels between children with (36.98%) and without (43.27%) malabsorptive conditions.
Conclusions
The prevalence of insufficient and sub-optimal vitamin D levels was higher than previously reported. Our study found that adolescents and overweight children are at risk of sub-optimal or lower vitamin D levels. Supplementation with regular review could be extended to these groups.

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P033

Novel *HNF1*Avariant associated with congenital hyperinsulinism in infancy and maturity onset diabetes of young (MODY 3) in later life

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Introduction
Congenital Hyperinsulinism (CHI) is the most common cause of persistent hypoglycemia in neonates, infants and children with an incidence of 1/25000-1/50000 live births. *HNF4A* and *HNF1A* mutations lead to maturity onset diabetes of the young (MODY 1 and 3 respectively) with a potential for causing CHI in the newborn period. Whilst *HNF4A* mutations causing CHI is well known, reports on CHI due to *HNF1A* mutations are very limited.
Case report
A baby boy was born by emergency caesarean section for foetal distress with a birth weight of 4.26 kg ($+1.65$SD). The mother had gestational diabetes mellitus managed on diet. He suffered a caecal perforation on day 3 of life and underwent right hemicolectomy with colostomy. His echocardiogram demonstrated persistent duct arteriosus and left ventricular hypertrophy. He developed persistent hypoglycaemia on day 2 of life and the hypoglycaemia screening

(blood glucose: 2 mmol/l, insulin: 406 pmol/l, c-peptide: 2095 pmol/l, 3-hydroxy butyrate: 87 umol/l, free fatty acid: 143 umol/l and cortisol: 659 nmol/l) confirmed CHI. He was initially managed with high concentration dextrose fluids [GIR: 21.5 mg/kg per min] and glucagon [10 µg/kg per hour] and subsequently he was commenced on diazoxide (3 mg/kg/day) and chlorothiazide (7 mg/kg per day) to which he responded well. The dose of diazoxide had to be gradually increased over the first year of his life to establish euglycaemia [up to 10 mg/kg per day]. His mother was subsequently diagnosed with Type 2 Diabetes Mellitus requiring metformin. The genetic analysis identified a novel heterozygous variant in *HNF1A* [c.713G>T p.(Arg238Met)], which was maternally inherited (consistent with MODY 3 clinical phenotype in mother).

Conclusion

We present a rare cause of diazoxide-responsive CHI due to a novel *HNF1A* mutation which has also caused MODY 3 in mother. Infants and children with transient, diazoxide-responsive CHI might merit from screening for *HNF4A* and *HNF1A* mutations, especially in the presence of family history of diabetes mellitus, to predict the long term risk of MODY in adulthood.

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P034

Hypoglycaemia in paediatrics – a quality improvement project

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Introduction

Hypoglycaemia is a common paediatric medical emergency, hence prompt treatment with appropriate investigations of causes is essential.

Aims

(1) Review current practice of investigating hypoglycaemia in children; (2) Improve awareness of local guidelines; (3) Overcome practical hurdles when investigating hypoglycaemia

Methods

- Retrospective audit of investigation of hypoglycaemic patients over a year using clinical notes
- Education regarding local guidelines with pre/post teaching quiz
- Introduction of 'Hypo-packs' containing sample bottles and list of investigations

Audit results

Over a 12-month period (May 2017–18), 20 hypoglycemic patients were identified.

Demographics

11/20= Male; Average age=35 months (7 months - 6 years); Most common presentation: gastroenteritis (11/20).

8/20 had BM < 2.6 at/during admission; 7/8 had a hyposcreen. 1/8 had an abnormal result: cortisol 17 – with a final diagnosis of hypoadrenalism.

9/20 patients had ketones measures with the initial low BM.

7/20 with BM > 2.6 at/during admission (range: 2.8–3.1) also had hyposcreens.

0/14 patients who had a hypo-screen had complete investigations as per our local guidelines.

Final diagnoses

13/20 ketotic hypoglycaemia, 3/20 - gastroenteritis, 1/20 - epilepsy, 1/20 hypoadrenalism, 1/20 suprasellar mass, 1/20 unknown (transferred out)

Hyposcreens were missed on 2 patients requiring extended overnight fast and resulted in delayed discharge. 2 patients were readmitted for further investigations.

Quiz results

18 responders pre-teaching and 19 responders post-teaching: medical students, GP trainees, paediatric trainees and consultants. Results pre-teaching in brackets.

- (22%) 47% correctly defined hypoglycaemia as < 2.6
- (89%) 89% recognised ketones as the most important bedside test
- (39%) 84% could locate trust guidelines
- (22%) 28% could list correct investigations and (56%) 74% correct sample bottles for a hyposcreen
- 100% thought that pre-made "hypo-packs" would be useful

Conclusions

- Preliminary results show that we may be over-investigating hypoglycaemia and that our current practice is variable in terms of investigation and mangement.
- Educating the clinical team has improved awareness of local guidelines.
- This project is ongoing; we are also reviewing our guidelines to define criteria for 1st and 2nd line investigationswe.
- We plan to re-audit in 6 months' time to evaluate the effectiveness of the introduction of hypo-packs and further education.

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P035

Use of recombinant human growth hormone in a neonate with Prader Willi Syndrome to improve respiratory status

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Background

Prader Willi Syndrome (PWS) is a disorder of genetic imprinting caused by uniparental disomy of chromosome 15. It can present in the neonatal period with dysmorphic features, hypotonia and feeding difficulties. In the UK, recombinant human Growth Hormone (rhGH) is licensed for use in PWS, improving body composition and motor development, as well as final adult height. Some studies have also demonstrated an improvement in respiratory function in children with PWS. The age at which rhGH treatment is initiated requires careful consideration of the intended benefits and risks of treatment, but is generally recommended to start by the the age of 2 years.

Aims

We describe a case of neonatal PWS, where rhGH was initiated at 16 weeks' gestational age, with the primary aim of improving respiratory function, in an infant requiring long term non-invasive ventilation (NIV).

Case report

Infant B was the second of DCDA twins. She was delivered by emergency caesarean section at 28 + 1 weeks' gestation. She displayed respiratory distress at birth and subsequently developed pulmonary haemorrhage and persistent pulmonary hypertension of the newborn, necessitating oscillatory ventilation, inhaled nitric oxide therapy and inotropic support. Following extubation to NIV, she was noted to be hypotonic with dysmorphic features. She was diagnosed with PWS at 9 weeks' gestational age. Due to her continuing need for NIV, rhGH was initiated at 16 weeks' gestational age. Her anthropometry moved from the 9th to the 50th centile and her tone improved. She was successfully weaned off NIV over the following 8 weeks.

Conclusion

Early genetic diagnosis of PWS enables consideration of initiation of rhGH treatment. In PWS, rhGH initiation is known to worsen respiratory compromise in those with pre-existing sleep disordered breathing. However, rhGH has also been shown to have a positive effect on respiratory function in PWS, primarily via a stimulatory effect on central respiratory centres. In addition, in this case we hypothesise that rhGH initiation in the neonatal period contributed to improved tone and thus weaning from NIV support.

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P036

Outcomes of a quality improvement project integrating continuous glucose monitoring systems into the routine management of neonatal hypoglycaemia

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Introduction

Empirical research studies suggest that continuous glucose monitoring systems (CGMS) are safe and could optimize neonatal hypoglycaemia management. However, they need to be tested within resource-limited, time-constrained clinical practice. CGMS was piloted in our Level 3 Neonatal Intensive Care Unit (NICU) in June 2017. Five key barriers to its effective implementation were identified: 1) Lack of NICU staff confidence in device usage 2) Infant discomfort during device removal 3) Calibration errors 4) Wireless connection disruptions during nursing cares 5) Bruising after device removal.

Methods

We designed a quality improvement project that aimed to reduce the number of problems per patient associated with CGMS use in our NICU from 5 to 0 over a one-month period. This study was conducted from June-July 2017. Eligible for inclusion were term neonates 1.5 kg who were admitted for hypoglycaemia (<2.6 mmol/l) within the first 48 hours of life. A New Generation Enlite™ Sensor (Medtronic, Northridge, California) was inserted into five consecutive babies admitted with hypoglycaemia and removed when normoglycaemia was achieved. The sensor transmitted interstitial glucose readings to a Minimed® REAL-Time Transmitter and displayed glucose values every 5 minutes on a MiniMed® 530G System (both Medtronic, Northridge, California). Five 'Plan-Do-Study-Act' (PDSA) cycles tested the change intervention.

Results

The first two cycles tested CGMS acceptability and practicality of the device using qualitative feedback from nursing staff and families and quantitative data from the Neonatal Infant Pain Scale (NIPS). Subsequent cycles focused on

optimizing the insertion process, trouble-shooting calibration errors, and on promoting NICU staff confidence in device usage. Key recommendations included manually inserting the device on smaller babies, using Duoderm® to reduce subcutaneous bruising, timely insertion of calibration readings to avoid sensor errors, adaption of nursing cares to avoid signal loss, and using near-peer teaching techniques to educate medical and nursing staff on CGMS usage. Bland-Altman analysis comparing point-of-care and sensor glucose readings showed no significant proportional bias.
Conclusion
PDSA cycles revealed aspects of CGMS use that need to be adapted for its successful implementation in real-life clinical practice. Further studies should assess the potential of CGMS as a decision-making tool in hypoglycaemia management.

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P037

PTRF novel mutation causing congenital generalized lypodistrophy type 4

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Introduction
Congenital generalized lipodystrophy (CGL) is a heterogeneous, rare, monogenic condition, characterized by loss of subcutaneous fat, muscular hypertrophy, acanthosis, hepatomegaly and impaired lipid metabolism. Four types have been identified, caused by mutations in *AGPAT2*, *BSCL2*, *CAV1* and, *PTRF*, respectively. Mutations in *PTRF* cause CGL type 4, characterized by muscular dystrophy, myopathy, cervical spine instability, high CK levels, cardiac arrhythmias, skeletal abnormalities and gastrointestinal dysmotility.
Case report
We report a 10 year old girl of Somali origin, with generalised lack of subcutaneous fat, acanthosis nigricans and, contractures. Parents were distantly related (3rd grade cousins). Father's sister has a similar phenotype but lives in Somalia. At the age of 9 years, genetic evaluation revealed a novel homozygous frameshift mutation in *PTRF* (exon 2 c.519dup p(Glu174fs)), consistent with a diagnosis of CGL type 4. She had normal glucose tolerance (OGTT: glucose 5.0→6.6 mmol/l; insulin 6.6→36 mU/l), raised ALT of 87 U/l and high CK of 2980 U/l, lipid profile was normal. Physical examination: Height 128 cm (−2.11SDS), weight 28.5kg, BMI 17.7 (+0.17SDS). Generalised lipodystrophy with obvious lack of subcutaneous fat and prominent muscles. Restricted movements and contractures in wrists, shoulders, elbows, knees and, ankles. Lordosis and thoracolumbar scoliosis. Mild umbilical hernia. Tanner A3 B2 P refused. Neurological review showed normal neurology with no signs of muscle weakness. Cardiac and orthopaedic review is pending.
Conclusions
CGL type 4 is an extremely rare autosomal recessive disorder caused by mutations in *PTRF*. So far, 11 mutations have been described. *PTRF* encodes the cavin protein, which is a highly abundant caveolae component and plays a role in the stabilization of caveolins. Caveolae are invaginations of the plasma membrane involved in many cellular processes (endocytosis, cholesterol transport, signal transduction). Knockdown of *PTRF* in mammalian cells and zebrafish leads to a reduction in caveolae density, and *PTRF* knockout mice mimic lypodystrophy in humans. Whilst the metabolic phenotype in CGL type 4 is mild, cardiac arrhythmias have been described, highlighting the importance of obtaining a genetic diagnosis and other specialist review.

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Thyroid

P038

Long-term outcomes of thyroid function in babies with Down syndrome and congenital or early hypothyroidism

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Introduction
Children with Down syndrome (trisomy-21/T21) are at risk of developing congenital and early (diagnosed ≤1 year) hypothyroidism. Our current monitoring follows the Down Syndrome Medical Interest Group (DSMIG) guidance: performing thyroid function tests (TFT) at birth and 12 months.
Aims/objectives
1) Determine the incidence of congenital/early hypothyroidism in babies with T21 and determine long-term thyroid function outcomes (by age 4-years).
2) Audit local practice against DSMIG guidelines.
Methods
We identified children with T21 born in our region over 10years: June 2007-June 2017. We reviewed their new-born screening (NBS), laboratory TFT, radiological results and follow-up input.
Outcome
Eighty-five children fulfilled the criteria (M:F sex ratio:1.58, incidence 0.95/1,000 livebirths). Day 5–7 NBS results were available for 84 patients (99%). Four children (4.8%, M:F 1:1) were diagnosed with congenital hypothyroidism requiring thyroxine treatment. Of these, 2 had normal NBS results (2.4%). 30/84 (36%) babies had transiently abnormal TFTs within 1 year. The majority occurred within month one of life ($n=25$, 83%), and were mostly elevated TSH values ($n=13$, 43%). 93% ($n=28$) had normal TFTs by 15months and of the remaining 2, one had normal TFTs by age 3-years and one has untreated persistent compensated hypothyroidism at age 2. Compliance with DSMIG guidelines:
- At birth: Between June 2007–2012, 40.5% (15/37 patients) had venous TFTs checked, compared to 81% (38/47) over July 2012–2017.
- 12-months: Between June 2007–2012, 76% (28/37) had venous TFTs; compared to 96% (45/47) over July 2012–2017.

Table 1

Patient	**NBS TSH** (Upper limit 6 or 10mU/l)	**Venous TSH at birth** (Upper limit 7.5 or 5.42mU/l)	**Current treatment dose** (micrograms) **and age** (years)
1	16.9	33.84	25 (Age = 1.0)
2	24.26	62.42	50 (Age = 4.1)
3	1.29	11.09	37.5 (Age = 4.8)
4	1.54	16.07	62.5 (Age = 4.75)

Discussion
Our regional sex and birth rates for T21 compare with national rates (SR 1.3; BR 1.08 in 1000). Our incidence of congenital/early hypothyroidism in children with T21 (4.8%) compares with reported rates (1–20%). The majority of abnormal TFTs are transient and don't require treatment. Over the second half of the 10-year period, compliance with DSMIG guidelines improved significantly.

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P039

Isolated central congenital hypothyroidism (CCH) due to (Immunoglobulin SuperFamily member 1) IGSF-1 gene deficiency

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Introduction
Central congenital hypothyroidism (CCH), undetected by TSH-based NewbornScreening, occurs from TSH synthesis or secretion defects. An extremely rare (<1:100,000) cause concerns the recently described ImmunoGlobulinSuperFamily member 1 (IGSF1) gene, critical in TSH biosynthesis. These 2 infants highlight intriguing clinical features.
Case-1
Term male (BW 3.95 kg) with poor feeding and persistent jaundice (max bilirubin 362 umol/l) despite phototherapy, had mildly elevated TSH on Guthrie (11.4 mU/l). Repeat TFTs demonstrated low fT4 (6.8 pmol/l) with low/normal TSH (9.46 mU/l) suggesting possible central hypothyroidism. Examination showed small umbilical hernia and large testes for age (3 ml). Broader evaluation showed normal Synacthen (592 nmol/l), LH 5.8 IU/l, FSH 3.7 IU/l, although low prolactin (66 mIU/l). MRI was normal. Genetic analysis confirmed novel variant mis-sense IGSF1 mutation, c.3691 T>C, p.(1231R).

Case-2
Term male (BW 2.7 kg) with polyhydramnios and short limbs on antenatal scans. Clinical features at 10 weeks were roving nystagmus, short limbs, relative macrocephaly and large anterior fontanelle prompting skeletal dysplasia radiological and genetic investigations. Radiology identified only mild skeletal immaturity. Array CGH identified Xq26.2 1.02Mb deletion, encompassing FRMD7gene (associated with X-linked congenital nystagmus) and IGSF1gene (associated with central hypothyroidism). CGH array interpretation prompted TFTs: low-normal TSH 3.3 mIU/l with low FT4 8.4 pmol/l. Clinical features at 5 months included large anterior fontanelle, persistent posterior fontanelle, flat nasal bridge, moderate sized umbilical hernia, testes 2ml. Broader evaluation showed normal Synacthen (475 nmol/l), LH 1.0 IU/l, FSH 2.1 IU/l, prolactin 284 mIU/l. Thyroxine initiation achieved rapid fT4 normalisation and good developmental progress in both boys.
Conclusion
Biochemical screening will not detect Isolated TSH-deficiency. So, remembering subtle features aid early diagnosis to achieve good neurodevelopmental outcome: appreciation of inappropriately low-TSH and low-fT4 on jaundice screening and of subtle hypothyroidism with skeletal abnormalities. New rarer causes of Isolated TSH deficiency add extra unusual clinic-points: IGSF1 mutations cause an X-linked disorder with intriguing additional features of macro-orchidism (boys) and ovarian cysts (girls) and variable prolactin deficiency. A high index of suspicion for CCH in appropriate clinical settings along with timely therapeutic intervention (thyroxine replacement) can help prevent long term sequelae.

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P040

MEN2B and MTC: the challenge of early diagnosis

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Introduction
Multiple endocrine neoplasia type 2B (MEN2B) is a rare autosomal dominant neuroendocrine neoplasia syndrome characterised by early onset medullary thyroid carcinoma (MTC) in all patients, phaeochromocytoma and multiple extra-endocrine features. We present a case of late diagnosis of MEN2B illustrating the challenge of early diagnosis.
Case report
A 12 year old boy presented after lifetime of investigation. There was no relevant family history. He had atypical left talipes equinovarus caused by a tethered spinal cord which was surgically released, swallowing difficulties, gastroesophageal reflux, constipation, left duplex kidney with grade 3 reflux, tracheomalacia, amblyopia, speech and language delay, articulatory difficulties, asthma and allergic rhinitis. At the age of 4, genetic investigation revealed normal karyotype, MLPA, and array CGH. At 10 he was enrolled into the pilot 100,000 genome project and about 2000 genes were analysed. This revealed a single pathogenic variant: a heterozygous missense pathogenic RET variant, c.2753T>C p.(Met 918Thr) diagnostic of MEN2B. Examination revealed marfanoid habitus with arm span exceeding height, hyperflexibility, prognathism, enlarged tongue with mucosal neuromas, high arched palate, full lips, eversion of upper lids and unremarkable thyroid examination but enlarged cervical lymph nodes. Biochemical measurements showed a Calcitonin level 7000 ng/l [0–12.7], CEA 28.7 µg/l [0–3.4] and normal plasma metanephrines. Thyroid ultrasonography revealed bilateral medullary thyroid nodules with local nodal involvement and chest CT showed bilateral lung nodules. The patient had total thyroidectomy with modified radical neck dissection, the cancer had also infiltrated the right recurrent laryngeal nerve. Pathology confirmed the presence of bilateral medullary thyroid cancer and involvement of 55/137 excised lymph nodes. Calcitonin levels decreased to 5010 ng/l. Postoperatively he had stridor from vocal cord paresis. He is currently well, no chemotherapy is planned presently.
Conclusion
MEN2B is a rare disease consisting of a *de novo* mutation in 90% of patients. Also, MTC may be asymptomatic until advanced stage of disease. However, different extra-endocrine features will be present in 100% of patients and awareness of these is essential for early diagnosis and improved outcome.

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P041

Single UK tertiary centre experience of newly presenting thyrotoxicosis in childhood and adolescence (2013–2018)

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Introduction
Thyrotoxicosis, the commonest cause of which is Graves' disease, is rare in childhood and adolescence.We report a consecutive series of patients referred to a single tertiary paediatric endocrine centre over 5 years.
Methods
Retrospective case note and database review of patients referred 01/2013–02/2018.
Results
27 patients (21F) with Graves' disease in 21, and Hashitoxicosis in 6. During the same period an additional 30 patients (29 Graves', 1 Hashitoxicosis) were referred to the service but managed jointly at their local General Hospital. We report the characteristics of patients managed solely at our Teaching hospital. Median age at diagnosis was 13 years (Range: 7 days – 17 years). 48% of patients were Black African/Caribbean origin. The majority were referred from primary care (52%). Ophthalmopathy was present in 11, proptosis being commonest (9); all were managed conservatively. Median fT4 was 69pmol/l; fT3 26pmol/l. 59% had TSH-Receptor antibodies (TRAB) measured: 94% positive. The two patients with negative TRAB had Hashitoxicosis. 72% had Thyroid Peroxidase antibody measured, (75% positive); 52% had Thyroglobulin Antibody measured (43% positive). Patients with Hashitoxicosis did not require treatment. Graves' patients received standard antithyroid treatment, usually 40 mg Carbimazole for a minimum 2 years initially. 17(81%) were treated with 'block and replace' therapy. Median time to euthyroid status was 6 weeks (range 3–20) before introduction of thyroxine 62% experienced side effects (commonest urticaria, 38%) patients. One patient developed 1st degree heart block within 48 hours of starting Atenolol, which resolved promptly with withdrawal of β-Blockade. 10 patients completed 1 course of treatment: seven patients remain in remission, 3 relapsed and restarted treatment. 9 patients presently remain on treatment. Two had care transferred to another hospital.
Conclusion
We report the profile a large Paediatric series of newly diagnosed thyrotoxicosis over the last five years from a single UK centre. The high incidence may be due to the high Afro-Carribean population in the catchment area. Ophthalmopathy was not uncommon. All patients responded to carbimazole which was generally well tolerated. Poor adherence was common. Longer term follow up of this cohort will inform us of treatment outcomes in this population.

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P042

Impact of iodine deficiency on thyroid function in vegan siblings

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Background
Iodine deficiency is the most common cause of acquired hypothyroidism worldwide. Incidence of iodine deficiency may be rising due to usage of vegan diet.
Case presentation
We present siblings aged 2.5 years boy and 6 years old girl from family who are strict vegans. Both children have been on vegan diet since birth. Boy attended hospital urgently due to significant concerns about hypothyroidism. His TSH level 2 months before admission was 187 mIU/l and fT4 was < 4 pmol/l. At the hospital admission his weight was between the 2nd and 4th centile and his height was below the 0.2nd centile. He was diagnosed with iron deficiency and vitamin B12 deficiency and hypothyroidism 2 months before admission and parents stated giving him multivitamins with iodine and iron. In terms of thyroid related symptoms, apart from growth the main issue was hair thinning and loss, which parents have noticed over the past few months. Energy levels seemed appropriate. He was not having any skin or nail manifestations. Developmentally no concerns at all and he was bilingual and his speech was appropriate for his age. His motor development had not been a concern either. At the admission in his bloods test he was still iron deficient, but his thyroid function was normal with TSH of 0.44 mIU/l and fT4 15.2 pmol/l. His 6 year old sister was referred to endocrine clinic due to goitre, which parents noticed at the age around 2½ years old. She also was found to have subclinical hypothyroidism with slightly elevated TSH with normal FT4 (FT4: 16 pmol/l, TSH: 7.04 miu/l) and an enlarged thyroid gland on

ultrasound scan. Following this the family started both children on vitamin supplements with iodine. Both children were referred to dietician to help family balance their diet.
Conclusions
This case highlights the risk for iodine deficiency in children on a vegan diet and that it can lead to acquired hypothyroidism and goitre. Doctors should be aware of the danger of not supplementing with iodine in a vegan diet children.

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P043

Audit of management of neonates born to mothers with thyroid disorders

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Introduction
Maternal thyroid disorders influence neonatal thyroid status. Neonatal thyrotoxicosis (NT) is a potentially fatal condition with high risk in those with clinical signs, high or unknown maternal thyroid receptor antibody (TRAb) status and where mother is clinically hyperthyroid or on treatment. The aim of post-natal management of these babies is to identify those at risk of NT and monitor them. There is, however, no available national or international consensus.
Aim
To evaluate local practice in order to develop local guideline to aid the management of these infants.
Method
This is a retrospective analysis of case notes and investigations of infants born to mothers with thyroid problems during a one-year period between 1/4/2017 to 30/3/2018. The following criteria were assessed – mother's thyroid disorder, cause of maternal hypothyroidism, maternal treatment, biochemical and clinical status, neonatal clinical review, timing of neonatal bloods, results and if treatment was started.
Result
There were 49 neonates born to 48 mothers with thyroid disorders (one set of twins). 38 women had hypothyroidism out of which 5 were post treatment for Grave's disease and 9 women were hyperthyroid. 14 neonates in total were at risk of NT with 11 being at high risk. Among these, maternal thyroid disorder details were recorded in 2 notes, none of the neonatal notes had maternal TRAb status documentation. Only one neonate had a clinical review. 3 infants had thyroid function tests, all performed after day of life 5 with no abnormal results and no infant required treatment. The audit showed that majority of babies at risk of NT were not recognized.
Conclusion
This audit served to highlight the importance of identifying neonates at risk of NT and to ensure appropriate monitoring and follow up of these infants. It highlighted the need to develop local guidelines which we have since completed.

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P044

Abstract Unavailable.

Diabetes

P045

A rare and unexpected cause of diabetes in a teenager

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Introduction
Pancreatogenic diabetes (Type 3c diabetes-T3cDM) is rare in children, and frequently underdiagnosed. The prevalence is 5–10% of all adult diabetes cases in the developed world. Over 78% of people with T3cDM have chronic pancreatitis.
Case
A 15-year old presented with polyuria, polydipsia, abdominal pain, weight loss (WL) and a three-generational family history of type-1 (T1DM) and type-2 diabetes mellitus (T2DM). Examination revealed mild epigastric tenderness, with moderate dehydration. Bloods showed high blood glucose (BG):18.8 mmol/L (NR: 4–7) and HbA1C: 90mmol/mol (NR: 20–42). Blood ketones were negative. Serum amylase was 185 IU/L (NR: 25–125). Further tests including diabetes autoantibodies: Islet cell, Islet antigen 2, Glutamic acid decarboxylase- were negative and OGTT results showed a 2-hour BG of 18.8 mmol/l; and c-peptide of 498pmol/L. The results confirmed diabetes but not conclusive of either T1DM or T2DM. Next generation sequencing for all known monogenic diabetes genes was negative, hence excluding genetic maturity onset diabetes of the young (MODY). He was started on subcutaneous insulin (Glargine and NovoRapid). Over several weeks he complained of on-going abdominal pain, WL (8 kg over 6 weeks) and early satiety. A repeat amylase was very high (415 IU/l) and an abdominal MRI revealed a large pancreatic pseudocyst with pancreatic duct disruption, confirming diabetes secondary to chronic pancreatitis, also referred to as type-3c diabetes mellitus (T3cDM). Following bloods for fat soluble vitamins (A, D and E) he was commenced on vitamin D supplementation. His clotting profile was normal. After endoscopic drainage of the pseudocyst his abdominal symptoms resolved, however he remains on insulin therapy. Genetic tests for idiopathic pancreatitis (SPINK1 and PRSS1 genes) were negative.
Discussion and learning points
T3cDM is often mis-diagnosed as T2DM.The pathophysiology is pancreatic inflammation and destruction of islet cells. It is often complicated by malabsorption and malnutrition, and patients with T3cDM require insulin therapy more urgently than those with T2DM. Making the correct diagnosis is important for managing both exocrine and endocrine pancreatic insufficiency. Avoiding alcohol and smoking will reduce pancreatic inflammation. Early pancreatic imaging is recommended in suspected cases.

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P046

Coming off the insulin pump- outcomes from a single centre

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Introduction
Continuous subcutaneous insulin infusion (CSII) can improve glycaemic control and quality of life in Type 1 Diabetes patients. It is uncommon for paediatric patients to discontinue CSII and return to multiple daily insulin injections (MDI) often due to concerns regarding worsening metabolic control. However a trial off CSII is a requirement before transition to the adult clinic. We review the outcomes of those who discontinued CSII in our centre (total 248 patients with ~50% on CSII).
Methods
Between 01/04/2014 and 31/03/2016, 7 patients <19 years old discontinued CSII. Data were collected from electronic patient records. Differences between groups were explored using paired *t*-tests. *P* value <0.05 (2- tailed) was considered significant.
Results
Seven (2 male) patients out of 112 pump patients (61 male) discontinued CSII and changed to MDI. The median (range) age of starting CSII was 11.3 (9.3–12.7) years and discontinuing CSII at 14.3 (11.8–18.5)years. Median (range) duration of CSII was 4 (1.8–7.9) years. Six of the seven patients chose to remain on MDI. 57.1% (4 patients) personally chose to discontinue CSII. Other reasons cited from the remaining 3 patients include poor control, physician recommendation and technology difficulties. Following CSII discontinuation, HbA1c remained unchanged for the first 12 months and fell over the 2nd 12 months (Table 1).
Conclusion
We describe outcomes in seven young people who discontinued CSII. Majority remained off CSII with no deterioration in control. Indeed, control improved after stopping CSII for 2 years although this cannot be directly attributed to coming off CSII. These data could give confidence to families and diabetes teams when making the choice to trial off insulin pump in preparation for transition.

Table 1 HbA1c before, during and after stopping CSII.

HbA1c (mmol/l)	**Median** (range)
Average HbA1c during 1 year before starting CSII	67.3 (60–81)
Average HbA1c during CSII	82 (49.6–90.4)
Last HbA1c before stopping CSII	89 (50–116)
Average HbA1c during 1st year after stopping CSII	88 (46–103.5)
Average HbA1c during 2nd year after stopping CSII	75 (42–90)*

*$P<0.05$ vs last HbA1c before stop.

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P047

Audit on the recognition and response to hypertension in young people with type 1 diabetes mellitus

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Background
Raised blood pressure (BP) in adolescents with type 1 Diabetes Mellitus (T1DM) has been associated with adverse cardiovascular outcomes independently of raised HbA1c. It is therefore of critical importance that these patients are identified early and appropriate treatment instigated. Of concerns, studies have recognised suboptimal management of hypertension in most of these young people, allowing them to succumb to complications of diabetes with hypertension in their adulthood. The aim of this audit is to assess our local practice in recognising and managing hypertension in adolescents with T1DM.
Methods
This audit reviewed recorded BP for adolescents with T1DM, aged between 12 and 16 in our trust over 12 months. The records were extracted from Twinkle Database where all clinical encounters were recorded. The primary endpoints of interest for this audit are i) frequency of BP measurements ii) intervention taken for abnormal BP.
Results
98 patients were included in this audit. 10 patients had no BP checked or documented for 12 months. A total of 230 clinic episodes were attended by these 98 patients over the year and adolescents were found to be hypertensive in 37 of them. Out of these 37 clinic episodes, BP was subsequently rechecked within 3 months in only 12 (32%) of them. One quarter of these adolescents remained hypertensive. No clear action was documented in response to these abnormal BP recordings.
Conclusion
Our audit has identified poor awareness in monitoring hypertension in adolescents with T1DM. Only a small fraction of children with recorded episode of hypertension had appropriate follow up as recommended by the American Diabetes Association. As a consequence the service is reviewing the screening tools and the management of adolescent with borderline and actual hypertension. We are also in a process of writing a regional guideline to ensure improved detection and management of borderline and actual hypertension in adolescents with T1DM.

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P048

Diabetic retinopathy in childhood – patient profiles

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Retinopathy is one of the more serious complications of type 1 diabetes. There is emerging knowledge re the development of retinopathy in childhod diabetes. We studied the clinical profiles of children with retinopathy in an industrial town in Northern England. The current clinic size is 160. 42 patients were identied from clinic records as having retinopathy. Formal screening is offered to all patients from age 12. The age range was 11–20 years; median age 16. 55% were female and 45% male. 41 patients had type 1 diabetes mellitus and 1 patient had glucokinase deficiiency We looked at average HBA1C of each of these patients since diagnosis. The average HBA1C was 80.38 mmol. The range of average HBA1c was from 41.7 to 112 mmol. The NPDA audit for the corresponding time period showed a clinic mean HBA1C of 68.8. The average duration of diabetes in the 42 patients was 8 years and 9 months. 40 out of the 42 patients had been admitted to hospital because of their diabetes (the North-West average is that 17.2% of paediatric diabetes patients get admitted annually). Altogether there were 167 admissions: 55 due to DKA, 25 due to a hypoglycaemic episode requiring third party assistance and 86 admissions as a result of high blood sugars. Only two patients never had a hospital admission related to their diabetes. Four patients had a history of hypoglycaemic seizures. Four patients had pre proliferative or proliferative changes. The others had background changes only. These four patients had an average HBA1c of 103.4 and a cumulative total of 10 admissions due to DKA. There were three cases of maculopathy This study shows that development of diabetes retinopathy correlates with higher HBA1C and longer duration of diabetes. The development of retinopathy in individuals with excellent HBA1C scores also indicates the presence of individual susceptibility to microvascular disease. There is clearly a much higher than usual number of admissions and episodes of severe hypoglycaemia and DKA in this group. Further research could show if the relationship between retinopathy and DKA/severe hypoglycaemia is in itself causative or merely an association with poorer control.

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P049

Use of diluted insulin in the management of very young children with type 1 diabetes: case report and literature review

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Introduction
The management of type 1 diabetes (T1D) in young children can be extremely challenging due to high insulin sensitivity, unpredictable eating and activity and difficulty recognizing symptoms of hypoglycaemia. Continuous subcutaneous insulin infusion (CSII) therapy is beneficial in managing young children, however the small insulin doses required challenge the accuracy of standard concentration (100 IU/ml) CSII.
Case report and literature review
A 15-month-old, previously healthy boy was admitted with the diagnosis of diabetic ketoacidosis in new T1D after presenting with a 7-day history of polyuria, polydipsia, lethargy, vomiting and increased work of breathing. Due to oscillating consciousness and refractory tachycardia he was transferred to a paediatric intensive care unit where he was treated for severe shock and cerebral oedema. During his admission he developed increasing abdominal distension and he was diagnosed with extensive bowel necrosis. Subtotal colectomy was performed and total parenteral nutrition started. Twenty-seven days into his admission sensor-augmented CSII was started and based on his low insulin requirements the following calculations were made: 3.5 IU/day at 0.025 IU per mini-bolus (lowest rate) = 1 bolus every 10 minutes. We believed this would be insufficient to achieve good glycaemic control and we turned to the literature for support. A study by Borot (J Diabetes Sci Technol. 2014) reports increased rates of flow errors and significant occlusion detection delays with low infusion rates. A study by Elleri (BMJ Open Diabetes Res Care 2014) showed a tendency towards reduced hypoglycemia and reduced glucose variability using diluted insulin. Finally, the study by Ruan (Diabetologia 2015) concluded that diluting insulin does not change its pharmacokinetics and may result in less variable absorption. The decision was made to start our patient on diluted insulin 10 IU/ml using diluting medium for insulin aspart (Novo Nordisk A/S). Good glycaemic control (HbA1c 47 mmol/mol) was achieved despite multiple challenges in his slow transition from parenteral to enteral nutrition.
Conclusion
Very young children with low insulin requirements challenge the accuracy of standard concentration CSII which may be overcome by diluting insulin. This report adds our experience to the limited evidence on using diluted insulin.

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P050

A survey of the use of medical identification in children and young people with diabetes at a large children's hospital

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Objectives
Children and young people (CYP) with Type 1 Diabetes Mellitus (T1DM) are at risk of acute clinical emergencies. Wearing medical identification (ID) is recommended by the National Institute for Clinical excellence (NICE). Information on adherence to this recommendation in CYP with T1DM is scarce.

This study aimed to assess parent and CYP's knowledge of the recommendation, to explore adherence and barriers to carrying ID and understand preferred forms of ID.
Methods
This was a prospective, cross-sectional questionnaire survey of CYP aged 10–19 years with T1DM of more than 6 weeks, and carers, conducted at diabetes clinics in a large diabetes centre between 6- 31/3/2018.
Results
Questionnaires were completed by 47/47 CYP (mean age 14.1 years), and 38/39 carers, accounting for 19% of registered 10–19 year olds. Medical ID was owned by 29/47 CYP(61.7%) and 81%(13/16) of 16–18 year olds with no significant gender differences. 25/33 (75%) of young persons recalled having advice on ID, in contrast to 17/38 (45%) of carers. Diabetes ID cards (44%), given free to CYP on diagnosis by the clinic, and ID wristbands (34.5%) were the most frequent forms of ID owned. Although 8/29 (27%) CYP reported carrying ID daily, only 7/29 (24%) wore it on the day they attended. 20/44 (45%) CYP and 13/30 (43%) carers identified forgetting ID was the greatest barrier to carrying ID. 20/30 (60%) carers thought appearance was a barrier in contrast to 8/44 (18%) of YP. For 10/32 (31%) YP, in contrast to 6/45 (13%) carers, 'feeling safe' was a factor in wearing ID.
Conclusion
Up to 40% of CYP do not possess medical ID and up to 85% of CYP are potentially at risk if experiencing a diabetes emergency away from their main carers. Professionals have a role in awareness of ID amongst CYP and carers by checking this at every clinic. Making ID cards available at every clinic, in addition to providing at diagnosis, may prove beneficial.

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P051

Audit to look at the effectiveness of sensor augmented pump in managing type 1 diabetes mellitus

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Aim
Type I Diabetes Mellitus is a chronic metabolic disorder with an incidence of 24,000 children in the UK. NICE has recommended the use of the sensor augmented pump (SAP) in managing short and long term diabetes related complications. Limited literature is available in the paediatric population. SAP is designed to allow continuous glucose monitoring, with real-time adjustment of insulin; making it superior to other pump systems. 0.8% of children suffer from Type I DM in the Wigan Borough. SAP was introduced in these children as a trial; who were previously on insulin pumps with limited success in managing hypoglycaemic episodes. The aim of the audit was to identify how effective SAP was in reducing HBA1c and preventing hypoglycaemic episodes.
Method
14 children were commenced on the SAP between 2016–17 March. Evidence was collected from electronic records, which, summarized clinic letters from the consultant and diabetic nurse team. Date of diagnosis and initiation of SAP following that was dictated. The number of hypoglycaemic episodes causing admission to hospital and HBA1c was compared before and after the SAP was started.
Results
There were equal number of males and females. The average age of Type I DM diagnosis was 6 years 2 months. The average age when SAP was commenced was 8 years 1 month. Average HBA1c prior to SAP was 63.1 and showed 5.3% improvement following SAP with 59.8. 64.3% showed improvement, whereas, 21.4% of children showed deterioration in HBA1c. These were males and belonged to an older age group (>5 years). 14.3% of children did not show any change in their HBA1c. 29% of children had severe hypoglycaemic episodes prior to SAP. Following SAP, 7.1% of children had a severe hypoglycaemic episode.
Conclusion
NICE 2016 has recommended the use of SAP in improving the quality of life for people with Type I DM. The audit highlighted improvement in glucose control with positive effect on HBA1c and reduction in hypoglycaemic episodes. This can be explained with increased adherence to treatment with the use of automatic insulin monitoring and delivery. Ultimately, SAP offers benefit to the NHS with cost and resource saving.

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P052

Improved inpatient hypoglycaemia management following implementation of a multipronged strategy

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Introduction
Recently a serious incident due to failure in rechecking blood glucose (BG) after hypoglycaemia treatment was reported in an adult inpatient. We evaluated adherence to network guidance on hypoglycaemia management in inpatients and changes in practice following an intervention based on education and system changes.
Methods
In an audit (audit-1), hypoglycaemia episodes (BG level <4 mmol/l) were identified in paediatric inpatients (age <17 years) with diabetes mellitus receiving insulin from electronic patient records between May-July 2017. Hypoglycaemia management was evaluated by three parameters: identification of hypoglycaemia, appropriate treatment and rechecking after treatment. Subsequently, we implemented following recommendations: availability of wider range of oral hypoglycaemia treatments, hypoglycaemia treatment orders sets in electronic patient record linked to clinical guidelines and an education programme for ward nurses. The effects of these changes were evaluated by a second audit (audit-2) between January and July 2018.
Results
21 hypoglycaemia episodes (Table 1) were identified in each audit [five patients with median age 10 (range, 1–16) years in audit-1; seven patients with median age 11.3 (2.3–16.5) years in audit-2]. A greater proportion (66.7% vs 14.3%; $P=0.0054$) of BG rechecking occurred within 30 minutes after treatment in audit-2 compared with audit-1.
Conclusion
This audit cycle demonstrated considerable improvement in rechecking BG after hypoglycaemia treatment which suggests effectiveness of the education programme and easier access to clinical guidance. However, these efforts need to be further intensified. We were unable to evaluate the appropriateness of treatment due to the large proportion of unrecorded treatments most likely due to self-administered treatments.

Table 1 Results of audit-1 & audit-2.

Audit standards	audit-1,n/21(%)	audit-2,n/21(%)
Appropriate identification of hypoglycaemia episodes	20/21 (95.2%)	20/21 (95.2%)
Treatment with rapid-acting carbohydrates	14/21 (66.7%)[#]	10/21 (47.6%)[#]
Recheck BG within 15 minutes after treatment.	2/21 (9.5%)*	11/21 (52.4%)*

[#]Treatment types were unrecorded in 19% (4) of hypoglycaemia episodes in audit-1 and 9 (42.9%) in audit-2. *P-value = 0.0027.

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P053

Using quality improvement [QI] in diabetes care to drive better outcomes for newly diagnosed patients - experience of RCPCH QI Programme

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Background
Our Diabetes Team look after approximately 220 T1DM patients aged 0–17 years. In 2014/15 NPDA we ranked amongst the top 5 paediatric units with mean HBA1c <65 mmol/mol. Susequently our ranking slipped, with increased mean HBA1c and fewer patients achieving HBA1c <58 mmol/mol.
Objectives
We recognised a particular problem with poor control in the first year after diagnosis and identified the need to drive change to be able to achieve improvement in outcomes for our patients. We also identified the need to provide our patients with bespoke education that will empower them to manage their Diabetes effectively.
Aim
HBA1c <48 mmol/mol at 3 & 12 months post diagnosis.

Methods
We joined the RCPCH National QI Initiative and over the past 7 months have planned and undertaken a number of small projects designed to help achieve our aim. First was the introduction of carbohydrate counting from diagnosis which required a huge amount of work to upskill ward staff and design new charts for use in educating staff and patients. Subsequent projects included early introduction of Expert Meters and downloading these at home via Diasend which allows team members to offer advice on blood glucose readings remotely and empower self-management. We are also developing a package of bite-sized teaching to deliver in clinic. PDSA cycles and Driver Fish Bone diagrams were used to design projects and metrics including time to first carbohydrate counting, HBA1c and average blood glucose are plotted on run charts. A knowledge survey prior to bite-sized teaching was performed and will be repeated once bite-sized teaching is embedded.
Results
Median HBA1c 44.5 mmol/mol at 3 months v' 53 mmol/mol pre-QI. Mean Blood Glucose at 30 days post discharge 6.7 mmol/l. Further data will be presented.
Conclusion
Participation in the National QI Initiative has been enormously valuable in terms of improved ways of working and innovative ideas to improve the care we deliver. We have learned to be brave, fail fast and change the way we do things based on 'Bright Spots' and 'Dark Spots' as well as the evidence accumulating on run charts.

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P054

Network-wide audit of 'hypo supplies' availability in children and adolescents with type 1 diabetes mellitus – interim results

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Introduction
Hypoglycaemic episodes (Hypos) can happen at any time in type 1 diabetes patients; sometimes quite unpredictably. Carrying 'hypo supplies' at all times is basic to good diabetes care; often delegated to parents for children with diabetes. The primary aim was to assess how this basic care activity is practised in real life; secondary aim was to correlate lack of hypo supplies with diabetes control or other patient characteristics.
Methodology
The prospective audit was conducted over 2 weeks, where all patients attending any paediatric diabetes clinic across both South East Coast (East & West) Networks were requested to show their hypo supplies, glucose meter & strips and bolus insulin present with them. Non-type 1 patients were not included in analysis due to small numbers. Non-identifiable patient data like age, sex, duration of diabetes, post code and HbA1c were collected.
Results
405 patients (87.9%) attended their appointment; and 52.4% were male. Age significantly differed between attenders (mean = 12.07, SD = 4.05) versus non-attenders (mean = 14.66, SD = 3.37) ($P < 0.001$); but no difference observed with gender or duration of diabetes. Patients age ranged from 1.5 years to 19 years (mean = 12.39, SD = 4.06) and duration of diabetes from 0.2 to 17 years (mean = 4.87, SD = 3.93). HbA1c ranged from 30-130 mmol/mol (mean = 65.33, SD = 17.88). Patients on 4+ injections had higher HbA1c (mean = 67.34, SD = 17.73) (mmol/mol) than those on pump therapy (mean = 58.98, SD = 11.96) ($P < 0.001$). 399 patients were checked and 308 (77.2%) had one or more hypo supplies with them (49.5% glucose tablets, 38.7% glucose drink and 31.3% sugar jelly beans). Patients with higher HbA1c were less likely to have hypo supplies ($P < 0.001$). Older children and patients with longer duration of diabetes had higher HbA1c (both $P < 0.001$). No correlation was observed between HbA1c and gender or having bolus insulin present ($P > 0.281$).
Conclusions
The majority of patients carried their hypo supplies with them. This study was conducted without fore-warning and very likely represents real life practice. Continued and targeted education for older children, those with longer duration of diabetes and higher HbA1c is needed, to promote good diabetes self-care.
Acknowledgement
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P055

RCPCH QI diabetes collaborative: improving the clinic experience

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Introduction
Gloucestershire Paediatric Diabetes Team has implemented several innovations including carbohydrate counting from diagnosis, annual review clinics and family events. We seek to improve our patient engagement and experience to improve health outcomes.
Aim
Improve the clinic experience for patients, their families and staff, based on their input, thereby encouraging greater engagement and patient attendance as part of the RCPCH quality Improvement programme.
Methods
We undertook mapping of our current clinic process and ideal clinic. We collected feedback from patients, families, clinic staff and our team members. We identified main areas for improvement. Interventions were implemented and evaluation done.
Interventions and results

Aim	Areas identified for improvement	Solutions implemented	Results based on patient survey
To improve clinic experience for patients	Clinic feeling 'interview like'	Clinic layout and furniture rearranged into 'coffee table' setting	88% were positive about changes in clinic layout, 12% neutral
Patient engagement in clinic and wanting greater involvement in care decisions	Development of 'getting ready for Clinic' sheet enabling patient-led consultation and to provide clear written action plans to be taken away from clinic	94% positive responses, 6% neutral	
Need for patients to have greater ownership of their diabetes management	Providing instruction leaflets and guidance on Diasend downloading in clinic to enable all patients to download from home Introduction of Hba1c record charts in clinic	86% found instructions valuable 72% were happy to download at home. Some indicating that knowing they would need to download in clinic would encourage to download at home prior to clinic.	
	Reduce time spent waiting in the MDT clinic	Data on clinic waiting times were collected. Amending appointment letters to request patients arrive 15 minutes early for clinic	Amendments made recently and clinic times being reviewed (as 3 monthly clinics)

Conclusion
Verbal and written feedback has shown families and children are engaging to a greater extent and more involved in their own diabetes management. They are more relaxed and have now found their voice. The project has enabled us to improve our team working.

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P056

Paediatric diabetes education and empowerment quality improvement project

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Aim
To empower our patients/parents to self-manage Type 1 diabetes (T1dm) by providing them with required knowledge and skills.
Method
We identified 10 motivated, mostly newly diagnosed T1dm patients and their families. We organised a master-class to educate them on how to use DIASEND to review blood sugars, identify patterns and adjust Insulin doses. We conducted weekly DIASEND clinics for 6 weeks and fortnightly for another 6 weeks (phone call/email). The whole diabetes team participated in this process including nurses, doctors and dieticians. An objective assessment was made on the degree of competence of patient/parents in identifying patterns in blood sugars and ability to make appropriate changes in Insulin doses at each DAISEND clinic using a standardised format. A qualitative questionnaire was completed by families at the beginning and end to feedback on the effectiveness of this project.
Results
100% of families were competently identifying patterns in blood sugars at week 5 and 89% of families were competently making appropriate adjustments in Insulin doses by week 5. Subsequently patient/parent engagement declined suggesting that 5 contacts are sufficient and practical for families. HbA1c improved in 75% of the patients, mean HbA1c before initiating QI project was 52.8 mmol/mol and 50.2 mmol/mol at the end. Qualitative feedback at the end of the project showed that 100% of families felt that this project helped them to gain more knowledge and understanding about their/their child's diabetes (60% reported 'definitely', 40% reported 'partly'). 100% of the families reported that they felt more confident and empowered in making changes to Insulin doses at the end of the project (75% reported 'definitely' and 25% reported 'partly'). 75% of the families reported that they would continue to review blood sugars at the end of the project and 45% of these reported that they would do so using DIASEND as opposed to 0% in the beginning of the project.
Conclusion
Frequent DIASEND download clinics with T1dm patients/parents is an effective way of educating and empowering T1dm them to competently self manage their diabetes by identifying patterns in blood sugars and adjusting Insulin doses.

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P057

Type 1 diabetes cohort with HbA1c $\leq$ 48 mmols/mol April 2017 – March 2018 – what have we learnt?

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Background
71/270 (26%) of our patients with T1DM, diagnosed for more than 1 year, had an ideal HbA1c of less than or equal to 48 mmol/mol. Are there factors within this group that may be transferred into groups with higher HbA1cs to improve control?
Methods
Clinical records were reviewed for the whole year and download data from a randomly selected 2 week period was reviewed. Age, gender, time from diagnosis, ethnicity, postcode, other medical conditions, social care involvement and number of contacts with the diabetes team were recorded. From the download, information was collected on: CGM/FGS/fingerprick blood glucose (SMBG) use, mean SMBG tests per day and number and severity of SMBG hypos, time in target (CGM/FGS/SMBG). Data was not included for 2 patients (closed loop research trial) and was unavailable for 1 patient who did not consent to downloads being saved.
Results
33/71 were female. Mean age was 11.5 yrs with 31/71 being teenagers. Mean duration of diabetes was 4 years and 4 months. 38/71 were treated with insulin pumps. Data from the two week period showed: mean number of daily SMBG tests was 6 for those not on CGM/FGS. Average time spent in target was 41%. Average number of hypos ($<$4.0 mmol/l) per patient was 7. Variability for all 3 factors, however, was large and there were no observed correlations. Hypoglycaemia was looked at in more detail. There were only 5 recorded SMBG levels under 2.5 mmol/l in total, with two thirds of SMBG readings being between 3 and 4 mmol/l. Contact with the diabetes team was overall much higher than the minimum specified by Best Practice Tariff (BPT) with the average being 32 (12–154).
Conclusion
Contact with the diabetes team was frequent in this group. This may be an important factor in enabling such high numbers to achieve an ideal HbA1c. We will look at our whole clinic cohort to determine whether this contact frequency has increased over time in line with improving clinic HbA1c.

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P058

Can Download Clinics' improve diabetes metabolic control?

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Introduction
Optimal care in Type 1 Diabetes (T1DM) requires intensive insulin management with regular dose adjustments. A Download clinic (DC) was created for all patients attending the Paediatric Diabetes clinic. Patients downloaded their glucometers, pumps and Continuous Glucose Monitors (CGM) either at home or hospital. After analysis, the diabetes team provided feedback by email and phone.
Objectives
To analyse the effects of the DC on the metabolic control of paediatric patients with T1DM
Methods
Retrospective study of all patients using the DC during its first 9 months of existence. Demographic, clinical and metabolic control data was recorded at the beginning and during 3 months follow up. Patients in partial remission, diagnosed within the past 6 months or with less than 2 DC were excluded. Primary outcome was the difference in HbA1c levels. Secondary outcomes were differences in hypoglycaemic events, average daily blood glucose testing, average blood glucose level and total daily insulin dose (TDI).
Results
21 (11 female) out of 39 patients fulfilled the study's conditions. Median age was 9 years old (min 3 – max 15). Median time of diagnosis was 3.9 yrs (min 1 – max 13.15). Median clinics per patient was 3 (min 2 – max 8). When DC started, 6 patients were on multiple daily injections (MDI), 15 had insulin pumps (IP), four of which had CGMs. One patient changed from MDI to IP two weeks after initiating DC. Median HbA1c significantly decreased from 8.1% (min 7.50 – max 12.4) to 7.91% (min 7 – max 9.74) after 3 months ($P<0.05$). Mean TDI/Kg significantly increased from 0.74 (SD 0.3) to 0.82 (SD 0.3) after 3 months ($P<0.05$). There was no statistical significance in hypoglycaemic events, average blood glucose levels and testing before and after using the DC. No patient required medical care because of poor metabolic control.
Conclusion
This study demonstrates an improvement of patients' HbA1c level after using the DC without significant increase of adverse events revealing a potential benefit of DC clinics in metabolic control of Diabetic patients.

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P059

Experience of FreeStyleLibreuse in the management of an asymptomatic child in the pre-diabetes state

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Introduction
Type 1 diabetes (T1DM) occurs as a result of autoimmune destruction of pancreatic β-cells which is supported by the presence of autoantibodies well before the onset of T1DM. Individuals at risk for T1DM are characterised by a deficient first-phase insulin response and impaired glucose tolerance which is present before the onset of T1DM.
Case
We describe a case of 6 year-old asymptomatic girl who took part in the TrialNet Pathway-to-Prevention (PTP) study in which relatives of people with T1D were screened to assess their risk of developing T1D. She was found to be positive for

all 5 autoantibodies thus increasing her risk of developing T1D. Moreover her HbA1c was 40 mmol/mol at presentation consistent with pre-diabetes state. Although she was clinically asymptomatic her blood glucose (BG) was intermittently above 11 mmol/l. Thus it was agreed to commence her on FreeStyle Libre for monitoring of her BG which demonstrated post-meal glucose excursion only after teatime with BG above 12 mmol/l. Therefore although asymptomatic she was commenced on Novorapid using ICR 1:50 to manage her evening meal. Within 6 months she was found to have post-meal BG excursion at breakfast and was started on Novorapid. Currently 18 months after the introduction of sc insulin for only breakfast and teatime her glycaemic control is excellent as is demonstrated from the Libre download and HbA1c of 36 mmol/mol.

Conclusion

We present 6 year-old asymptomatic girl who was found to have 5 positive autoantibodies which were identified as part of the TrailNet research and had her BG levels monitored by FreeStyle Libre flash glucose monitoring system which detected post-meal BG excursion at breakfast and tea and were managed on small amount of sc Novorapid. She has remained asymptomatic 18 months since started on insulin with excellent glycaemic control. This case raises interesting question about how best to manage asymptomatic children with high risk of developing T1D. Further studies are required to determine which factors contribute to prevention and delayed progression of pre-diabetes to type 1 diabetes in paediatric population.

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P060

Co-designing purpose between three hospital diabetes teams within the same trust

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Introduction

The aim of having an away day was to enhance relationships across three sites by improving the understanding of each other's roles, their contributions and ways to provide mutual support. Also the intention was to establish parity through co-designing common practices of working effectively and developing quality improvement projects.

Method

Staff members from three Paediatric Diabetes Teams within the same trust were invited to attend an away day led by a leadership development specialist. To unite and focus the group, after outlining the programme of the day, staff were set a picture profiling icebreaker, where participants split into pairs to assess strengths, gaps and opportunities in the workplace. The group then reconvened to engage in a quality improvement exercise, identifying just one QI project that could be immediately implemented, with the aim of initiating a model for future collective action plans that could be introduced across the trust.

Results

From the comprehensive list of possible QI projects generated, it was mutually agreed through visual voting, that the first initiative following the Plan Do Study Act (PDSA) cycle would be to encourage all patients to upload their own Diasend data either before visiting the clinic or in the waiting room.

Other QI suggestions.

Quotations from day:

'There was very much a feeling that we worked through our problems together and that our views were considered and taken seriously'

'I valued the time away from clinic. I could think without being interrupted or hurried'

'Listening to the questions and the issues that the other sites face was really helpful'

Conclusions

Focus was encouraged and distractions minimised by organising this Away Day off site. In order to facilitate group harmony and productivity, using an impartial leadership development specialist was paramount. It was clear that communication, purpose and understanding was improved between the three hospitals within a Trust. We easily came to a decision regarding which improvement project we wanted to take forward, which all three sites implemented that same week and staff are still developing this idea using the PDSA tool.

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P061

Moving on: a review on the diabetes transfer care of young people

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Introduction

Young people with type 1 diabetes (T1DM) face great challenges in managing their disease. Puberty poses strains on glycaemic control. Transferring from paediatric to adult diabetic services is another obstacle. The study aims to evaluate our local transition and transfer service provision and monitoring of the young people's HbA1c control during this challenging period.

Methods

T1DM patients transferred from our hospital's paediatric to adult diabetic services from 1/9/10 to 31/8/14 were identified. Those who left adult service within 2 years following transfer were excluded. Case notes and electronic lab records were analysed.

Results

Over 4 years, 21 patients were transferred from paediatric to adult services. 4 moved out of region within 2 years of transfer, leaving 17 patients in the study. 94% (16/17) received transition care. The mean age of transition was 17.9 years (range 15.8–19.4) while the mean age of transfer to adult care was 19.2 years (range 17–20.9). Thus, the mean duration in transition was only 1.3 years. The clinic attendance rate also dropped significantly from 82.7% while in transition to 71.3% after transfer to adult care ($P=0.037$). Only 58.8% patients were offered their first adult clinic within 3 months after transfer. Overall, first adult clinics were attended at a mean of 4.8 months (range 3–9) post-transfer. Their mean HbA1c was 84.1 mmol/mol before transition and peaked at 89.6 mmol/mol after 1 year in adult care ($\sim$20.2 years), before significantly improving ($P=0.01$) to 83.7 mmol/mol 2 years after transfer ($\sim$21.2 years).

Conclusions

HbA1c worsened first year after transfer, peaking at an age and level that is later and higher than literature reports, thus exposing these young people to a longer period of poor glycaemic control. This study has identified areas for improvement: start transition clinic at an earlier age to allow longer transition and reduce gap between last transition and first adult clinics for continuity of care.

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P062

KISS Advanced Bolus System for managing the post-prandial glycemic effect of fat and protein in young people with T1D

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Objectives

The Diabetes Team at Birmingham Children's Hospital modified the advanced bolus algorithm suggested by Bell (2015), to develop the KISS (Keep it Simple and Safe). KISS involves adding 25% extra insulin to meals identified as very high fat and protein, and spreading the insulin by a split bolus, 50% now and 50% over 2.5 hours. KISS also has an adjustment tool allowing extra insulin to be added and the split modified from monitoring. KISS is intended to be a simple. The purpose of this one year audit was to assess the effectiveness of KISS, and identify key determinants of when extra insulin is needed. It was hypothesized over half of the patients would use KISS, and that meal carbohydrate grams per kilogram (CHOg/Kg) of the high fat and protein meals would be the main determinant of the need for extra insulin.

Methods

From April 2016 to April 2017, 25 children aged 10.8 years (s.d. 3.7) were initiated onto insulin pump therapy. On the 3rd education session, KISS was taught. All 25 patients pump downloads were analyzed 2 weeks after the session.

Results

Of the 25 patients educated, 68% ($n=17$) tried KISS at least once. The KISS users were significantly older than the non-users (11.9 years vs 8.5 years, T-Test $P<0.01$) and no patients aged under 7 years used KISS. Default 1 shows the 28 high fat and protein meals grouped by the extra amount of insulin they required. There was a significant difference between groups for CHOg/Kg. Posthoc analysis shows the meals requiring more than 25% extra insulin had significantly higher CHOg/Kg, when compared to 0% ($P<0.01$), and 25% extra ($P<0.05$).

Conclusions

The audit results highlight KISS is simple to use, but may not be used by children under seven years. When deciding if to add extra insulin to defined high fat and protein meals, it may be possible to use the meal CHOg/Kg to determine the extra required. Specifically, no extra insulin for meals under 2.0 CHOg/Kg, 25% extra for 2.0 – 2.5 CHOg/Kg and more than 25% extra for more than 2.5 CHOg/Kg.

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P063

An annual review questionnaire in children and young people with type 1 diabetes

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Objectives
To evaluate the usefulness of an Annual Review Questionnaire (ARQ) which was introduced as a clinical tool to assess Knowledge and Compliance of Children and Young People (CYP) with Type 1 diabetes with aspects of good clinical care as defined by National Institute of Clinical Excellence (NICE) guideline.
Methods
All CYP with Type 1 diabetes, were expected to complete the ARQ as part of annual review. The questionnaire asked about compliance and knowledge of aspects of good clinical care. CYP with diabetes duration $<$ 3 months prior to audit period and those with Type 2 diabetes were excluded.
Results
Data on the first 80 patients who completed the questionnaire between Feb-march 2018 was analyzed. 48.8% were males, 50% $>$12, 43.8% 12-5 and 6.3% $<$5 years old. 60.8% were White, 26.6% Asian, 11.4% African and Caribbean and 1.3% mixed race. 47.5% were on insulin pump. They were divided into 3 groups according to HbA1c level. Group A: HBA1c $<$7.5% (29/80), Group B: HBA1c = 7.5–9% (36/80) and Group C HBA1c $>$ 9% (15/80). Compared to the whole group, significantly more children in group A were aware of their glucose targets (89.7% vs 70% $P=0.01$), reported never missing insulin bolus (85.7% vs 79.5% $P-0.00$) and reported testing blood glucose $>$4 times a day (93.1% vs 75.9% $P=0.00$). Only 76.3% of all patients were using level 3 carbohydrate counting to determine premeal bolus insulin dose and only 57.5% were bolusing insulin with snacks.
Conclusions
The ARQ identified areas of both good and poor compliance and knowledge amongst CYP with Type 1 diabetes. This helped the diabetes team to try to target education to individual CYP in problem areas identified. CYP in group A showed statistically significant better compliance in some areas.

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P064

A case of HHS mixed with DKA and severe hypernatraemia

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Introduction
A 7 year old boy with history of Joubert's syndrome presented with first presentation of type 1 diabetes mellitus in Diabetic ketoacidosis (DKA) and a hyperglycaemic hyperosmolar state (HHS). His underlying neurological condition made clinical assessment difficult and he had reduced GCS with intermittent apnoeas but no respiratory compromise. Using the BSPED guideline (2015) for DKA he was managed with cautious fluid replacement despite his hyperosmolar state as he did not demonstrate clinical evidence of shock.
Methods
IV fluids were started at maintenance rates with 5% rehydration as 0.9% saline and replacement of urinary losses ml for ml. First laboratory blood glucose was 95.7 mmol/l, pH 7.21, blood ketones 5.9, serum osmolality 422 osmol/l. Blood pH and ketones first normalised at 18 hours from starting insulin therapy at 0.05 units/kg per hour. Intravenous heparin infusion was used to reduce risk of thrombosis.
Results
Serum sodium (corrected for glucose level) was 148 and rose to 200 mmol/l (estimated as laboratory assay range usual cut off 183 mmo/l) on day 3. iv Fluid rates were unchanged but content changed to 0.45% sodium chloride. Rhabdomyolysis ensued from day 3 (peak CK 40,000 day 5). Serum sodium normalised by day 10 with no further intervention. Renal function (peak creatinine 290 mmo/l) normalised by day 8 of admission. Serum antibodies were high for GAD, IA-2 and Zn transporter antibodies confirming likely type 1 diabetes mellitus. The child made a full recovery and is now managed on MDI insulin regimen of 0.5 units/kg per day.
Discussion
HHS is more typically seen in adult patients or adolescents usually with type 2 diabetes mellitus. It has high associated mortality rate (10–20%) and high volume iv fluid resuscitation and haemofiltration are recommended due to paucity of paediatric data in the literature. However, this case illustrates that DKA and HHS can co-exist in a young patient with type 1 diabetes. There is limited literature to suggest it more commonly occurs in children with type 1 DM and learning difficulties. Despite very high osmolality and severe hypernatraemia slow fluid replacement was associated with a successful outcome in this case.

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P065

Audit of management of diabetic ketoacidosis in children and young people at the Children's Hospital for Wales

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Introduction
Diabetic Ketoacidosis (DKA) is a life-threatening complication of Type-1 diabetes mellitus (T1DM) in children and young people (CYP). An Integrated Care Pathway (ICP) for management of DKA is established in Wales with the 3rd edition published in March 2016. This is based on the 2015 British Society for Paediatric Endocrinology and Diabetes (BSPED) guidelines.
Aims
To audit the management of DKA in a teaching hospital following the introduction of the third edition of the ICP, with a focus on fluid therapy.
Methodology
Retrospective case note review of all children admitted in DKA to the Children's Hospital between June 2016 and June 2018.
Results
A total of 24 episodes of DKA were recorded in 23 patients (13 female). The median age was 11 years (range 1–16 years). 9 of the DKA episodes were in newly diagnosed CYP. Omission of insulin was the most common precipitant in those with established TIDM. In all episodes, the diagnosis of DKA was made using blood glucose $>$11 mmol/l, blood ketones $>$3 mmol/l and pH $<$7.3. Eleven patients presented with a pH of $<$7.1, of which 10 received a 10 ml/kg fluid bolus of 0.9% saline, 6 of whom required a further fluid bolus following clinical assessment. Of the 13 patients with a pH $\geq$7.1, 6 required 10 ml/kg of 0.9% saline fluid boluses, 2 of whom required the bolus after 2-3 hours of initiation of DKA management, and 1 required a further 10 ml/kg bolus. The maintenance fluid infusion rate was increased in 1 case. Hypoglycaemia was documented in 10 of the 24 episodes whilst on the pathway, despite having dextrose in their fluids.
Conclusion
A significant proportion of CYP being treated for DKA needed a change in fluid therapy when treated in accordance with the current guideline. This change was made based on ongoing clinical assessments. No adverse outcomes were identified. There was an increased incidence of hypoglycaemia despite a reduction in the rate of insulin in the current guideline. This audit suggests that fluid therapy in DKA requires further evaluation and comparison with other centres using the ICP and BSPED guidance.

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P066

Are we getting it right? An evaluation of diabetes transitional service at a district general hospital

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Introduction
Poorly managed transition could adversely impact upon adjustment to diabetes and potentially result in non-adherence to treatment, loss to follow-up and worsening of health-related outcomes. In our DGH, approximately 20 Young Person (YP) with T1DM get transferred to YP Clinic every year. YP between 17–19 years of age attend a joint clinic before the transfer. The YP Clinic provides a continuity of diabetes care up to the age of 25 years.
Aim of the study
To evaluate the experiences and satisfaction of YP with current diabetes transitional service at a DGH, identify aspects of the service that could be improved and propose plans to improve the service.
Methods
A survey was conducted evaluating the experiences and satisfaction of YP transitioned in the years 2014 and 2015. The challenges faced by the current transitional service was evaluated through a survey of paediatric and adult diabetes professionals. The patient and professional survey was conducted using SurveyMonkey.

Results
Thiryt out of 40 YP responded to our survey. 22 YP responded that transition was first discussed after 15 years of age. 23 YP reported their involvement in planning their transition care but only 30% reported that their transition care plan (TCP) was specific to their needs. 90% had a key worker at transition. 14 YP reported attending age-specific 'Teen Diabetes Clinic' between 14–17 years of age. 80% met with YP diabetes team at the joint/transfer clinic. 86% reported attending their first appointment at the YP Clinic. Majority expressed high rate of satisfaction with the transition support. Provision of peer support, reminders for appointments and an opportunity to familiarise with YP Clinic environment before the transfer were highlighted as most crucial by YP. Clinic capacity and lack of in-house dietitian and psychology support were the major challenges identified with the YP Clinic.
Conclusion
There was high rate of attendance at the handover as well as first clinic post-handover. Majority respondents reported good satisfaction with the service. Recommendations were made to improve the TCP, to assess YP's transitional readiness using 'Ready Steady Go' and to address the gaps in post-transfer dietetic and psychology support.

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P067

Pump Vs MDI: Which is the superior treatment option for the management of type 1 diabetes in the paediatric population?

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Aims
To understand whether insulin treatment for type 1 diabetes mellitus (T1DM) in the paediatric population is most effective at providing diabetic control when delivered by Multiple Daily Injections (MDI) as compared to Continuous Subcutaneous Insulin Infusion (CSII).
Methods
A District General Hospital's submissions to the National Paediatric Diabetes Audit (NPDA) between 2012 and 2018 were analysed to establish if either method of insulin delivery is superior. Patients newly diagnosed with type T1DM and established on a single treatment regimen, either CSII or MDI, for a minimum of 2 years were identified. Over the 6 years of NPDA submissions analysed, a total of 43 patients newly diagnosed with T1DM, established on a single treatment regimen for a minimum of 2 years were identified. Data for patients treated for 3, 4 and 5 years was also obtained, however as length of treatment increased, the number of patients eligible for inclusion decreased.
Results
MDI and CSII produce similar reductions in levels of glycated haemoglobin, and similar attainment of national targets between two and five years post diagnosis, whilst patients are established on a single insulin regimen. There was no statistical significance between the CSII and MDI results at 2 and 3 years. Four and 5-year datasets were too small to be statistically analysed.
Conclusion
There is no significant difference in diabetic control achieved by multiple daily injections of insulin and continuous subcutaneous insulin infusions. To improve the reliability and validity of these results, readily available data could be obtained from other units across England and Wales, using NPDA submissions, to increase the sample size. With larger samples, it will be possible to further analyse the data, for example according to age and sex, to ascertain whether there are superior treatment options for specific groups of patients.

	MDI Users	CSII Users		
Years of Treatment	Average HbA1c reading at diagnosis	Average HbA1c reading after treatment	Average HbA1c reading at diagnosis	Average HbA1c reading after treatment
2	75.1	62.0	76.5	62.3
3	72.1	63.1	76.8	62.0
4	70.6	63.6	80.7	60.4
5	71.3	69.7	82.2	63.1

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P068

Characteristics of pre-school children diagnosed with type 1 diabetes at University Hospital of Leicester

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Background
There is an increased incidence of Type 1 diabetes in preschool children and the management of diabetes in this group is challenging. Preschool children are dependent on others for all aspects of their care. Normoglycaemia in preschool children reduces the likelihood of acute and chronic complications.
Objectives
Our goals were to:
1. Outline the demographic characteristics of children diagnosed with diabetes before 5 years of age.
2. Compare HbA1C levels at diagnosis, one and two years of diagnosis.
3. Outline the clinical mode of presentation of diabetes in this age group.
4. Review diabetes auto-antibodies profile in this group.
5. Benefits of early initiation of insulin pump therapy in this age group.

Methods
We studied 75 children under 5 years with Type 1 diabetes diagnosed between January 2009 and December 2017. Patients' data were collected from local diabetes database, medical notes, and electronic notes.
Results
The median age was 3.1 years at diagnosis and 41% were boys. Caucasians represented 74% followed by Asian 21%. 28 (37%) children presented in diabetic ketoacidosis (DKA). 66 children had diabetic antibodies checked with GAD being the commonest (60%) followed by IA2 (55%) and Islet cell antibodies (33%). 58 out of 67 children had 1 or more positive antibodies. Insulin pump therapy is used presently by 51 (68%) children.
Conclusions
Over one-third of children in our study presented in DKA. Median HbA1c levels improved at 1 year and 2 years since diagnosis and the best improvement was in the group started on insulin pump within 1 year of diagnosis. Table comparing HbA1c levels at diagnosis, 1 year and 2 years.

	Number of children	Median HbA1c at diagnosis (mmol/mol)	Median HbA1c 1 year since diagnosis (mmol/mol)	Median HbA1c 2 years since diagnosis (mmol/mol)
Pump start within one year of diagnosis	14	82	56	60.5
Pump start 1 year after diagnosis	37	83.5	66	62
Not on pump	24	95	65	67
All children	75	87	64	63

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P069

Annual lipid checks in children and young people with Type 1 Diabetes: Just statin the obvious

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Background
As per 2011–15 National Paediatric Diabetes Audit (NPDA) data set, the paediatric diabetes units (PDU) contributed data on annual lipids levels check for children and young people (CYP) over 12 years of age. Blood cholesterol were used to stratify the risk of complications of diabetes. National Institute of Health and Care Excellence (NICE) guideline NG18 did not recommend lipid screening during annual review of type 1 diabetes due to lack of robust evidence. A survey of members of Association of Children's Diabetes Clinicians (ACDC) published in 2017 revealed significant number of respondents still measured cholesterol on annual basis. The NPDA dataset 2017 mentions annual cholesterol check in type 1 diabetes as optional.
Aim
To check if cholesterol screening in CYP with type 1 diabetes complied with NICE NG18 in our unit.

Materials and Methods
Paediatric diabetes database was used to identify CYP who had blood cholesterol checked between 1-4-16 and 31-3-17. Results were confirmed from Pathology system. Medical records of CYP with cholesterol level > 5.2mmol/L were reviewed to identify treatment strategies and subsequent cholesterol levels were followed till 28-2-18.
Results
Out of 144 CYP, 138 had cholesterol levels checked during audit period. Out of these 138 CYP, 20 (14.5%) had cholesterol level above 5.2mmol/L including 7 (5%) with levels above 6.2 mmol/L. All CYP received dietary advice. In all except one CYP, subsequent cholesterol testing revealed the levels were improving. The highest cholesterol level was 9.4mmol/L at diagnosis that reduced to 4.2 mmol/L with diabetes treatment. One CYP in late teens with cholesterol level 7.7mmol/L was started on lipid lowering medicine in transition clinic. This CYP was diagnosed with type 1 diabetes over 10 years ago and had poor compliance and control for several years.
Discussion
Our local audit revealed no benefit of routine annual cholesterol checks in CYP with established diabetes thus we have changed to a more targeted approach. In addition, it is not clear if inclusion of cholesterol checks in old NPDA data set was driving PDUs across country to do this test on annual basis.

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P070

Additional appointments for children and young people with high HbA1c: Does it work?

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Introduction
This is an audit on the outcome of children and young people (CYP) with Type 1 Diabetes with high HbA1c who were offered extra appointments with a paediatric diabetes specialist nurse (PDSN) over a three-year period at Harrogate District Hospital.
Patient population
26 CYP with Type 1 Diabetes with HbA1C more than 75mmol/mol, were offered extra diabetes clinic appointments with a PDSN.
Audit Methodology
A retrospective audit was carried out between January 2013 and December 2016. 26 CYPs were identified. Their extra clinic appointments ranged from 1 to 10 with an average of 3.6.
Outcome
Any causation is hard to establish, but 15 patients showed an improvement in HbA1C readings. Their average HbA1c at the beginning was 91.8mmol/mol and after the appointments it had come down to 65 mmol/mol. Interestingly 11 patients showed deterioration in HbA1C readings. Their average HbA1c at the beginning was 85 mmol/mmol and after the appointments it had gone up to 107 mmol/mol. This reminds us that education and training can only produce results if it is put into action. Ways of engaging patients to actually implement training, should be the focus of our intervention to achieve our goals. The most important finding was high numbers of clinics appointments don't seem to have an extra effect on improving diabetes control.

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P071

Standardising the management of hypoglycaemia in paediatric patients with type 1 diabetes mellitus

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Background
During 2017–2018 the diabetic team at our Foundation Trust participated in the RCPCH diabetes quality improvement collaborative to support work in reducing the mean HbA1c of our patient cohort. It is widely acknowledged that a consistent approach is vital in working towards HbA1c targets. One area of focus of our quality improvement work was to standardise the management of hypoglycaemia. As a team we decided to follow the BSPED hypoglycaemia guideline (2016) giving clear and personalised recommendations for treating hypoglycaemic episodes with 0.3 g/kg of fast acting carbohydrates.
Aim
The aim of this audit was to evaluate patients' management of hypoglycaemia in accordance to BSPED guidance and to assess the impact of standardising advice on patient management and patients' HbA1c.
Patient Population
Our Trust has a caseload of 230 patients with T1DM across two hospitals.
Method
Between January and March 2018, patients' management of hypoglycaemia was reviewed with a questionnaire when they attended a multidisciplinary clinic. They were educated and given a patient leaflet including an individualised plan in line with BSPED guidance. Their management of hypoglycaemic episodes was subsequently re-evaluated at future clinic appointments.
Results
Of the 121 patients initially assessed, 83% used the correct threshold of blood glucose <4mmol/L to treat hypoglycaemia and 34% managed hypoglycaemic episodes appropriately. After education in clinic and the provision of a patient leaflet this improved to 90% of patients using the correct threshold. For the 52 patients who were assessed pre and post education, initially 23% had appropriate management of hypoglycaemic episodes and this improved to 60%. The individual reduction in HbA1c was not significant however over the audit period the average HbA1c dropped from 66.6 to 64.7 mmol/mol at one hospital and 70 to 66 mmol/mol at the other site.
Conclusion
This audit shows that implementing a standardised approach to the management of hypoglycaemia improves adherence to BSPED guidance and giving a consistent message with individualised written plans has a positive impact on reducing overall HbA1c.

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P072

A diabetes transition programme: outcomes and scope for improvement

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Introduction
'Transition' is the period of movement from paediatric to adult healthcare. These patients are in their adolescence when the brain is maturing, causing changes in behaviors including greater risk-taking. The period of transition can be associated with poor adherence to insulin and blood glucose monitoring regimens and an increased risk of diabetic ketoacidosis (DKA). This study looks into how effective our transition programme has been at addressing this.
Method
We have assessed the outcomes of diabetes transition healthcare from 2013–2017 by looking at attendance at appointments, HbA1C levels and emergency admissions for hypoglycaemia, overdose, insulin omission and DKA. We studied 60 patients, within the age range of 16–19 years, previously diagnosed with Type 1 or Type 2 diabetes and who had continued to attend the young adult service after transition clinic.
Results
Out of the 60 patients studied 36 were female. The mean age when they first attended transition clinic was 17.5 years. Duration of transition spanned from 0-21 months with a mean duration of 7.8 months. A mean of 3 appointments were offered and a mean of 2 were attended. The overall attendance rate to transition clinic was 63%. Two out of the 60 patients attended no appointments in transition clinic. The table below depicts the HbA1C values before the first transition

HbA1c	Pre-transition 66.2 mmol/mol		Post-transition 75.2 mmol/mol	
Emergency admissions	Total number	Number of patients	Total number	Number of patients
DKA	6	5	22	5
Hypoglycaemia	10	8	4	4
Overdose or intentional insulin omission	10	5	6	4

appointment and one year after the last transition appointment. Emergency admissions shown include all records outside of the transition period, excluding new diagnoses of diabetes.
Conclusion
Diabetes control, measured by HbA1C, deteriorates post-transition. 87.5% of all young people completing transition had a recorded HbA1C one year post-transition, showing they were still engaged with the adult services. Admission rates also increase for DKA (albeit affecting the same 4 patients with recurrent DKA pre-transition). Improving support for young people in the young adult service is imperative to improve outcomes.

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Psychological spectrum in DM1

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Abstract
The psychosocial impact of diabetes in childhood is ubiquitous and involves the entire family, as well as schools and society as a whole. The International Society for Pediatric and Adolescent Diabetes (ISPAD) developed guidelines in 2000 to assist health professionals in the management of young people with diabetes. These guidelines are based on the St. Vincent Declaration, the Declaration of Kos, and the Declaration of the Americas, which define the rights of all people with diabetes and focus on significant areas of responsibility for those involved in the care of diabetic children and adolescents. We, at our trust, undertook a prospective, observational, quantitative study in order to get an idea about the nature and intensity of major psychological issues faced by the patients and families with DM1.
Aim
- to formulate a template for 'meeting-the-threshold' criteria; in term of major psychological issues affecting the patient/family.
- to determine the top three major psychological issues in the study group.
- to design the (psy) services in such a way as to target the specific psychological issues, during follow ups.

Study
- recruting patients from DM1 clinics over 6 months
- segregated them according to age groups - pre-school/school/adolescents

Main Findings
- PRE-SCHOOL - Major Psy factor is anxiety-depression in parents from the fear of Hypoglycaemia (3.3 times relative-risk)
- SCHOOL - Major Psy factor is 'PEER-PRESSURE/BULLYING' (2.9 time RR)
- ADOLESCENT - Major psy factor was 'Eating-disorder'(2.3 times RR)

Action
- AS a part of BPT, psy services are offered to all the patients.
- After the study, the follow-ups were more 'targetted' and 'focussed'
- Data is being collected to see the impact of this intervention.

Misc
- Some of the other psy issues, prevalent (but not making in to the top three causes) were also innumerated and discussed.
- However the cost-benefit-analysis did not support the specific/targetted psy sessions for those psy issues, and rather the standard general psy sessions were continuted.

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Deaths within the first year of handover from transition diabetes clinic

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Background
Self-management of Type 1 diabetes (T1DM) is difficult and complex, particularly so during the transition period. Deterioration in glycaemic control is common, in part due to psychosocial and environmental changes (going to college or university), poor adherence to insulin regimens, risk-taking behaviours and family stressors. Transition to adult diabetes services can be a traumatic period for young people with diabetes, who commonly fall between services and are lost to follow up if appointments are not kept. Our Children's diabetes service follows the NICE guidelines and cares for diabetic patients up to 18 years old. University students are handed over to the adult diabetes team of their university town. Two 18-year old boys are described here. One who just started university and was living in a medically supported flat (NB). The other was at home (NP) and had been independently travelling and self-caring at home on his own before.
NB
NB was diagnosed at the age of 11 years not in ketoacidosis. He was carbohydrate counting a year later. He was handed over to the adult diabetes team of his university town after numerous letters to support safe residence. HbA1c at handover was 8.1%. He contacted his family with gastroenteritis symptoms and abdominal pain and self managed as before. He was discovered by his flat mate the next morning.
NP
NP was diagnosed at the age of 7 years not in ketoacidosis. He was initially on pre-mixed twice daily insulin injections and subsequently on the basal bolus regimen 2 years later. He had high HbA1c (11.1% when transitioned) for several years. Flash continuous glucose monitoring was offered with self funding but he did not use it. He left a family holiday to return home to celebrate his 18th birthday with friends. He felt unwell with abdominal pain and went to bed and was discovered by a family member and died in intensive care 3 days later. His insulin pens were not unpacked.
Conclusion
Both boys never experienced diabetic ketoacidosis and were on an ultra long-acting basal insulin. Perhaps they never knew the red flags to call for help.

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Case series of monogenic diabetes due to HNF1B mutation

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Introduction
A case series of three children diagnosed with MODY at a university hospital between November 2015 and May 2018. All of them was found to have HNF1B mutation.
Background
HNF1β-MODY (MODY5) is a rare form of monogenic diabetes that is often associated with a wide range of urinary tract anomalies including renal cysts. It's a dominantly inherited disease including maturity-onset diabetes of the young (MODY), pancreatic insufficiency and some psychological disorders. Clinical presentation of renal cyst and diabetes syndrome (RCAD) includes renal involvement, deranged liver function, hyperuricemia and early-onset gout and reproductive tract abnormalities. In this case series report, we describe 3 cases of atypical non-autoimmune diabetes associated with a confirmed HNF1β mutation.
Management
Two children needed insulin for their diabetes management. Emphasis should be on lifestyle modifications such as weight loss and diet control. All three cases and their families had extensive genetic counseling and advise.

Table 1

	Case 1	Case 2	Case 3
Age at diagnosis (years)/sex	15/Male	13/Male	12/Male
BMI at diagnosis kg/m^2 (SDS)	33 (2.96)	18.4 (0.06)	34 (3.35)
HbA1c at diagnosis (mmol/mol)	117 (12.8%)	55 (7.1%)	52 (6.9%)
Initial treatment	MDI regime	Gliclazide	Metformin
Renal scan findings	Normal	Echogenic kidneys and single cyst	Single renal cyst
MODY genetics	HNF1B whole gene deletion	Chromosome 17q12 micro-deletion including HNF1B gene deletion	HNF1B c.884G>A
Other morbidities	Depression, ASD, ADHD	Exocrine pancreas insufficiency	Depression
Present treatment	MDI insulin + Metformin	Insulin BD regime	Metformin
Family history	Type 2 diabetes	Mother and half-sister have same mutation	Mother type1, grandmother type2
Recent HbA1c (mmol/mol)	42 (6%)	51 (6.8%)	42 (6%)
Diabetes antibodies	Negative	Anti-GAD antibody 28	Negative

Conclusion
In our case series, we have shown that early diagnosis of HNF1B disease in childhood can help in early detection and management of diabetes and other co-morbidities. Co-morbidities include electrolytes imbalance, liver enzymes derangement, exocrine pancreas insufficiency and Psychological disorders were detected in case one and three. Molecular diagnosis has huge implications for the counselling and treatment of the patients and their family members.
Clinical presentations
See Table 1.

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Feeding and autoimmunity in down's syndrome evaluation study (FADES)

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Introduction
Children with Down's Syndrome (DS) have altered immunity with higher rates of diabetes, thyroid autoimmunity, coeliac disease, respiratory tract infections and leukemia. Diabetes in children with DS appears to be accelerated with an earlier age of onset compared with the general population, with 22% diagnosed before the age of 2 years. Increased HLA class II DR3/4 susceptibility is seen in in children with DS and diabetes but the prevalence is reduced compared children with diabetes in the general population. FADES (Feeding and Autoimmunity in Down's Syndrome Evaluation Study) aims to study the association between early infant feeding, infections, antibiotic use and the gut microbiome in the development of autoimmunity in DS.
Methods
FADES is a longitudinal UK birth cohort of children with DS, with follow up until the age of seven years. Parents complete detailed medical and feeding questionnaires online close to birth, at six months and annually. DNA samples are collected at recruitment and samples for urine C peptide, gut microbiome and blood samples are collected close to birth at 6 months, 12 months and annually.
Results
The study has to date, enrolled 80 infants (Male $n=41$), mean age at recruitment 17.3 weeks (S.D.10 weeks). Initial analysis of questionnaires from 61 participants reveals that all had hospital admissions during infancy. Hypothyroidism was diagnosed during infancy in 2 cases, one before the age of three months. Transient abnormal myelopoiesis was diagnosed in 5% of participants. HLA class II analysis of the first 62 participants shows that 6% have the highest risk genotype for Type 1 diabetes compared to 3% in the general population. Analysis of questionnaires and samples to further characterise the cohort for the presence of markers of autoimmunity and associations with feeding and health is ongoing.
Conclusion
This longitudinal birth cohort of children with DS is an important resource for understanding the causes of autoimmunity including Type 1 diabetes in a 'high risk' population.

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Audit of HbA1c improvement in newly diagnosed type 1 diabetes paediatric patients in Gloucestershire Hospitals NHS Foundation Trust

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Aim
To investigate the trend of HbA1c levels of newly diagnosed type 1 diabetes paediatric patients in Gloucestershire Hospitals NHS Foundation Trust.
Methodology
The Infoflex diabetes database was used to collate information on the type 1 diabetes paediatric patients, diagnosed in Gloucester NHS Trust between September 2015 and December 2017. The cohort totalled 74. Their HbA1c levels at diagnosis, 4–7 weeks, 3–4 months, 6–8 months and 12–16 months were recorded and compared. The cohort was sub-divided into smaller subgroups so that the outcomes for different age groups and genders could be calculated and compared. These groups were: boys; girls; 0–4 years; 5–9 years; 10–14 years; and $\geq$15 years old. Outpatient appointments and any other contact with the diabetes team were recorded in the first 12 weeks.
Results
At 12 weeks post diagnosis, the mean HbA1c for the whole cohort was 47.39 mmol/mol which is below the target level ($\leq$48 mmol/mol). At 6–8 months and 12–16 months the mean HbA1c level of the cohort was 52.71 mmol/mol and 58 mmol/mol respectively. These were above the target level. The 10–14-year-old group at 12 weeks was the only age group to achieve a mean HbA1c level below the target (44.89 mmol/mol). The mean number of contacts with the diabetes team in the first 12 weeks was 31.97 for boys and 34.69 for girls.
Conclusion
The post-diagnosis interventions were effective in improving the HbA1c levels for all the sub groups. However, sustaining the HbA1c level below target over a longer period was problematic. Increasing age in itself does not appear to be an exacerbating factor as the most successful group in this audit was the 10–14-year-old age group. The HbA1c level for boys was consistently lower at all check points than for girls. There appears to be no correlation between the number of contacts with the diabetes team and improved HbA1c level control.

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Our experience in the use and effect of insulin dugludec in children with diabetes in a secondary care setting

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Introduction
Insulin Dugludec is an ultra- long acting basal insulin. The management of diabetes in children is challenging due to the need of regularly injecting insulin, risk of hypoglycaemia, variation in the activity of different insulins available. Dugludec has a long half-life (25 hrs), lower variability and lasts 42 hours. Currently there are no guidelines or NICE recommendations advising the use of insulin dugludec in children with diabetes. Studies are few but have shown improved glycaemic control and reduced episodes of diabetic ketoacidosis and hypoglycaemia.
Methods
Retrospective study looking at clinic letters, blood results of children and adolescents with diabetes on dugludec over 4 years (2014–2018).
Results
Twenty-four children and adolescents (41.6% males, 58.3% females) with a mean age of 15.2 years were started on Degludec, of which 21 had type 1 diabetes and the remaining, type 2. Majority (92%) were commenced due to poor glycaemic control and poor compliance to other insulins. 1 child was started on it to reduce episodes of hypoglycaemia. 1 was started at diagnosis from overseas. Mean HbA1c levels before dugludec was 98 mmol/mol (69–134). HbA1c levels decreased in 15(63%), increased in 6(25%), static in 2(8%) and is too early to assess in 3(12%). The mean reduction of HbA1c levels was 12.5 mmol/mol (2–34). Social difficulties was the main deterrant to improvement.13(54%) patients had no hypoglycaemia episodes noted and 9 (37.5%) had hypoglycaemia.
Conclusion
Dugludec should be considered in patients with poorly controlled diabetes, multiple emergency admissions for hypoglycaemia/diabetic ketoacidosis and difficulty with injections. Choosing the cohort of patients most likely to benefit from dugludec is likely to be cost-effective.
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Maturity onset diabetes of the young (MODY): A report of 7 related and unrelated cases in a university hospital

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Introduction
MODY is a group of monogenic disorders contributing to about 1% of diabetes due to a primary defect in the function of the beta cells of the pancreas. Although increasingly recognised, it is often misdiagnosed as type 1 or Type 2 Diabetes Mellitus(T2DM). We describe 7 cases of MODY of which 6 were genetically confirmed.
Case reports
Siblings with loss of function mutation of ABCC8 gen. 2 brothers were diagnosed to have diabetes at 15 and 12 years of age. The first was thought to have T2DM but was investigated based on a normal BMI. A loss of function mutation of ABCC8 gene was identified. The brother had chronic ITP, hyperglycaemia and the same mutation. Siblings with deletion of HNF-1beta gene. Two siblings aged 12 and 16 were identified to have deletion of HNF-1beta gene. The younger sibling was screened based on a strong family history of diabetes. Her renal scan was normal. The brother who was already diagnosed to have diabetes at the time, and had weakly positive islet cell antibodies, was screened based on this report. He also had severe unilateral hydronephrosis. Whole gene deletion of HNF1beta was confirmed. He was not treated with drugs. Parents were found to be gonadal mosaics for HNF1B mutation. Another sibling was a carrier and was referred for annual surveillance. Mutation of HNF-1alphaP291fsinsC gene. This 13-year-old girl had diabetes in both grandparents. Her sister, an adult, was diagnosed to have type 1 Diabetes Mellitus. Splicing mutation of the GCK (Glucokinase) gene. This 15-year-old boy with a strong family history of diabetes has impaired OGTT. Undiagnosed but likely GCK-MODY. This 5-year-old boy with high random blood glucose and impaired Oral Glucose Tolerance Test (OGTT) and negative antibodies is thought to have GCK-MODY though no mutations have been identified.
Conclusion
A high index of suspicion is necessary for diagnosis of MODY, which in turn allows for a different approach to management compared to Type 1 or T2DM. Diagnosis also makes it possible for screening of family members and surveillance of asymptomatic carriers.

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P080

Optimal use of resources and teamwork improves glycaemic control in a multi-ethnic population-Evidence from the National Paediatric Diabetes Audit (NPDA)

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Introduction
Patients who have diabetes are at risk of complications, both acutely and in the long term. Although care is individualised, it may not be practical to continuously review this on an individual basis. An audit evaluating outcomes is a useful tool to reflect on multidisciplinary team management. We describe how effective use of resources led to better results in a multi-ethnic population.
Population
A total of 130 children and young people who received care at North Middlesex Hospital(NMH) were included.
Methodology
The Paediatric Diabetes Unit at NMH has been participating in the National Paediatric Diabetes Audit (NPDA) since 2010. Data currently submitted is based on routine care, screening, outcomes and admissions. Data collated from electronic recording systems is submitted to the Royal College of Paediatrics and Child Health(RCPCH). Once centrally analysed, reports are released to participating units and also published in public domain.
Results
Of the 130 children, 62% were above 10 years of age. The population was multiethnic and included 28.5% white, 23% black ad 5% Asian. Nearly 18% were on insulin pumps. Over 90% had Type 1 Diabetes Mellitus and 7% Type 2. There was sustained and remarkable improvement in median HbA1c levels over the past years, dropping from 74 mmol/mol in 2013/14 to 63 mmol/mol in 2015/16, thus dropping below the average for London (65.5 mmol/mol) and England (65 mmol/mol).
Conclusion
The remarkable improvement in glycaemic control was achieved through provision of adequate resources such as recruitment of staff to facilitate initiation of insulin pump therapy, providing more intensive support and teaching carbohydrate counting from diagnosis. This was boosted by team commitment and cohesiveness leading to improved patient engagement. The achievement is commendable given the patients' diverse cultural and ethnic backgrounds, which are more marked compared to some other boroughs in London and outside.

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Introduction of carbohydrate counting from diagnosis is associated with significant reduction in HbA1c in children with type 1 diabetes

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Introduction
NICE NG18 recommends level 3 carbohydrate counting from diagnosis for CYP diagnosed with Type 1 Diabetes. Our unit introduced in-patient level 3 carb counting from day 1 in 2015 in response to an audit demonstrating sub-optimal control in the first year of treatment.
Methods
We carried out a longitudinal study of HbA1c in paediatric patients during the first year of diagnosis in two time periods, before and after the introduction of carb counting from day 1; December 2012 – October 2014 ($n=39$) and August 2015 – August 2017 ($n=42$).
Results
The mean HbA1c achieved 12 m post diagnosis reduced from 62.9 mmol/mol in the first group to 54.3 mmol/mol in the second group ($P=0.0015$).
Conclusions
Introduction of immediate level 3 carbohydrate counting from diagnosis was associated with a clinically and statistically significant reduction in mean HbA1c 12 months after diagnosis.

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P082

An alternative approach to beating the September school rush!

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The management of children and young people (CYP) with diabetes is forever evolving, with tools and management strategies becoming much more intense. Year on year this has led to an overwhelming burden of educating schools when providing training for over 300 patients with type 1, type 2 and rarer types of diabetes. Children spend on average 1,267.5 hours per year in school – it is essential children's diabetes management is optimised during this time, and health care professionals must ensure their diabetes care needs are met in school. Our historical approach was to attend each school, fighting Birmingham traffic and roadwork's taking up to 15 minutes to travel just 1 mile! A new paradigm was needed to meet the school training demand. The Diabetes Team created a bold new vision by mind mapping. The concept was to invite schools to attend a 'school clinic' at the diabetes centre. Six separate training slots every Monday, June to October, prioritising those new to diabetes/changing school. The training aimed to deliver comprehensive, consistent training that met the needs of school personnel and CYP diabetes. The 'School Clinic' approach was calculated to meet demand, and half the nursing and dietetic time required for school training. The 'School Clinic' approach was piloted in 2015. Findings from our first year were, schools being initially resistant to change, no consistency in paperwork and training resources and time pressure. Each year the training has been evaluated and audited by both the diabetes team and the schools. The time taken to educate all schools was halved a significant efficiency. The team is in the process of delivering their 4th successive year of this innovative approach to training schools in the management of childhood diabetes. There is now a standard operating procedure, teaching slides, equipment and standardised care plans for each type of therapy, MDI, CSII, Sensors & Libre along with exercise formulation charts.

Feedback from both sets of staff is positive, and the team will continue to develop and respond to technological advances in diabetes in the future.

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P083

A review of the freestyle libre's use in a paediatric clinic over 3 months

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Objectives
The purpose of this study was to review the effectiveness of the Freestyle Libre flash glucose monitoring system at improving glycaemic control in a paediatric clinic.
Methods
Data from 13 participants with type 1 diabetes for the first 3 months of use of the Freestyle Libre system either continuously or intermittently was collected using both clinic readings of glycated haemoglobin (Hba1c) and from the Libre itself using the Diasend diabetes management and analysis web platform. Retrospective analysis was carried out to evaluate improvements in glycaemic control over this period using the following parameters; Hba1c, %time spent above and below normal range (4–8 mmol/l) and average blood glucose.
Results
Results obtained showed modest mean reduction in Hba1c over 3 months (−2.9 mmol/mol). Reductions in time spent below normal range were observed with a 8.7% reduction in time spent in hypo seen. Unexpectedly, a 7.1% increase in time spent above range was observed as well as a 0.5 mmol/l increase in average blood glucose after 3 months.
Conclusions
Although reductions in Hba1c and time spent in hypoglycaemia were observed, increases in mean blood glucose and patients do not seem to be gaining maximal benefit from use of the Freestyle Libre System which has the potential to hugely improve glycaemic control in most patients. The key to improving engagement and effective use of the Freestyle Libre system is through education of patients, parents, care-givers and healthcare professionals. Improvements in education across these groups should lead to greater improvements in glycaemic control in type 1 patients.

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P084

Impact of transition on diabetes related outcomes

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Introduction
The period of adolescence for young people (YP) with diabetes is a significantly high-risk time and is linked with worsening metabolic control, non-adherence to treatment, and increased risk of mental health issues. Arranging an efficient and smooth transfer for young person with type 1 diabetes (T1DM) from paediatric to adult care is one of the great challenges facing the diabetes multidisciplinary teams.
Aim of the study
This audit looks at the diabetes related health-outcomes for YP who transitioned over a 2-year period in a DGH.
Methods
A retrospective audit of diabetes related outcomes for YP who transitioned in the years 2014 and 2015 was conducted. Data was collected from paper and electronic patient records with regards to number of clinic attendances, HbA1c, keyworker, support from dietitian and psychologist. The data for the 12 months preceding the transfer was compared to that for 12 months post-transfer.
Results
40 YP were transitioned from paediatric to adult diabetes service over the 2-year period. The median age at transfer was 17.9 years. 90% had a key worker at transition. 78% attended the joint transfer clinic and 80% attended the first clinic post-handover. However only 28% had their first appointment within 3–4 months post-transfer. In total 63% were seen within 6 months of transfer. Median HbA1c was 77 mmol/mol post-transfer compared to 66 mmol/mol in 12 months preceding the transfer. Only 30% YP attended 3 or more YP Clinics compared to 75% in the pre-transfer period. 40% missed their annual review in YP Clinic. There was no significant difference in the incidence of diabetes related complications or hospital admissions. The YP Clinics had significantly less dietetic support and no psychology support.
Conclusion
The metabolic control worsened, and the clinic attendance rate reduced post-transition. However, there was no change in diabetes related acute or chronic complications. This audit showed the challenges faced by the YP diabetes team in terms of clinic capacity and lack of access to specialist service like exercise and psychology. The audit helped in developing action plans to address and re-design the elements of current transitional service.

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